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Cytisine versus Nicotine for Smoking Cessation

Natalie Walker, Ph.D., Colin Howe, Ph.D., Marewa Glover, Ph.D., Hayden McRobbie, M.B., Ch.B., Ph.D., Joanne Barnes, Ph.D., Vili Nosa, Ph.D., Varsha Parag, M.Sc., Bruce Bassett, B.A., and Christopher Bullen, M.B., Ch.B., Ph.D.

ABSTRACT

BACKGROUND
Placebo-controlled trials indicate that cytisine, a partial agonist that binds the nicotinic acetylcholine receptor and is used for smoking cessation, almost doubles the chances of quitting at 6 months. We investigated whether cytisine was at least as effective as nicotine-replacement therapy in helping smokers to quit.

METHODS
We conducted a pragmatic, open-label, noninferiority trial in New Zealand in which 1310 adult daily smokers who were motivated to quit and called the national quitline were randomly assigned in a 1:1 ratio to receive cytisine for 25 days or nicotine-replacement therapy for 8 weeks. Cytisine was provided by mail, free of charge, and nicotine-replacement therapy was provided through vouchers for low-cost patches along with gum or lozenges. Low-intensity, telephone-delivered behavioral support was provided to both groups through the quitline. The primary outcome was self-reported continuous abstinence at 1 month.

RESULTS
At 1 month, continuous abstinence from smoking was reported for 40% of participants receiving cytisine (264 of 655) and 31% of participants receiving nicotine-replacement therapy (203 of 655), for a difference of 9.3 percentage points (95% confidence interval, 4.2 to 14.5). The effectiveness of cytisine for continuous abstinence was superior to that of nicotine-replacement therapy at 1 week, 2 months, and 6 months. In a prespecified subgroup analysis of the primary outcome, cytisine was superior to nicotine-replacement therapy among women and noninferior among men. Self-reported adverse events over 6 months occurred more frequently in the cytisine group (288 events among 204 participants) than in the group receiving nicotine-replacement therapy (174 events among 134 participants); adverse events were primarily nausea and vomiting and sleep disorders.

CONCLUSIONS
When combined with brief behavioral support, cytisine was found to be superior to nicotine-replacement therapy in helping smokers quit smoking, but it was associated with a higher frequency of self-reported adverse events. (Funded by the Health Research Council of New Zealand; Australian New Zealand Clinical Trials Registry number, ACTRN12610000590066.)

From the National Institute for Health Innovation (N.W., C.H., V.P., C.B.), the Centre for Tobacco Control Research, Department of Social and Community Health (M.G.), the Department of Pacific Health (V.N.) and the School of Population Health and the School of Pharmacy (J.B.), University of Auckland, Auckland, and the Quit Group, Wellington (B.B.) — all in New Zealand; and Queen Mary University of London, Wolfson Institute of Preventive Medicine, and UK Centre for Tobacco and Alcohol Studies, Barts and the London School of Medicine and Dentistry — all in London (H.M.). Address reprint requests to Dr. Walker at the National Institute for Health Innovation, School of Population Health, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand; or at n.walker@auckland.ac.nz.

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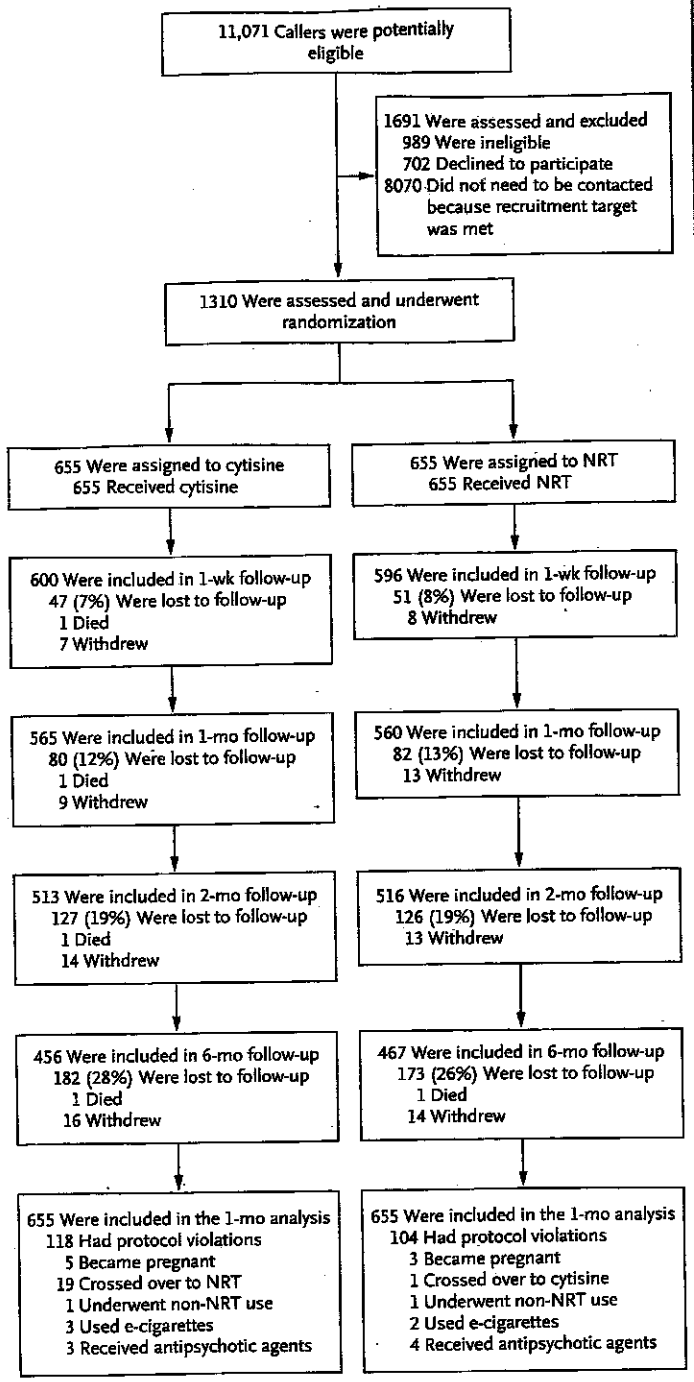

Figure 1. Recruitment and Retention of Participants throughout the Trial.
At initial assessment, the main reasons for ineligibility were current use of other smoking-cessation products or services (71%), schizophrenia (9%), uncontrolled blood pressure (9%), and pregnancy or breast-feeding (4%). For the 1-month analysis, protocol violations (as defined in the study) included loss to follow-up, death, and study withdrawal. NRT denotes nicotine-replacement therapy.

Table 1. Baseline Characteristics of the Participants.*

Characteristics	Cytisine (N=655)	NRT (N=655)
Female sex — no. (%)	372 (57)	372 (57)
Age — yr	37.8±11.8	38.4 (11.9)
Ethnic group — no. (%)†		
New Zealand Maori	215 (33)	213 (33)
Non-Maori	440 (67)	442 (67)
Less than 12 years of schooling — no. (%)	344 (53)	329 (50)
Cigarettes smoked per day‡	19.3±11.9	19.0 (10.0)
Cigarette dependence§	5.4±2.1	5.3 (2.3)

* Plus–minus values are means ±SD. No significant differences were observed between groups in baseline characteristics. NRT denotes nicotine-replacement therapy.
† Ethnic group was self-reported. Maori are indigenous New Zealanders; all others are non-Maori.
‡ The number of cigarettes smoked per day includes hand-rolled cigarettes.
§ Cigarette dependence was measured with the Fagerström Test of Cigarette Dependence. On a scale of 1 to 10, a score above 5 indicates high cigarette dependence and a score of 5 or below indicates low cigarette dependence.