

Smoking Cessation Treatment Outcomes in Men and Women in Taiwan: Implications for Interpreting Gender Differences in Smoking Cessation

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Abstract: Several clinical trials of both behavioural and pharmacological treatments across Europe and the US have reported lower smoking cessation rates in women than in men, while population data and data from smokers attending routine stop-smoking services show little or no gender differences in outcome. Data from countries with a large gender difference in smoking prevalence can clarify whether self-selection could be responsible for this discrepancy. We analyzed data from a smoking cessation clinic in Taiwan, where 47% of men and 4% of women smoke. 1,090 smokers (963 men and 127 women) seeking help at a Taiwanese smokers' clinic between 2002 and 2007 received nicotine patches and up to 8 support sessions. Several baseline variables were collected together with self-reported smoking status at 3 and 6 months. Sustained abstinence rates (abstinent at both 3 months and 6 months) were significantly lower in women than in men (18.0% vs 30.3%, $p=0.04$), as were point-prevalence abstinence rates at both 3 (28.3% vs 38.5%, $p=0.026$) and 6 months (22.0% vs 35.0%, $p=0.004$). In a multiple regression including all baseline variables, only gender and cigarettes per day were significant predictors of sustained abstinence. In conclusion, among a cohort of treatment-seekers in Taiwan, there was a significant gender difference in smoking cessation outcomes. Given that such an effect is small or non-existent in countries where the prevalence of smoking across genders is similar, this suggests that sporadic gender differences could be an artifact of self-selection.

Keywords: Smoking cessation, sex, gender, nicotine patches, tobacco dependence.

INTRODUCTION

There is a long-standing debate over whether women find it harder than men to stop smoking. Clinical trials are the main source of data in support of the assertion that they do. Women have been observed to be less successful than men when using nicotine replacement treatment (NRT) [1, 2], bupropion [3, 4], behavioral support without medication [5], and unaided smoking cessation attempts [6]. However, not all studies have found such a difference [7-9]. A meta-analysis of nicotine patch trials found no gender difference [10], whilst an update performed by another research group found a marginally lower quit rate in women [11]. Another analysis merged data from nicotine patch, gum, inhaler, and nasal spray trials, and reported that women were less likely to quit [12].

In contrast to clinical trials, the other sources of data suggest little or no gender differences in quit rates. General population studies report no gender differences in the proportions of ex-smokers among men and women. Early population level analyses reported less smoking cessation success among women [13], but the gender difference was shown to be an artifact of a failure to include data on the number of ex-cigarette smokers who had switched to cigar and pipe smoking; these products tend to be smoked predominantly by men and when such data were included, the gender difference disappeared [14, 15]. It has been suggested that differences among the types of men and women who present for clinical trials, i.e. self-selection bias, rather than an inherent gender effect, may explain the gender difference sometimes observed in clinical studies [15].

Smokers who receive stop-smoking treatment in 'real-life' settings are the third source of information on this issue. By far the largest data source in this area is the United Kingdom (UK) NHS Stop Smoking Service, which had 816,444 smokers setting a quit date in 2012; 51% of men versus 48% of women reported abstinence four weeks after their target quit date [16]. The figures were similar in

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previous years, i.e. 50% and 48% in 2011 and 51% and 48% in 2010. The prevalence of smoking in men and women is similar in the UK (men vs women = 21% vs 20%), but women are slightly more likely than men to attend for treatment (52.7% vs 47.3 %). A study of 3,398 smokers attending the Mayo Clinic in the United States (US) found no gender difference in outcome [17].

While in the UK and US there are only marginal differences in smoking prevalence among men and women, in most other countries the prevalence of smoking is higher among men. If in such countries the gender difference in outcome is larger than in countries where male and female smoking has a similar prevalence, it would suggest that any gender differences in quitting smoking are more likely due to smoker self-selection than due to any biological effects of gender. Data from 'real life' settings in such countries are needed to test this hypothesis.

The present study adds to the existing literature by comparing smoking cessation outcomes in men and women treated at an outpatient smoking cessation clinic in Taiwan, where in 2002 (when this study began) 47% of men and 4% of women smoked [18].

MATERIALS AND METHODOLOGY

Design and Setting

This was a naturalistic cohort study. The Department of Health in Taiwan has been funding Smoking Cessation Clinics since 2002. Taiwanese smoking cessation clinics and clinical trials have so far reported similar outcomes to Western studies [19, 20]. The Clinics provide stop-smoking medications, brief advice, and printed guides to quitting. The National Health Insurance covers NT\$250 per visit/wk (US\$ 8.5), the patients pay NT\$ 450 (US\$ 15.0) for nicotine transdermal patches per week and NT\$ 100-150 (US\$ 3.3-5) for each Clinic visit. The Clinics are based in hospitals and run by physicians (mainly family doctors but other specialties can provide the treatment if trained and certified by the Bureau of Health Promotion in Taiwan). The national service was initially advertised regularly *via* TV, radio, and press for several months around its launch in 2002. Adverts were then placed every few months to maintain awareness of the programme.

The study Clinic is based at the Department of Family Medicine at Kaohsiung Veteran General Hospital, and it is run by five family physicians.

Participants

The study sample included 1,096 smokers who started treatment between September 2002 and July 2007. The majority of patients were self-referred. During the study period, all patients were treated with nicotine patches. Treatment is available for smokers ≥ 18 years old, smoking ≥ 10 cigarettes per day (CPD) or scoring ≥ 4 on the Fagerström Test for Nicotine Dependence (FTND) or scoring ≥ 5 on the Fagerstrom Tolerance Questionnaire (FTQ), not pregnant, and not treated for acute cardiac or stroke conditions in the past 3 months.

Six clients died prior to the 6 months follow-up and were excluded from the analysis. The final sample includes 1,090 patients; 963 men and 127 women. Approval from the

Kaohsiung Veteran General Hospital IRB was obtained prior to the start of the study.

Intervention and Follow-Up

At the first visit, patients received support and advice from clinicians, educational materials and a prescription for nicotine patches for one or two weeks. Patch strength was tailored to number of CPD. For $CPD \geq 20$, Nicotinell 21mg was prescribed for four weeks, followed by Nicotinell 14mg for two weeks and Nicotinell 7mg for two weeks. For $CPD < 20$, Nicotinell 14mg was prescribed for 6 weeks and Nicotinell 7mg for 2 weeks. Patch dose was lowered if needed at the following visits (e.g. if higher dose patches caused skin irritation/itching or insomnia).

Patients were encouraged to attend every 1 to 2 weeks for a maximum of 8 visits over 90 days. The initial session lasted ~15-20 minutes, while the follow-up visits were briefer. Support and advice focused on physical dependence, managing and reassurance about withdrawal symptoms, patch adverse effects, and perceived barriers to quitting. Patients had to attend the clinic to receive patch prescriptions for the next week or two, depending on their visit schedule.

Measures

At the first visit, patients were asked to complete a questionnaire that collected demographic information and smoking history, reasons for quitting and past medical history.

Smoking status at 3 and 6 months was established by telephone calls. Three call attempts were made at each of these time points. Patients were asked whether they smoked any cigarettes at all over the past seven days [21]. Patients for whom smoking status was not established (unable to contact, moved to unknown address, refused contact, etc.) were classified as smokers. In addition to sustained abstinence, defined as self-reported abstinence at both 3 and 6 months, we also report separately on point-prevalence abstinence at each time point.

Statistical Analyses

Baseline characteristics and smoking cessation outcomes at 3 and 6 months were compared between men and women using independent t-test and chi-square or Fisher's Exact Test. Forced-entry logistic regression using baseline variables was used to predict smoking cessation outcomes. All variables collected at baseline were entered into the regression models. Data were analyzed using SPSS 12.0.

RESULTS

Table 1 shows baseline characteristics of the 1090 clients of whom 12% were female. The sample comprised of heavy smokers mostly in their 30's and 40's. Men and women differed in a number of variables including age, cigarette consumption, education, health status and reasons for wanting to stop smoking.

Table 2 shows abstinence rates for men and women. Women had significantly lower sustained quit rates and also point-prevalence quit rates at both 3 and 6 months.

There was no gender difference in the percentage of participants lost-to-follow-up at 3 months (male=13%,

Table 1. Baseline Characteristics

	Men N=940-963*	Women N=124-127*	Difference (p-Value)
Age in years; mean (SD)	47.0(16.4)	38.8(13.7)	<0.001
Years of smoking; mean (SD)	26.0(14.7)	16.2(11.1)	<0.001
Cigarettes per day; mean (SD)	25.1(12.5)	21.3(8.4)	<0.001
High dependence score ^{**} ; N (%)	551 (57.2%)	74 (58.3%)	0.822
Tried to quit before; N (%)	642 (62.3%)	85 (57.4%)	0.258
Education Level; N (%)			<0.001
Elementary	65 (6.7%)	12 (9.4%)	
High school	413 (42.9%)	87 (63.8%)	
University Unknown	436 (45.3%)	27 (21.3%)	
49 (5.1%)		8 (5.5%)	
Medical history; N (%)			
Cancer/ Malignancy	19 (2.0%)	5 (3.9%)	0.187
CVA or Stroke	25 (2.6%)	1 (0.7%)	0.350
Liver disease	51 (5.3%)	6 (4.7%)	0.786
Kidney disease	15 (1.6%)	1 (0.8%)	1.000
Heart disease	104 (10.8%)	7 (5.5%)	0.064
Diabetes	86 (8.9%)	5 (3.9%)	0.056
Lung disease	73 (7.6%)	4 (3.1%)	0.067
Hypertension	144 (15.0%)	8 (6.3%)	0.008
Reasons for wanting to stop smoking; N (%)			
Health	813 (86.5%)	108 (87.1%)	0.852
Family	519 (55.2%)	60 (48.4%)	0.151
Work	100 (10.6%)	14 (11.3%)	0.825
To save money	170 (18.1%)	17 (13.7%)	0.229
Doctor's advice	160 (17.0%)	9 (7.3%)	0.005
Friend's advice	158 (16.8%)	31 (25.0%)	0.025
Prescribed 21mg (rather than 14mg) patch; N (%)	760 (78.9%)	88 (69.3%)	0.014

*N varies due to missing data.

**Scored ≥ 7 on FTQ or ≥ 6 on FTND.

female=15%; $p=.54$), but men were less likely to be lost-to-follow-up at 6 months (male=16%, female=26%; $p=.007$).

Table 2. Abstinence Rates in Men and Women

	Men (N=963)	Women (N=127)	Difference (p-Value)
Abstinent at both 3 and 6 Months	292 (30.3%)	23 (18.0%)	0.004
Abstinent at 3 Months	371 (38.5%)	36 (28.3%)	0.026
Abstinent at 6 Months	337 (35.0%)	28 (22.0%)	0.004

All baseline and treatment variables, including rate of lost-to-follow-up were entered into forced-entry regression models, with sustained abstinence and abstinence at 3 and 6 months as the dependent variables (Table 3). Compared to patients who continued to smoke, those who were abstinent

at both 3 and 6 months were significantly more likely to be lighter smokers and male. Gender also remained a significant predictor of outcome for 3 month and 6 month point prevalence abstinence.

DISCUSSION

In a sample of Taiwanese smokers seeking treatment, women had significantly lower abstinence rates than men. The difference remained significant after controlling for a range of baseline variables.

There were a number of differences in baseline and treatment variables between men and women. Men were, for example, older and smoked a greater number of cigarettes and for longer than women. These differences are typical of smoking patterns seen in Taiwan, where smoking among women is uncommon, but those who do are mostly below the age of 40 [18]. Although women were more likely than men to be lost-to-follow-up at 6 months, it is important to

Table 3. Significant Predictors of Quitting at 3 Months, 6 Months, and Both

	Abstinent at Both 3 and 6 Months		3 Months*		6 Months*	
	aOR [§] (95% CI)	p-Value	aOR [§] (95% CI)	p-Value	aOR [§] (95% CI)	p-Value
Male	1.836 (1.06-3.17)	0.029	1.767 (1.10-2.84)	0.019	1.965 (1.16-3.32)	0.012
Age (years)	1.015 (1.00-1.04)	0.125	1.032 (1.01-1.05)	0.001	1.015 (1.00-1.04)	0.120
Years of smoking	0.989 (0.97-1.01)	0.274	0.974 (0.95-0.99)	0.012	0.989 (0.97-1.01)	0.288
Cigarettes per day	0.959 (0.94-0.98)	<0.001	0.968 (0.95-0.98)	<0.001	0.960 (0.94-0.98)	<0.001
Tried to quit before	1.348 (0.99-1.84)	0.062	1.502 (1.12-2.02)	0.007	1.295 (0.96-1.75)	0.095
History of cancer	0.310 (0.08-1.16)	0.081	0.238 (0.07-0.77)	0.017	0.454 (0.15-1.40)	0.170

*7-day point prevalent abstinence, [§]aOR = Adjusted odds ratio.

note that in smoking cessation programmes drop-out is a consequence, rather than a predictor, of treatment outcome. People who do not succeed often feel embarrassed and are much less likely to attend follow-up appointments. After controlling for these differences, however, gender remained a significant predictor of abstinence.

The study had several limitations, especially in measuring smoking cessation outcome. Self-reported abstinence was not biochemically validated and only 7-day point prevalence abstinence rates were collected. Such soft outcome measures can be expected to inflate the abstinence rates and to generate 'random noise' which can obscure real predictors of outcome. However, this also implies that a baseline predictor which remains significant despite these problems is probably fairly robust.

Smokers in this cohort were all treated with nicotine patches. It has been proposed that there may be a specific gender difference in reaction to NRT [22], and future research should compare gender outcomes among users of non-NRT medications. However, a previous analysis of a cohort of NRT and bupropion users found no gender by medication interaction effect on outcome [17], and the UK Service has consistently observed roughly equal rates of success in the two genders during the period when 80% of clients used NRT (mostly patches) and 6% used bupropion, and the period when 66% used NRT and 25% used varenicline [16, 23].

It has been suggested previously that where gender differences in difficulty quitting are detected, these may be related to a range of presumably universal gender factors. These include gender differences in nicotine metabolism [24], that women are influenced less by nicotine and more by non-nicotine factors [25], and that there is a gender difference in fear of or reactions to post-cessation weight gain [26], or post-cessation depression [27]. The present data cannot exclude such explanations.

Another possible interpretation which may be more parsimonious involves the self-selection hypothesis, i.e. that any gender differences in difficulty quitting smoking may be instead related to the fact that people attracted to smoking where smoking behavior among their peers is common differ from those who pick up smoking where only a minority of their peers do so and where such behavior carries a degree of social stigma. Such 'rare' smokers may be more likely to have a strong reaction to cigarettes or have other

characteristics which make quitting smoking more difficult, and which are not necessarily gender-specific.

In summary, while there are only small or no genuine population-wide gender differences in difficulty quitting smoking in the US and UK, we detected a significant gender difference in a country with a 10-fold difference in smoking prevalence among men and women. Further research is needed to clarify whether sporadic gender differences are an artifact of self-selection or a reflection of any universal gender factors.

CONFLICT OF INTEREST

PH and HM have provided consultancy to, and received research funding from, manufacturers of smoking cessation medications.

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