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The Inclusion of Women and Minorities in Smoking Cessation Clinical Trials: A Systematic Review

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Abstract

This study assesses the impact of the 1993 NIH Revitalization Act on the inclusion and subgroup analysis of women and minorities in trials of FDA-approved smoking cessation pharmacotherapy. Female representation, while commensurate with population levels, declined significantly for trials that began recruitment after 1993 ($M = 47.2\%$ vs. $M=53.9\%$) and fewer than half reported analyses by gender. Minorities continued to be under-represented in later trials, however, significant improvement in representation ($M=16.1\%$ vs. $M=10\%$) and analysis by race occurred. Industry sponsored studies had lower minority representation than NIH funded studies. Recommendations are offered to improve subgroup analyses and minority inclusion.

Keywords

females; minorities; smoking cessation; research methods

Introduction

Tobacco use is the most common cause of preventable death in the United States and contributes to increased morbidity and mortality from a variety of diseases including cancer, heart disease, and stroke (1). The risk of cancer associated with tobacco use is especially pronounced. Approximately 85% of cases of head and neck cancer diagnosed each year are associated with tobacco use. The relative risk of lung cancer-related morbidity attributable to smoking is over 90% and between 60–70% for other forms of cancer (e.g., larynx, and urinary cancers) (2). According to recent estimates, 20.8% of the United States population smokes (3) and 12.8% of the population met criteria for nicotine dependence (4). Given that 46.2% of smokers (20.5 million) are women and 23.0% (10.05 million) are minorities (5), the health

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Dr. O'Malley has consulted to GlaxoSmithKline, Eli Lilly and Ortho McNeill. Dr. O'Malley is an inventor on unlicensed patents held by Yale University for the use of naltrexone in smoking cessation treatment.

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effects of smoking faced by members of these groups affect a considerable proportion of the United States population. Unfortunately, women and minorities historically have been under-represented in clinical research (6). The extent to which this historic under-representation applies to smoking cessation research is an important topic, given the significance of smoking cessation in cancer prevention efforts and the large number of minority and female smokers.

In response to concerns about representation of women, the National Institutes of Health (NIH) established a policy in 1986 urging that women be included in clinical research (7). In 1987, a similar policy was published encouraging the inclusion of minorities in clinical research (7). These recommendations subsequently became requirements following the passage of the 1993 NIH Revitalization Act (6). This act directed the NIH to ensure the inclusion of women and minorities in clinical research and, in 1994, the NIH began requiring researchers to address the inclusion of women and minorities explicitly in their research designs. The NIH stipulated that, as part their research plans, investigators should provide the female and minority composition of the population they intend to study and provide a rationale for the selection of these research participants. The 1994 NIH requirements further stipulated that Phase III clinical trials must include subgroup analyses to assess gender and racial/ethnic differences in treatment efficacy. While subgroup analyses were required only for Phase III trials, the NIH stated that these analyses should be conducted in all clinical studies, even in cases where small sample size limits the statistical power of these analyses (1).

The importance of adequate representation of women and minorities in clinical trials was also noted in The Food and Drug Modernization Act of 1997 (8). An amendment addressing Women and Minorities that was added to Section 115 (b) of this Act states, “The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).” Recognizing the full range of individuals from various racial and ethnic backgrounds who will ultimately receive approved drugs, the FDA has put forth efforts towards ensuring that drug safety and efficacy are adequately studied among women and minorities (9).

In a study analyzing adherence to the NIH requirements in federally funded randomized clinical trials, women were found to be generally underrepresented in studies published in top tier journals (10). Another review of papers published in major medical journals concluded that the release of the 1994 NIH requirements did not appear to have improved enrollment of women irrespective of funding source (11). In addition, three studies found that a majority of clinical trials did not report subgroup analyses by sex (10,11,12). Consistent with this conclusion, the May 2000 General Accounting Office (GAO) Report to Congress addressing women’s health noted an improvement in clinical trial participation among women (13) but not in reporting of subgroup analyses.

Reviews of minority representation and analysis in clinical trials have also found inadequate inclusion and failure to conduct subgroup analyses based on race/ethnicity. For example, Murthy, Krumholz and Gross found lower enrollments of Hispanic and African American patients in a population-based analysis of participants in breast, colorectal, lung, and prostate cancer clinical trials (14). Also, in a study analyzing reports of clinical trials in areas of known health disparities (i.e., HIV/AIDS, diabetes, cancer and cardiovascular disease), the majority of trials did not report race and almost none reported analyses by race/ethnicity, findings that did not differ by funding source (15). In addition, in an analysis of 165 K-awarded clinical trials associated with diabetes and obesity, only 37% reported the ethnic/racial breakdown of their samples (16). Thus, not only have minorities been inadequately represented, neither race nor racial/ethnic breakdown and subgroup analyses have been reported in many clinical trials covered in prior reviews.

To our knowledge, no systematic analysis has been conducted to assess the impact of the NIH Revitalization Act and the ensuing NIH requirements on the inclusion of women and minorities in clinical trials of pharmacotherapy for smoking cessation. Further analyses with regards to the impact of the NIH Revitalization Act are important since Food and Drug Administration (FDA)-approved pharmacotherapy may assist in reducing the morbidity and mortality associated with tobacco use among women and minorities. Among smokers, women appear to be at increased risk of developing chronic obstructive pulmonary disease (17), and while lung cancer rates are dropping for men, they continue to climb for women (18). This latter trend may be explained by the decline in gender differences in smoking rates observed during the second half of the 20th century. According to estimates from the National Health Interview Survey, the percentage of males who were current smokers was about 53% greater than the percentage of females who were current smokers in 1965 (51.9% versus 33.9%, respectively), compared to a 26% higher rate among males estimated for 2004 (23.4% versus 18.5%, respectively) (5). The decline in gender differences in smoking rates has been attributed to more women than men taking up smoking (19) and the lower rates of success women have had in smoking cessation treatment compared with men (20). With regard to health disparities among members of minority groups, African American smokers have higher rates of tobacco-related morbidity and mortality than Caucasian smokers (21). Among Hispanics, five of the ten leading causes of death are attributable to smoking compared to one of five in the general U.S. population (22). American Indians and Alaska Natives have the highest rates of smoking at approximately 35% (23). Furthermore, unlike some other racial and ethnic groups, the high tobacco prevalence rates among American Indian adults have not decreased significantly since the 1970's and rates are increasing among Blacks (1).

The purpose of this study was to analyze participation of women and minorities in smoking cessation trials of FDA-approved pharmacotherapy conducted in the United States and published in English within the scientific literature. These FDA-approved pharmacotherapies include nicotine replacement products (e.g., nicotine patch, gum, lozenge, nasal spray and inhaler), bupropion and varenicline. This review addresses three main topics: 1. the extent to which gender and racial/ethnic sample breakdowns were reported; 2. the extent to which analyses to assess differences in outcomes based on gender or race/ethnicity were reported, and 3. whether female and minority representation was adequate. We compared trials beginning recruitment before and after passage of the NIH Revitalization Act, and trials funded by NIH and by pharmaceutical companies.

Based on the findings of the 2000 GAO Report (13), we anticipated that recent representation of women would be adequate, but that reporting of subgroup analyses would continue to be insufficient. Due to reports of continued under-representation of minorities in clinical trials in other areas of medicine, we hypothesized that minorities would be under-represented and their response to treatment typically unexamined following the NIH Revitalization Act. Because the NIH requirements only apply to NIH sponsored studies, we predicted that pharmaceutical sponsored trials would have lower enrollment of minorities, be less likely to report subgroup analyses, and show less change in these parameters following the implementation of the NIH requirements compared to NIH sponsored studies.

Method

The present review examines studies that were included in a prior review of FDA-approved pharmacotherapy for smoking cessation (24). The Leeman et al. review included reports of clinical trials published in English by July 2006 involving pharmacotherapies that had been FDA-approved as of that time. This included clinical trials of five forms of nicotine replacement therapy (NRT), bupropion sustained release (SR) and varenicline. Procedures for this review, including the databases that were searched and the inclusion criteria that were used, were

similar to those employed in meta-analyses of NRT (25) and antidepressants for smoking cessation (26) as found in the *Cochrane Database of Systematic Reviews* (see Leeman et al. for detailed procedures).

Only trials originating from the U.S. were included because the requirements for inclusion of women and minorities originated from NIH, which funds research primarily within the U.S. Reports were searched for the gender and racial/ethnic breakdown of their samples. As per NIH guidelines, minority groups included Hispanic or Latino, American Indian or Alaska Native, Asian, Black or African American, and Native Hawaiian or Other Pacific Islander. Published papers reporting the primary findings from a given trial as well as secondary publications were evaluated. Given that the NIH Revitalization Act was passed in June 1993 and the resulting NIH requirements for the inclusion of women and minorities were released in 1994, we compared trials initiating subject recruitment before 1994 with trials initiating subject recruitment during and after 1994. When date of initiation of subject recruitment was not included in a report, we contacted the corresponding author to obtain this information. We also identified funding source (i.e., NIH or pharmaceutical company) wherever possible and reviewed published reports for results of subgroup analyses to determine whether gender or racial differences existed in outcomes. All information was retrieved from articles by two investigators in order to reduce the likelihood of error.

Statistical Analysis

Our analysis plan was similar to a prior review of female and minority representation in clinical trial research (15). First, separate Chi-square analyses were conducted to compare the number of studies reporting the gender and ethnic/racial breakdowns of their samples and the number of trials reporting results of outcome analyses by gender and by race/ethnicity according to 1. recruitment period (before 1994 and from 1994-on) and 2. funding source (NIH versus pharmaceutical sponsored). Funding comparisons were limited to NIH versus pharmaceutical sponsored because there were insufficient numbers of trials funded through other means to permit a comparison. Hierarchical logistic regressions were then used to examine effects of all variables of interest in the same analysis. Recruitment period, funding source and sample *N* were entered in the first step of the analysis. The purpose of the sample *N* variable was to assess impact of the sample size of the trial. In the second step, we examined the interaction of recruitment period and funding source to address the possibility that the passage of the NIH Revitalization Act led to a greater change in reporting in NIH-funded trials than in pharmaceutical sponsored trials. Trials enrolling exclusively females or exclusively members of minority groups were not included in these analyses because neither examination of representation nor subgroup analyses was possible.

An analogous procedure was used to assess differences regarding the percentage of female and minority participants included in trials that reported this information. Separate *t*-tests were used for preliminary analyses examining each of the three comparisons individually. *ANCOVAs* were used to address multiple variables simultaneously. In the first set of *ANCOVAs*, sample *N* was included as a covariate and recruitment period was the sole independent variable. A second set of *ANCOVAs* was then conducted including these two variables as well as funding type and the recruitment period x funding interaction. Trials enrolling exclusively females or members of minority groups were excluded from these analyses because the inclusion of these trials would dramatically alter sample variance and potentially produce misleading results.

Confirmatory analyses were conducted by collapsing across trials and comparing the overall representation of females and minorities among the group of trials beginning recruitment before 1994 and the group of trials beginning recruitment from 1994 to the present, using chi-square. Trials enrolling only females or members of minority groups were included in the confirmatory analyses collapsing across trials.

Results

A total of 127 published reports from 80 United States-based smoking trials were included in the review. Forty-four trials (55%) began recruitment before 1994 and thirty-six (44%) began recruitment during 1994 or later. We were able to identify the funding source for 75 of the 80 trials (NIH-sponsored = 40, pharmaceutical-sponsored = 31, other funding = 4). Sixty-two of the trials tested NRT, 14 tested bupropion, 1 tested varenicline, 2 tested both varenicline and bupropion, and 1 tested NRT and bupropion.¹ Only reports cited in the text are included in the References section. A complete list of the references included in the review is available from the authors.

Reporting of gender breakdown and analyses comparing participants by gender

Two of the 80 trials included in this review enrolled exclusively females (27,28). These two trials were not included in any statistical analyses related to gender with the exception of the final, confirmatory analysis collapsing across trials. As shown in Table 1a, a gender breakdown was provided for 76 of the remaining 78 trials (97.4%). Given that gender breakdown was reported in such a high percentage of trials, there was no reason to conduct comparisons regarding likelihood of including gender breakdown. Gender analyses were reported in 36 of the remaining 78 trials (46.2%). Regarding the likelihood of reporting a gender analysis, neither comparison showed a significant difference (recruitment period [X^2 (1df, $N = 78$) = 0.40, $p = .53$] or funding source [X^2 (1df, $N = 70$) = 0.21, $p = .65$]). In the hierarchical logistic regression, the only significant predictor was sample N . The recruitment period x funding interaction was not significant in the hierarchical logistic regression, thus results from the first step of the regression are reported: N [$\beta = 0.002$, $SE = 0.001$, $OR = 1.002$ (95% $CI = 1-1.003$), $p = .016$], recruitment period [$\beta = -0.19$, $SE = 0.52$, $OR = 0.83$ (95% $CI = 0.30-2.29$), $p = .71$] and funding type [$\beta = 0.50$, $SE = 0.53$, $OR = 1.66$ (95% $CI = 0.59-4.65$), $p = .34$].

Comparisons of female representation in smoking cessation trials

In the individual analyses, trials beginning recruitment before 1994 had significantly higher female representation [$t(74) = -2.37$, $p = .021$], and there was no difference in the inclusion of females by funding type [$t(66) = 0.14$, $p = .89$] (Table 1a). In the ANCOVA, the recruitment x funding interaction term was not significant. Omitting the interaction term, recruitment period was significant [$F(1, 64) = 4.65$, $p = .035$], but funding type [$F(1, 64) = 0.06$, $p = .80$] and sample N [$F(1, 64) = 0.44$, $p = .51$] were not.

Collapsing across trials, the overall representation of females was 52.5% (18,152 out of 34,590). In trials beginning recruitment before 1994, female representation was 55.5% (8,468 participants out of 15,269), compared with 50.1% from 1994 on (9,684 out of 19,321). As in the analysis comparing inclusion of females by trial, this decrease in the later trials was significant [X^2 (1df, $N = 34,590$) = 97.42, $p < .001$].

Reporting of ethnic/racial breakdown and analyses comparing participants by race/ethnicity

Two of the 80 trials enrolled exclusively African-Americans (29,30) and were not included in any statistical analyses related to race/ethnicity with the exception of the final, confirmatory analysis collapsing across trials. As shown in Table 1b, 45 of the remaining 78 trials (57.7%) reported racial data. The percentage of trials providing a breakdown of participants by ethnic/racial status was significantly higher from 1994 to the present [X^2 (1df, $N = 78$) = 9.84, $p = .002$], but did not differ by funding source [X^2 (1df, $N = 70$) = 1.02, $p = .31$] (Table 1b). The

¹There were other trials included in this review that tested multiple active medications however, in these other trials, only one of the drug conditions met criteria for inclusion in a *Cochrane Review*. The trials are listed only according to the drug conditions that met or would have met criteria for inclusion in a *Cochrane Review*

recruitment period x funding interaction was not significant in the hierarchical logistic regression, thus results from the first step of the regression are reported. Significant effects were obtained for N [$\beta = 0.003$, $SE = 0.001$, $OR = 1.003$ (95% $CI = 1.001$ – 1.006), $p = .006$] and recruitment period [$\beta = 1.21$, $SE = 0.59$, $OR = 3.36$ (95% $CI = 1.05$ – 10.76), $p = .041$] but not funding type [$\beta = 1.09$, $SE = 0.63$, $OR = 2.96$ (95% $CI = 0.85$ – 10.26), $p = .09$].

With respect to whether a study reported race/ethnicity subgroup analyses in the individual analyses, trials beginning recruitment since 1994 were more likely to report such results [X^2 (1 df , $N = 78$) = 5.20, $p = .023$] and there was a trend for the funding comparison [X^2 (1 df , $N = 70$) = 3.60, $p = .06$] (Table 1b). In the hierarchical logistic regression, the recruitment period x funding interaction was not significant, thus results from the first step of the regression are reported. Sample N [$\beta = 0.002$, $SE = 0.001$, $OR = 1.002$ (95% $CI = 1$ – 1.003), $p = .009$] and funding source were significant with NIH-funded studies being more likely to report results of a race/ethnicity subgroup analysis [$\beta = 2.55$, $SE = 1.10$, $OR = 12.81$ (95% $CI = 1.49$ – 109.85), $p = .02$]. Recruitment period was not statistically significant [$\beta = 1.67$, $SE = 0.88$, $OR = 5.29$ (95% $CI = 0.94$ – 29.62), $p = .06$].

Comparisons of minority representation in smoking cessation trials

Two trials in which authors reported that the sample was predominantly composed of Caucasians without providing their exact representation in the sample were excluded from these analyses. In the individual analyses, trials beginning recruitment during or after 1994 had significantly higher minority group representation [$t(41) = 2.14$, $p = .039$] and NIH-funded studies had significantly higher minority representation than pharmaceutical trials [$t(39) = 3.29$, $p = .002$] (Table 1b).

In the *ANCOVA*, the recruitment x funding interaction term was not significant. Omitting the interaction term, recruitment period [$F(1,37) = 9.13$, $p = .005$] and funding [$F(1,37) = 13.40$, $p = .001$] were significant, however sample N was not significant [$F(1,37) = 0.73$, $p = .40$].

Collapsing across trials, overall minority representation in trials was 14.8% (3,939 out of 26,627). This figure can be broken down among the following racial/ethnic groups: African American 5.9% ($n = 1561$), Asian 0.4% ($n = 96$), Hispanic .07% ($n = 18$), American Indian/Alaskan Native .02% ($n = 4$), unspecified 8.5% ($n = 2,260$). Minority representation among all trials beginning recruitment before 1994 was 13.8% (1422 participants out of 10,333), compared with 15.4% from 1994 to the present (2517 out of 16,294). As in the analysis comparing inclusion of minorities by trial, this represented a significant increase in the later trials [X^2 (1 df , $N = 26,627$) = 14.25, $p < .001$].

Discussion

Consistent with the 2000 GAO report (13), we found that females were well-represented in smoking cessation pharmacotherapy trials, but that less progress has been made in reporting outcomes by gender. Funding source did not appear to influence female inclusion or analysis by gender. However, female representation was actually higher than male representation in smoking cessation pharmacotherapy trials that began recruitment before 1994. Although the percentage of women participating in trials declined in the period following the NIH requirement, the mean percentage of women among participants in these trials approximated the estimated percentage of smokers in the U. S. population who are women (approximately 46% as of 2004) (5). Nonetheless, further attention regarding this potential trend is recommended so that further declines do not occur. In addition, reporting of the results of gender analyses needs to be improved. Even in trials beginning recruitment from 1994 to the present, only half reported the results of a gender analysis and there was no significant improvement from the time before the requirement was implemented.

Among those trials in which racial representation was reported, there was significant improvement with regard to representation of minorities in U.S. based trials of FDA-approved pharmacotherapy for smoking cessation. Nonetheless, minorities continued to be underrepresented. The mean representation of minorities in the trials that began enrollment after 1993 was about 16%, however minorities currently represent about 23% of smokers in the U.S. (5). Representation of American Indians and Alaska Natives continues to be exceptionally low (four participants reported among all studies) despite the fact that these groups have the highest smoking rates. Thus, while improvements have been made, it is clear that further effort on the part of researchers, institutions involved in smoking related research, funding agencies, and journal editors will be required in order to make minority participation in smoking cessation trials commensurate with their representation among smokers in the U.S.

Racial representation was reported for just over half of the trials included in this review. The large proportion of trials not reporting this information makes it difficult to assess accurately the level of representation of members of minority groups. Although racial/ethnic breakdown was more likely to be reported in trials begun in 1994 or thereafter, this information was still unavailable in almost ¼ of these more recent trials. This problem could potentially be alleviated if journal editors required that authors report the racial/ethnic breakdowns of their samples as a prerequisite to publication for all clinical studies.

Funding source influenced the percentage of minorities included and, at a trend level, the reporting of results of ethnic/racial analyses, with NIH-funded studies performing better than industry sponsored studies. Higher minority inclusion in NIH-funded studies may be due to the fact that these trials are subject to NIH requirements. However, while industry sponsored studies may not be subject to NIH requirements, adequate representation of women and minorities in clinical trials funded by the pharmaceutical industry needs to be ensured because results of these trials often play a key role in the FDA approval process. Improvements in representation could be brought about through further endorsement of the need to include women and minorities by the FDA. For example, the NIH now requires grant applicants to specify an action plan for the recruitment of women and minorities. Similar standards could be adopted for industry sponsored studies.

Although historical events, such as the Tuskegee Syphilis Trial of African American males, have been proposed as possible causes for decreased minority participation in research (31), additional contemporary reasons for inadequate representation of minorities in clinical trials have also been recognized. These factors include poor minority recruitment planning and monitoring by researchers (32), need for increased cultural competency within the research setting (33), logistical limitations, including lack of transportation and need for child care services (34) and strict exclusion criteria, such as co-morbid medical and psychiatric conditions that often occur at higher rates among minority groups (34,35). Given that various minority groups are more likely to experience poorer health status (34) and higher rates of mental disorders (35), it may be necessary to make inclusion criteria less restrictive in order to increase representation of minorities to acceptable levels. This issue may be particularly pertinent for industry-funded trials, as these studies often carry more restrictive inclusion and exclusion criteria than NIH-funded trials. In order to assess accurately the efficacy of treatment among these groups, further adequately powered studies recruiting exclusively members of under-represented minorities, such as the trials of African-American smokers conducted by Ahluwalia and colleagues (29,30) are recommended. Forums should be provided for the dissemination of findings regarding treatment efficacy among minorities, including meetings/conferences and special issues of journals, such as the recent special issue of the journal *Addiction* on tobacco-related health disparities which contained several articles concerning minority smokers (36,37).

Results of ethnic/racial analyses were reported infrequently and while there was significant improvement observed in trials beginning in 1994 or later, even in the later trials, about ¾ did not report these analyses. Sample size was significantly associated with likelihood of reporting an ethnic/minority or a gender analysis. This is not surprising given that larger sample sizes afford greater statistical power for these analyses. Indeed, results of subgroup analyses from studies with small sample sizes should be interpreted with caution in order to avoid “overstated and misleading results” (38). However, the NIH requirements state that *all* studies should conduct ethnic/minority and gender analyses regardless of sample size. Unfortunately, there was no improvement observed in the reporting of either gender or ethnic/minority analyses for studies that began recruitment following the 1994 requirements. Further improvements would be realized if journals required that manuscript authors report results of analyses to detect differences in outcome based on gender and race/ethnicity. A bill called The Fair Access to Clinical Trials Act, which was introduced in the U. S. Senate in 2005, would require that *both publicly and privately funded* medication trials register in a publicly accessible data bank, which might facilitate secondary analyses of efficacy by minority groups and gender. This bill, if passed, could certainly help to broaden the base of knowledge we are able to acquire from the available data, but enhanced representation of minority groups through more aggressive and effective approaches is still needed in order to maximize the power and, accordingly, the utility of these analyses.

Various limitations are evident in our study. As in the Leeman et al. (2007) review (24), our focus was on trials of FDA-approved pharmacotherapy that met criteria for inclusion similar to those used in meta-analyses from the *Cochrane Database of Systematic Reviews*. Thus, the main limitation of the present review is that our findings do not apply to nonpharmacological, behavioral treatments for smoking cessation. Our findings also do not apply to pharmacotherapies not approved by the FDA or to trials of approved pharmacotherapy not meeting standards for inclusion in a Cochrane review.

The provisions in the 1993 NIH Revitalization Act pertaining to women and minorities were the result of concern about their under-representation in clinical research. Unlike a number of prior reviews (10,11,14), findings from this review suggest improvement in the representation of minorities. At the same time, rates of minority representation in clinical trials remained lower than population levels even in more recent trials. This was particularly true for pharmaceutical-sponsored trials. The present finding of adequate representation of females is in accordance with the report of the GAO (2000) (13), although it is important to note that rates were lower in trials beginning enrollment from 1994 to the present compared with those beginning earlier. Similar to prior reviews (10,11,15), we conclude that results of gender analyses were not reported often or consistently in the trials included in this review and the frequency of minority subgroup analyses was low. In order to comply fully with the NIH Revitalization Act of 1993 and the ensuing NIH requirements in smoking cessation as well as in other fields, a concerted effort by researchers, funding agencies, and journal editors is needed. Through adequate inclusion of minorities and continued representation of women, treatments can be identified that improve their health and well-being.

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Table 1a. Summary of gender group reporting in clinical trials of FDA-approved pharmacotherapy for smoking cessation

	Total N ^a	Year recruitment began		Funding source	
		Before 1994 ^b	1994 & after	NIH-sponsored trials ^b	Industry ^b
Number of trials overall	78	42	36	39	31
Number of trials reporting gender breakdown (percentage of total)	76 (97.4%)	40 (95.2%)	36 (100%)	38 (97.4%)	30 (96.8%)
Number of trials reporting results of a gender analysis (percentage of total)	36 (46.2%)	18 (42.9%)	18 (50%)	21 (53.8%)	15 (48.4%)
Mean percentage of females in trials(SD)	50.7% (12.6%)	53.9% (9.9%)	47.2% (14.4%)	51.1% (11.3%)	50.7% (11.5%)
Table 1b. Summary of minority group reporting in clinical trials of FDA-approved pharmacotherapy for smoking cessation					
Number of trials overall	78	43	35	39	31
Number of trials reporting ethnic/racial breakdown (percentage of total)	45 (57.7%)	18 (41.9%)	27 (77.1%)	26 (66.7%)	17 (54.8%)
Number of trials reporting results of an ethnic/racial analysis (percentage of total)	12 (15.4%)	3 (7%)	9 (25.7%)	9 (23.1%)	2 (6.5%)
Mean percentage of minorities in trials(SD)	13.8% (9.4%)	10% (6.1%)	16.1% (10.3%)	16.8% (9.4%)	8.1% (6.1%)

* $p < .05$

** $p < .01$, significant difference according to a chi-square analysis for categorical data or according to a t -test for continuous data

^aFor the minority group summary, this figure excludes two trials one involving NRT and one involving bupropion that enrolled only African-Americans (29,30). For the gender summary, this figure excludes two NRT trials enrolling only females (27,28)

^bA trial stating that subjects were primarily Caucasian without providing their exact representation in the sample was included as a trial reporting ethnic/racial background, but was excluded from analyses involving percentages of minority participants