
The Epidemiology and Genetics of Smoking Initiation and Persistence: Crosscultural Comparisons of Twin Study Results

Pamela A. F. Madden¹, Nancy L. Pedersen², Jaakko Kaprio³, Markku J. Koskenvuo⁴, and Nicholas G. Martin⁵

¹ Department of Psychiatry, Washington University School of Medicine, St. Louis, USA

² Department of Medical Epidemiology, Karolinska Institutet, Stockholm, Sweden

³ Department of Public Health, University of Helsinki and Department of Mental Health and Alcohol Research, National Institute of Public Health, Helsinki, Finland

⁴ Department of Public Health, University at Turku, Turku, Finland

⁵ Queensland Institute of Medical Research, Brisbane, Australia

We examined whether there are crosscultural differences in the magnitude of genetic and environmental contributions to risk of becoming a regular smoker and of persistence in smoking in men and women. Standard methods of epidemiologic and genetic analysis were applied to questionnaire data on history of cigarette use obtained from large samples of male and female like-sex twins from three different countries: Australia ($N = 2284$ pairs), Sweden ($N = 8651$ pairs), and Finland ($N = 10,948$ pairs). Samples were subdivided into three age groups (AG), 18–25 years, 26–35 years, and 36–46 years of age. The magnitude of genetic influence for lifetime smoking was found to be consistent across country and AG for women (46%) and men (57%), and estimates of the contribution from environmental influences shared by twin and co-twin could be equated across all countries by AG for the women (from youngest to oldest AG: 45%, 35%, and 26%), but not for men, with separate estimates obtained for the Scandinavian (33%, 29%, and 19%) and the Australian men (26%, 9%, and 11%). There was no evidence for an important role for shared environmental influences on persistent smoking, and the genetic contribution was found to be consistent in magnitude in men and women, and the same across country and AG (52%). There are strong genetic influences on smoking behavior, and that risk of becoming a smoker (but not persistence in smoking) may be modified by experiences shared by twins that differ by AG and, at least for men, cultural background.

Cigarette smoking remains an important risk factor for morbidity and mortality from disorders such as lung cancer, heart disease, emphysema and bronchitis (Doll et al., 1980; Doll & Peto, 1976; Risch et al., 1993) in both industrialized and developing countries

(WHO, 1997). In the United States alone, as many as 400,000 lives are lost each year to smoking (Peto et al., 1992; USDHHS, 1989).

The availability of information about the health problems related to cigarette use has increased over the past 30 years. While there have been changes in trends in smoking, some of which appear to follow changes in the availability of health-related information, shifts in the prevalence of smoking and the use of tobacco (especially by gender) have not been consistent either across or within cultures (Grunberg et al., 1991). Because the link between an increase in health-related information and trends in smoking are not fully in agreement, there is a need to know whether there are age, sex or societal-related factors that may modify susceptibility for regular cigarette use and maintenance of the smoking habit.

Provided that appropriate attempts are made to measure and adjust for characteristics of the twin environment, the classical twin design, comparing monozygotic and dizygotic twins reared together, is a powerful behavioral genetic design for analyzing the joint effects of genes and environment on a trait such as smoking, which is subject to rapid developmental and secular changes. Because evidence for genetic effects comes from intra-generational comparisons (in contrast to the inter-generational comparisons which provide most of the power of adoption and nuclear family designs), and from comparisons of individuals who are of the same age, problems such as age-effects (e.g., the incidence of smoking onset varies by age), cohort effects (e.g., attitudes towards smoking behavior may vary in persons born in different eras) and secular effects (e.g., differences in the availability of

Address for correspondence: Pamela A.F. Madden, PhD, Department of Psychiatry, Washington University School of Medicine, 40 N.Kingshighway, Suite 2, St. Louis, Missouri, 63108 USA. Email: pam@matlock.wustl.edu

cigarettes due to changes in cost or to policy changes on the distribution of cigarettes), are minimized, and the possible effects of age or of environmental circumstances on risk for some characteristic may be studied through the comparison of subgroups or different populations of twins (Heath & Madden, 1995).

In most, but not all (Kaprio et al., 1984), twin studies on the etiology of smoking behavior, evidence has been found for genetic influence on risk of cigarette use in both women (Crumpacker et al., 1979; Edwards et al., 1995; Hughes, 1986; Kaprio et al., 1982; Pedersen, 1981; Raascho-Nielsen, 1960; Hetta et al., 1999; Kendler et al., 1999; Kendler et al., 2000) and men (Carmelli et al., 1990; Carmelli et al., 1992; Crumpacker et al., 1979; Eaves & Eysenck, 1980; Hannah et al., 1985; Heath et al., 1993; Hetta et al., 1999; Hughes, 1986; Kaprio, 1978; Kaprio et al., 1982; Kendler et al., 2000; Raaschou-Nielson, 1960; Swan et al., 1990; True et al., 1997), and in adolescent boys and girls (Boomsma et al., 1994; Han et al., 1999; Kaprio et al., 1995; Maes et al., 1999). However, less is known about whether the importance of genetic influences on smoking varies as a function of societal differences, age, or other circumstances (i.e., genotype \times environmental interaction).

Heath and his colleagues (1993) have evaluated sources of risk for the initiation of smoking, including smoking by co-twin, in three large samples of adult twins from different countries and birth cohorts: Australia, Virginia (US), and the American Association of Retired Persons (US). Substantial differences in estimates of heritability were found between the Australian and the US twins, and between men and women. However, despite wide differences in the estimates of prevalence, there was no evidence to suggest that factors responsible for changes in the numbers of smokers affected the estimate of heritability for risk of becoming a smoker in men or women by birth cohort. For instance, although an increase in smoking by US women born before 1916 to those born 1960–1967 was observed in their data (from about 30% to over 45%), in both the younger and older cohorts of US women up to 51% of the variance in smoking onset was found to be due to additive genetic factors. Similar results were found in a Dutch study of smoking behavior in which no significant differences in heritability estimates were observed in adolescent boys and girls across three age groups, 13–14, 15–16, and 17–18 years of age (Boomsma et al., 1994).

Twin studies have consistently reported a strong genetic contribution to risk of persistent smoking (i.e., long-term continuation in the smoking habit by those who have become smokers; Heath & Martin, 1993; Heath & Madden, 1995; True et al., 1997), but, as with smoking initiation, the relative impact of smoking-related social factors on maintenance of the smoking habit remains largely unknown. Findings from some (Heath & Madden, 1995; Heath &

Martin, 1993; True et al., 1997), but not all (Heath, 1990), twin studies on smoking behavior suggest that familial factors that increase risk for smoking initiation are substantially different from factors influencing whether or not a smoker quits cigarettes (Heath & Martin, 1993; Heath & Madden, 1995; True et al., 1997).

Here we use data on smoking behavior obtained from large samples of twins assessed at similar ages from in Australia, Finland and Sweden to examine crosscultural differences. Comparable assessments of smoking behavior were available for these samples. In previous analyses of these data evidence was found for a genetic influence on various smoking behaviors (Crumpacker et al., 1979; Heath & Martin, 1993; Heath & Madden, 1995; Kaprio et al., 1982). In this paper, the primary questions addressed are: (1) Is the relative importance of genes consistent across country, age and sex?, (2) Do environmental influences shared by co-twins (i.e., including familial smoking behaviors and attitudes, shared neighborhood and school-related experiences) contribute to risk of the onset and to maintenance of smoking? and if so, (3) Does the importance of environmental influences on smoking behavior vary across age, country or sex?

Methods

Samples

The samples for this study were drawn from three nationwide adult twin registries maintained for research purposes in three different countries: the Australian Twin Registry, the Finnish Twin Cohort, and the New Swedish Twin Registry. Almost all subjects were of European descent, and in all cases, zygosity was determined by questionnaire. The accuracy of ascertaining zygosity using this method has been estimated to be at least 95% (Cederlöf et al., 1961; Eaves, Eysenck & Martin, 1989; Sarna et al., 1978).

The Finnish and Swedish twins were both ascertained from population registries, while enrolment in the Australian registry was dependent on volunteerism, with twins recruited throughout Australia using newspapers and other forms of advertising media. The numbers of twin pairs used in this study are presented in Table 1 by country, age group and sex.

The New Swedish Data were obtained by a mailed questionnaire survey conducted in 1973 with Swedish male and female like-sex twin pairs born between 1926–1958 (about 14,000 like-sex pairs; Medlund et al., 1977). For purposes of this project, only twins aged 18–46 years (born 1926–1954) were included in the Swedish sample, and the deletion of cases with missing data left for analysis 2,332 MZ and 3,584 DZ female, 1,923 MZ and 3,109 DZ male like-sex twins, and one twin only from an additional 2,514 pairs, with a mean age in women of 31 years ($SD = 8$) and in men of 30 years ($SD = 8$).

The Finnish Data used in this study were obtained by a mailed questionnaire survey conducted in 1975

Table 1Numbers of Like-sex Twin Pairs from Each of the Three Societies by Sex, Age Group, and Zygosity Used in the Analysis of Regular Smoking and (in Parentheses) of Persistent Smoking^a

Age Range	Australian Pairs		Finnish Pairs		Swedish Pairs	
	Women	Men	Women	Men	Women	Men
18–25 Years						
MZ	354 (117)	185 (57)	673 (260)	526 (253)	755 (346)	613 (272)
DZ	215 (67)	149 (40)	1270 (489)	1179 (542)	1093 (528)	1078 (485)
26–35 Years						
MZ	379 (129)	186 (31)	492 (144)	445 (253)	906 (393)	750 (364)
DZ	237 (66)	101 (34)	1009 (252)	1020 (506)	1347 (545)	1130 (505)
36–46 Years						
MZ	225 (67)	85 (34)	308 (40)	287 (155)	671 (192)	560 (233)
DZ	125 (29)	43 (19)	686 (81)	756 (393)	1144 (259)	901 (366)
Total Pairs	1535 (475)	749 (248)	4438 (1266)	4213 (2102)	5916 (2263)	5032 (2225)

Note: ^aGenetic model-fitting for persistent smoking used pairs concordant for lifetime history of regular smoking.

that was completed by 4,936 male like-sex and 5,545 female like-sex pairs born before 1958, with both co-twins alive in 1967 (the overall rate of response was 89%; Kaprio & Koskenvuo, 1988; Kaprio et al., 1978). For comparability with the Swedish and the Australian samples, only twins aged 18–46 years (born 1929–1957) were included in the Finnish sample, and the deletion of cases with missing data left us with 1,473 MZ and 2,965 DZ female, 1,258 MZ and 2,955 DZ male like-sex twins, and one twin only from an additional 1,636 pairs, with a mean age in both men and women of 29 years ($SD = 8$).

The Australian data used in this study were obtained by a mailed questionnaire survey conducted in 1980–81 which was returned by 1,232 complete MZ female pairs, 747 DZ female like-sex pairs, 567 MZ male pairs, and 350 DZ male like-sex pairs (respectively, 72%, 67%, 63%, 63% pairwise response rates; Heath et al, 1995; Jardine & Martin, 1984; Kendler et al., 1986). For the purposes of this study, only same-sex twins aged 18 to 46 years (born 1935 to 1963) in the Australian sample were analyzed here, and the deletion of cases with missing data left us with 958 MZ and 577 DZ female, 456 MZ and 293 DZ male Australian like-sex pairs, and one twin only from an additional 292 pairs with a mean age in women of 29 years ($SD = 8$ years), and in men of 28 years ($SD = 7$).

Measures

Subjects from all three countries completed mailed questionnaires which obtained self-report measures of smoking status and history, and other aspects of lifestyle, as well as measures of personality, attitudes and sociodemographic variables (e.g., education, marital status, and religious affiliation). The Finnish and Swedish questionnaires were designed to be used together in research, and many survey questions,

including those on cigarette use, had similar wording. A history of regular smoking was measured in Scandinavians who endorsed smoking at least 5–10 packs of cigarettes in their lifetime by the question “Do you smoke or have you at some time smoked regularly, in other words daily or almost daily?” and in the Australian survey by the question “Have you EVER been a smoker?”. Lifetime regular smoking was coded as a two-level variable, never versus ever a regular smoker, by combining current and ex-smokers into a single category.

Among the lifetime regular smokers, persistent smoking in the Scandinavian twins was measured by the question “Do you still smoke regularly?” and for the Australian twins was indicated by the non-report of an age for quitting cigarette use among those who had endorsed ever smoking.

In 1988–1989 an 8-year follow-up survey (“1989 survey”) of Australian pairs where both twins had responded in 1981 was conducted by mailed questionnaire or abbreviated telephone interview, with responses obtained from 84.5% of the female and 80.5% of the male pairs born 1935 to 1963 who took part in the 1981 survey. In the Australian 1989 survey questionnaire, the extent to which twins experienced similar environments while growing up was measured by having each twin rate how often self and co-twin: (i) had the same playmates, (ii) shared the same room, (iii) dressed alike, and (iv) were in the same classes as children (*never, sometimes, usually, or always*). A measure of the similarity of the environments experienced by twins as adults was also obtained by having each rate how often self and co-twin had seen one another in 1981 (as well as each subsequent year until 1989) using a 7-point scale: (i) *we lived together*, (ii) *almost every day*, (iii) *at least once a week*, (iv) *once or twice a month*, (v) *a few times a years*, (vi) *less often*, and (vii) *not at all*.

Data Analysis

Differences in rates of lifetime regular smoking and smoking persistence as a function of sex, age group and society were examined by logistic regression (SAS, 1990). To correct for the statistical non-independence of the observations from pairs of twins, for these analyses, which were descriptive in nature, data obtained from only one twin of a pair was used.

Before attempting a genetic analysis, the data set was evaluated for certain assumptions and population characteristics including representativeness of sampling, the assumption of equal environments between MZ and DZ twins (in the Australian sample), and the effects of age. Since significant age effects were observed across all samples, before genetic analyses were conducted, these data were further subdivided into three age groups (AG) which included twins aged 18–25 years, 26–35 years, or 36–46 years (see Table 1 for numbers of pairs by subsample).

The data were summarized into contingency tables for each twin group (MZ and DZ) by society, sex and AG ($2 \times 3 \times 2 \times 3 = 36$ twin groups) for the genetic analyses of these data, where twins were cross-tabulated with co-twins by smoking status. In all samples, twins 1 and 2 were designated according to birth order or by random selection if birth order was unknown.

Genetic Analysis

The contributions of genetic, shared environmental and non-shared environmental effects on risk of becoming a regular smoker (and risk of persistent smoking) was evaluated under a multifactorial threshold model, which assumes a continuous normal distribution of “liability”, with distinct thresholds superimposed. These are standard assumptions used in the genetic analysis of categorical data under a polygenic model, as used in the estimation of tetrachoric or polychoric correlations (Jöreskog & Sörbom, 1993).

In the analysis of these data, the variance was decomposed into three sources: genetic effects, shared environmental effects (i.e., influences that are shared by individuals reared in the same household), and non-shared environmental effects (for a detailed technical account of the basic principles underlying the genetic analysis of twin data, see Neale & Cardon, 1992). If variance in a trait is entirely environmentally determined, equal MZ and DZ correlations are predicted; whereas if the trait is influenced by additive genetic as well as shared and non-shared environmental effects, the DZ correlation should be less than the MZ correlation, but still greater than half of the MZ correlation; and if explained only by genetic plus non-shared environmental effects, a 2:1 ratio of the DZ to MZ correlation is predicted (or a greater than 2:1 ratio if some of the genetic variance is non-additive, i.e., due to genetic dominance or epistasis).

Hypothesis testing was conducted by fitting models to summary contingency tables (for binary or

ordinal variables) by maximum likelihood, using the same methods used in structural equation modeling (Neale & Cardon, 1992). Our approach involved fitting univariate models, estimating genetic effects, shared and non-shared environmental components to two sets of $18 \times 2 \times 2$ contingency tables, one for each sex, by the method of maximum likelihood, yielding an overall Chi-square test of goodness-of-fit (MX; Neale, 1994). The goodness-of-fit of the full model, that allowed for differences in the magnitudes of influence by age group and by society, was compared by likelihood ratio Chi-square tests to submodels in which genetic and environmental components were constrained to be equivalent across age group and/or society. For example, constraining all estimates of genetic influence to be equivalent implies the hypothesis that similar magnitudes of genetic influence are responsible for smoking behavior across all three AGs in all three societies; whereas estimating all parameters of genetic influence separately across age group (but constraining estimates to be equivalent across society) implies that the magnitude of genetic influences varies by age group, but is consistent across society; and alternatively, estimating all genetic parameters separately across society (but constraining the estimates to be equivalent across age group) suggests that society (but not year of birth) is an important modifier of genetic risk.

Once the best models were chosen to explain these data in men and women, parameters were equated across sex to test for differences in the magnitude of genetic and environmental influences on the initiation and persistence of smoking behavior in the male and female twins.

Representativeness of Sampling

To test for potential sampling biases, we examined the improvement in fit obtained when threshold values were allowed to vary between MZ and DZ pairs (indicating a zygosity difference in the prevalence of smoking in MZ and DZ pairs), and between a group of “complete” twin pairs (both members participated) and a group of “incomplete” pairs (or singleton twins, where the co-twin did not to participate in the questionnaire survey) (Heath et al., 1989). If smoking was found to be more prevalent in singleton twin respondents, this would imply that the non-responding twin was also more likely to be a smoker (since smoking is highly familial), and that there was under-representation of smokers. However, because of the large sample sizes, we did not correct for threshold differences in the MZ versus DZ and the complete versus incomplete twin pairs in the genetic analyses of these data.

Equal Environments for MZ and DZ Twins

The basic genetic variance decomposition rests upon the assumption that identical twin pairs are no more highly correlated for their environmental experiences than fraternal pairs. A strong association between

twin pair concordance for smoking behavior and some environmental experience more likely to be shared by identical than fraternal twins may result in the overestimation of genetic influences. Using self-report measures of early life experiences obtained from Australian twins (i.e., how close the twins were as children across four domains of potentially shared experiences including sharing the same room, having the same playmates, being dressed alike, and being in the same classes at school) and of the frequency of contact between twins as adults, we tested the appropriateness of this assumption for smoking behavior in MZ compared with DZ pairs. Once the best genetic model to explain the data on lifetime regular smoking was determined for men and women, these models were fitted to the Australian data on lifetime regular smoking, subdivided into twin pairs with more similar experiences and those with different experiences for each of a range of early environmental variables (e.g., sharing the same friends when growing up). Similarly, data on smoking persistence were fitted to genetic models after subdividing the sample into pairs who reported seeing one another frequently (we lived together, almost every day, at least once a week), and infrequently (once or twice a month, a few times a year, less often, not at all) in 1981, the year of heaviest data collection for the 1981 Australian survey. A strong association between twin pair concordance for a substance-related behavior and the degree to which twins reported sharing experiences, by likelihood ratio Chi-square tests of heterogeneity might suggest an overestimation of the importance of genetic effects. However, such an association would also be consistent with the hypothesis that more highly similar twin pairs are more likely to seek out similar environments.

Results

Sample Characteristics

Table 1 gives the number of like-sex twin pairs from each of the three societies by sex, AG and zygosity. Smaller numbers of pairs were used in analyses on persistent smoking, which were conducted only with pairs concordant for lifetime regular smoking. As expected with twins from volunteer registries, the Australian sample, in contrast with the Swedish and Finnish samples that were identified through national registries, have more MZ than DZ pairs, and nearly twice the number of female to male twins (Lykken et al., 1987).

Epidemiologic Comparisons

Table 2 presents differences in rates of lifetime regular smoking, persistent smoking, age-of-onset of regular smoking, and among persistent smokers, rates of heavy smoking (i.e., those smoking more than 20 cigarettes per day) and the average duration of cigarette use by sex, age group, and country.

Significant associations were found between sex, age group, society, and regular and persistent

smoking. Because strong first-order interaction effects were found for all three combinations of sex, age group, and society, further comparisons were conducted stratifying on these variables.

Differences in Men and Women, by Age Group and Society

Regular Smoking

Among those 18–25 years of age, in Finland (but not Australia or Sweden), men were significantly more likely to have become regular smokers than the women (OR: 1.53, 95% CI: 1.34–1.74). However, in later adulthood, a significant discrepancy in rates of lifetime smoking was observed between the sexes in all three societies, especially in the oldest aged group (Finland: 26–35 years, OR: 3.05, 95% CI: 2.62–3.54; 36–46 years, OR: 5.79, 95% CI: 4.77–7.02; Sweden: 26–35 years, OR: 1.28, 95% CI: 1.13–1.45; 36–46 years, OR: 2.06, 95% CI: 1.79–2.37; Australia: 26–35 years, OR: 1.41, 95% CI: 1.08–1.84; 36–46 years, OR: 1.60, 95% CI: 1.09–2.35).

Persistent Smoking

Among Swedes with a lifetime history of cigarette use, women had significantly higher rates of persistent smoking than did men across all three age groups (18–25 years, OR: 0.64, 95% CI: 0.52–0.78; 26–35 years, OR: 0.60, 95% CI: 0.51–0.72; and 36–46 years, OR: 0.47, 95% CI: 0.38–0.58), and there were nonsignificant trends in the same direction among Australians. However, among ever smoking Finns, it was the men 18–25 years of age who were significantly more likely to be persistent smokers than the women (OR: 1.26, 1.02–1.56), and a nonsignificant trend in the same direction was observed in the intermediate-aged group. Only in Finns from the oldest age group was a trend observed for higher rates of persistent smoking in the women compared with men.

Controlling for heavy cigarette use (20 or more cigarettes per day) and age onset of regular smoking, evidence for male–female differences for smoking persistence remained the same in most cases, with two exceptions: (1) the small difference in rates of persistent smoking among Finnish male and female lifetime smokers surveyed at 18–25 years of age (78% vs. 75%, respectively) became nonsignificant, and (2) evidence for lower rates of smoking cessation among Australian women than men, 36–46 years of age, became significant (OR: 0.54, 95% CI: 0.30–0.97). These findings suggest that discrepancies in rates of quitting cigarettes in men and women, especially those from Sweden, may not be entirely due to differences in lifetime patterns of heavy smoking or in age of initiation of regular cigarette use.

Crosscultural Comparisons, by Sex and Age Group

Regular Smoking

Among women surveyed in early adulthood, aged 18–25, the Australians were significantly less likely

Table 2Sample Characteristics by Sex, Age Group, and Country^a

	Women			Men		
	Age Groups			Age Groups		
	Youngest (18–25 yrs)	Intermediate (26–35 yrs)	Oldest (36–46 yrs)	Youngest (18–25 yrs)	Intermediate (26–35 yrs)	Oldest (36–46 yrs)
Numbers of Individuals						
Australia	1194	1296	739	714	630	288
Finland	4063	3280	2184	3674	3366	2418
Sweden	3711	4519	3651	3400	3773	2936
Mean Age (\pm SD)						
Australia	21 (\pm 2)	30 (\pm 3)	41 (\pm 3)	21 (\pm 2)	31 (\pm 3)	40 (\pm 3)
Finland	21 (\pm 2)	30 (\pm 3)	41 (\pm 3)	21 (\pm 2)	30 (\pm 3)	41 (\pm 3)
Sweden	22 (\pm 2)	30 (\pm 3)	41 (\pm 3)	22 (\pm 2)	30 (\pm 3)	41 (\pm 3)
Mean Age Onset of Regular Smoking (\pm SD)						
Australia	15 (\pm 2)	18 (\pm 3)	19 (\pm 4)	15 (\pm 3)	17 (\pm 5)	17 (\pm 4)
Finland	17 (\pm 2)	19 (\pm 3)	23 (\pm 6)	16 (\pm 2)	18 (\pm 3)	19 (\pm 4)
Sweden	16 (\pm 2)	18 (\pm 3)	21 (\pm 5)	16 (\pm 2)	17 (\pm 3)	19 (\pm 4)
Mean Years Smoked (\pm SD) (Among Persistent Smokers)						
Australia	6 (\pm 2)	12 (\pm 4)	22 (\pm 5)	7 (\pm 3)	14 (\pm 4)	23 (\pm 6)
Finland	5 (\pm 2)	10 (\pm 4)	17 (\pm 6)	5 (\pm 3)	12 (\pm 4)	21 (\pm 5)
Sweden	5 (\pm 3)	12 (\pm 4)	20 (\pm 6)	6 (\pm 3)	13 (\pm 4)	22 (\pm 5)
% Lifetime Regular Smokers (LRS)						
Australia	43%	45%	42%	42%	51%	57%
Finland	49%	40%	24%	59%	65%	67%
Sweden	58%	55%	40%	57%	61%	57%
% Persistent Smokers (Among LRS)						
Australian	74%	61%	58%	69%	56%	48%
Finland	75%	66%	66%	78%	68%	61%
Sweden	78%	73%	72%	71%	63%	55%
Heavy Smokers (20+ Cigarettes per Day: Among Persistent Smokers)						
Australia	36%	48%	57%	41%	57%	77%
Finland	9%	15%	15%	24%	41%	45%
Sweden	12%	17%	16%	20%	28%	32%

Note: ^aIncludes twins whose cotwin did not participate in the survey.

(OR: 0.82, 95% CI: 0.68–0.99), but the Swedish (OR: 1.44, 95% CI: 1.27–1.64) significantly more likely, than the Finnish to have a history of regular smoking. However, by later adulthood, from 26 years onward, women from both Australia and Sweden had significantly higher rates of lifetime regular smoking than did women from Finland (Australia: 26–35 years, OR: 1.29, 95% CI: 1.08–1.56, and 36–46 years, OR: 2.38, 95% CI: 1.85–3.06; Sweden: 26–35 years, OR: 1.94, 95% CI: 1.70–1.22, and 36–46 years, OR: 2.09, 95% CI: 1.76–2.48).

A different story was observed in the men: Finnish men of all ages had significantly higher rates of lifetime smoking than did men from Australia (18–25 years, OR: 0.48, 95% CI: 0.38–0.60; 26–35 years, OR: 0.60, 95% CI: 0.47–0.76; and 36–46 years, OR: 0.66, 95% CI: 0.47–0.93) or did men more than 25

years of age from Sweden (26–35 years, OR: 0.82, 95% CI: 0.71–0.94; 36–46 years, OR: 0.74, 95% CI: 0.63–0.87), and there was a nonsignificant trend in this same direction compared to Swedish men in early adulthood, aged 18–25 years (OR: 0.94, 95% CI: 0.82–1.08).

Persistent Smoking

Among lifetime smokers, across all age groups, men from Australia and Sweden were less likely than were men from Finland to be smoking at the time of survey (Australia: 18–25 years, OR: 0.59, 95% CI: 0.40–0.87; 26–35 years, OR: 0.52, 95% CI: 0.38–0.73; and 36–46 years, OR: 0.60, 95% CI: 0.38–0.95; and Sweden: 18–25 years, OR: 0.60, 95% CI: 0.49–0.73; 26–35 years, OR: 0.75, 95% CI: 0.63–0.90; and 36–46 years, OR: 0.77, 95% CI: 0.63–0.94).

The story in women was more complex. There were no significant crosscultural differences observed in rates of persistent smoking among female lifetime smokers 18–25 years of age. However, among those with a history of smoking surveyed between 26 and 35 years of age, Australian women were observed to have lower rates of continued smoking compared with the Finnish (OR: 0.73, 95% CI: 0.55–0.98), while the Swedish were observed to have significantly higher rates of persistent smoking than the Finnish throughout later adulthood (26–35 years, OR: 1.42, 95% CI: 1.15–1.76; 36–46 years, OR: 1.42, 95% CI: 1.04–1.94).

Controlling for heavy cigarette use and age at onset of regular smoking did not change the results of any crosscultural comparison in men or women, suggesting that societal differences in smoking persistence may not be due to the widely differing rates of lifetime heavy smoking or in average age-of-onset of regular smoking observed across countries.

Age Group Differences, by Sex and Society

Regular Smoking

Age at survey was a significant predictor of rates of lifetime smoking in Scandinavian, but not in Australian women. Finnish women 18–25 years of age, and Swedish women 18–35 years of age had significantly higher rates of lifetime smoking than did women from these countries surveyed in later adulthood (Swedish: 36–46 years, OR: 0.49, 95% CI: 0.43–0.56; Finnish: 26–35 years, OR: 0.66, 95% CI: 0.58–0.76; and 36–46 years, OR: 0.34, 95% CI: 0.28–0.40). By contrast, in both the Finnish and the Australian (but not Swedish) men, rates of smoking were significantly higher in the intermediate and the oldest aged groups than among men 18–25 years of age (Australian, 26–35 years, OR: 1.66, 95% CI: 1.23–2.24, and 36–46 years, OR: 1.77, 95% CI: 1.21–2.61; Finnish, 26–35 years, OR: 1.32, 95% CI: 1.14–1.52, 36–46 years, OR: 1.28, 95% CI: 1.09–1.50).

Persistent Smoking

Not surprisingly, among ever smoking men, across all societies, rates of continued smoking were significantly lower among those in the intermediate and the oldest age groups, who had a longer history of cigarette use, than in men between 18 and 25 years of age (Finland: 26–35 years, OR: 0.57, 95% CI: 0.46–0.69; 36–46 years, OR: 0.40, 95% CI: 0.32–0.50; and Australia: 26–35 years, OR: 0.50, 95% CI: 0.32–0.79; 36–46 years: OR: 0.41, 95% CI: 0.23–0.71; Sweden: 26–35 years, OR: 0.71, 95% CI: 0.59–0.85; 36–46 years: OR: 0.51, 95% CI: 0.42–0.62); and a similar pattern was observed in the women. Among Finnish female ever smokers, rates of persistent smoking were significantly lower in those surveyed between 26 and 35 years (OR: 0.66, 95% CI: 0.58–0.76) and 36–46 years of age (OR: 0.34, 95% CI: 0.28–0.40), than in those

surveyed between 18 and 25 years of age, and this was also true for female Swedish lifetime smokers 36–46 years (but not 26–35 years of age; OR: 0.49, 95% CI: 0.43–0.56). Although the results were not significant, a similar decrease in rates of smoking persistence was found in Australian and Swedish women aged 18–25 years to those 26–35 years with a history of regular cigarette use.

Similar to our previous findings for smoking persistence, controlling for heavy cigarette use and age-of-onset of regular smoking did not alter these results, suggesting that discrepancies in rates of smoking persistence among regular smokers in early versus later adulthood may not be entirely accounted for by differences in the proportions of lifetime heavy smokers or by cohort differences in average age-of-onset of regular smoking.

Representativeness of Sampling

Before conducting genetic analyses we tested for differences in rates of lifetime regular smoking and of persistent smoking by zygosity status (see Figures 1a–1d).

DZ prevalences tended to be larger than MZ for lifetime regular smoking across age group and society in men and in women. Consistent with this observation, a model where thresholds in MZ and DZ twins were constrained to be equivalent provided a significantly worse fit to these data than did a model where thresholds were estimated separately (women: $\chi^2 = 27.15$, $df = 9$, $p = 0.001$; men: $\chi^2 = 23.25$, $df = 9$, $p = .01$).

There were also prevalence differences in MZ and DZ twins for persistent smoking in women and in men, as shown in Figures 1c–1d, respectively. However, unlike for lifetime regular smoking, there was no evidence of a consistent pattern in DZ versus MZ rates of smoking persistence. Models where thresholds in MZ and DZ twins were constrained to be equivalent provided a significantly worse fit to data in the men ($\chi^2 = 20.54$, $df = 9$, $p = .01$), but not the women ($\chi^2 = 13.73$, $df = 9$, $p = .13$). In all subsequent analyses, separate thresholds were estimated for each zygosity group.

Prevalences for lifetime and persistent smoking were higher in the incomplete than the complete pairs of twins (see Figures 2a–2d). Consistent with this observation, models where thresholds in the complete and incomplete pairs were constrained to be equivalent provided significantly worse fits to these data for lifetime regular smoking in men and women from each society (women — Australian: $\chi^2 = 9.11$, $df = 3$, $p < .05$; Finnish: $\chi^2 = 23.76$, $df = 3$, $p < .001$; Swedish: $\chi^2 = 15.37$, $df = 3$, $p < .01$; men — Australian: $\chi^2 = 13.01$, $df = 3$, $p < .01$; Finnish: $\chi^2 = 20.12$, $df = 3$, $p < .001$; Swedish: $\chi^2 = 29.38$, $df = 3$, $p < .001$), and the findings for persistent smoking were similar. This implies that there has been significant undersampling of smokers in the three samples.

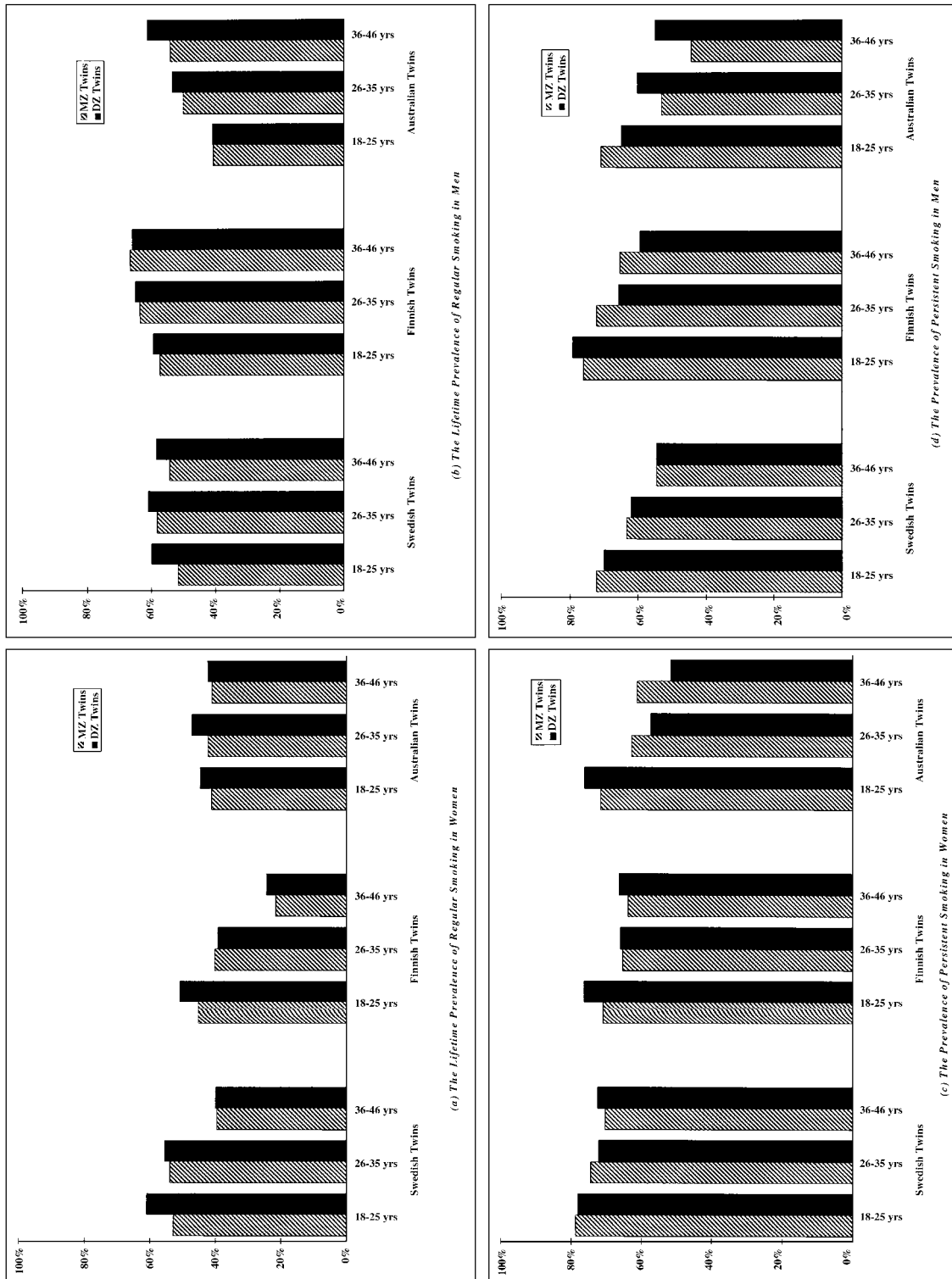


Figure 1 MZ and DZ prevalence estimates by country and age group for lifetime regular smoking in (a) women, and (b) men; and for persistent smoking in (c) women, and (d) men.

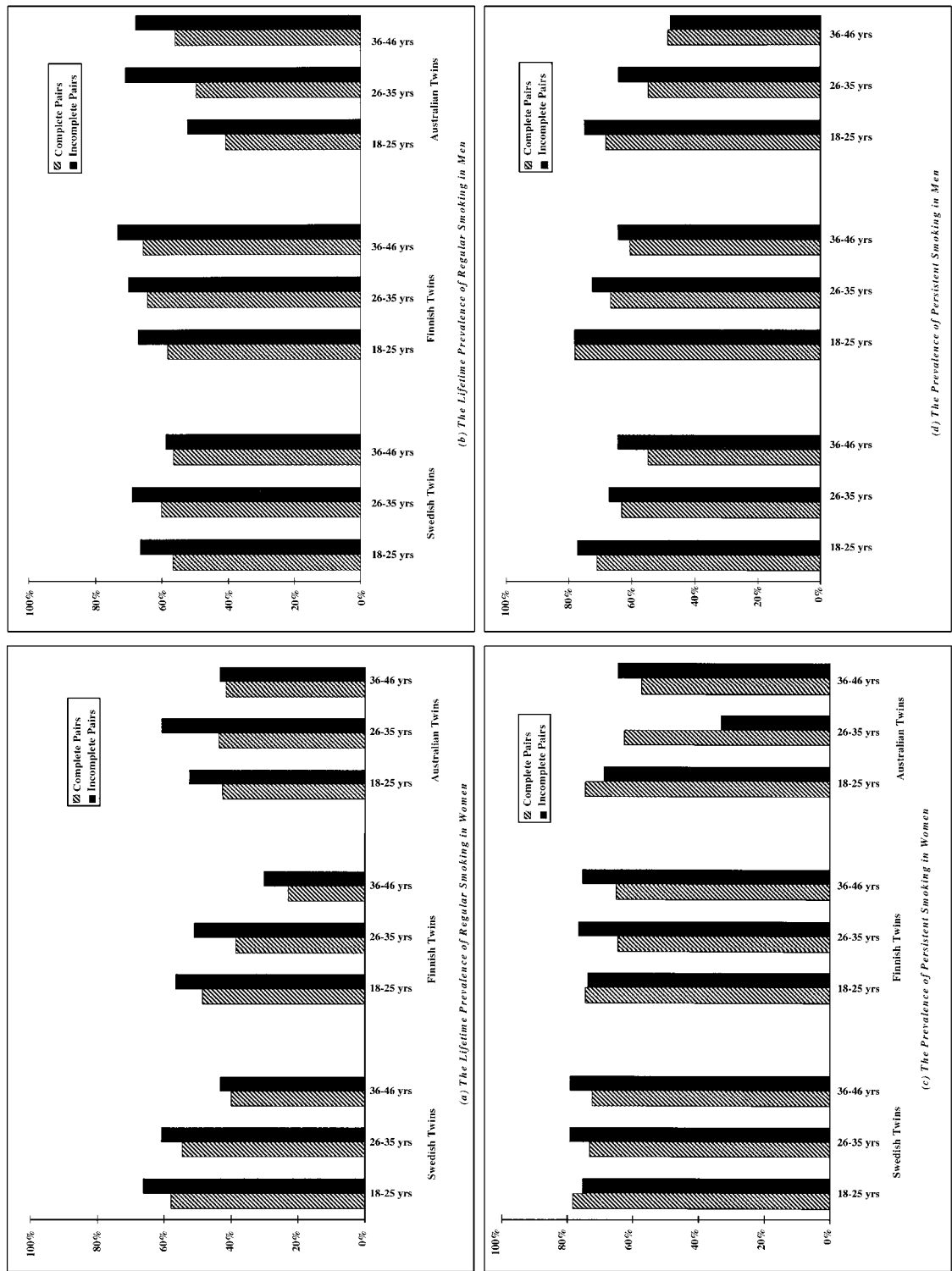


Figure 2 Prevalence estimates in the complete and incomplete pairs of twins by country and age group for lifetime regular smoking in (a) women, and (b) men; and for persistent smoking in (c) women, and (d) men.

Genetic Influences on the Initiation of Regular Smoking

The top half of Table 3 presents maximum likelihood estimates of twin tetrachoric correlations for the onset of regular smoking by country, age group, sex, and zygosity. Across all countries and AGs (except for the Australian women in the 25–36 AG) the DZ correlation in men and women was more than one half of the corresponding MZ correlation, consistent with the hypothesis that family resemblance for the initiation of regular smoking was determined by both additive genetic and shared environmental influences. Consistent with these observations, a model allowing for additive genetic, shared and unshared environmental influences, where these parameters were estimated separately by AG and country, provided a good fit to these data in both men ($\chi^2 = 17.40$, $df = 18$, $p = .50$) and in women ($\chi^2 = 13.66$, $df = 18$, $p = .75$) by Chi-square goodness-of-fit criteria; while a model including additive, non-additive genetic influences (i.e., due to genetic dominance or epistasis) and unshared environmental influences gave quite a poor fit (men: $\chi^2 = 93.29$, $df = 18$, $p < .001$; women: $\chi^2 = 170.62$, $df = 18$, $p < .001$). Therefore, all further genetic analysis of these data on the initiation of regular smoking used a full model that included

parameters to estimate shared environmental plus additive genetic effects.

Despite the wide variation in prevalence, and ages-of-onset by society and by age group, model-fitting analyses determined that the magnitude of estimated additive genetic effects did not differ significantly by country or AG, and the magnitude of shared environmental effects differed only by AG in men and women.

In women, a model with additive genetic parameter estimates constrained across country and AG did not provide a significantly worse fit to the data compared to the full model where these parameters were estimated separately in Swedish, Finnish and Australian women by AG ($\chi^2 = 12.85$, $df = 8$, $p = .12$), nor did the model constraining shared environmental parameter estimates within age groups across country ($\chi^2 = 10.38$, $df = 6$, $p = .11$). However, compared to the full model, significantly worse fits to the data were obtained in models where shared environmental estimates were either constrained to be equivalent across country and AG ($\chi^2 = 26.25$, $df = 8$, $p < .001$), or were estimated separately by country but constrained to be equal by age group ($\chi^2 = 16.27$, $df = 6$, $p = .01$).

The best-fitting model in women allowed for additive genetic estimates that were equivalent for all three countries and for all three AGs, and shared

Table 3

Twin Pair Tetrachoric Correlations (SE) for Lifetime Regular and Persistent Smoking by Country, Age Group, and Gender

	Women			Men		
	Sweden (1973) <i>r</i> (SE)	Finland (1975) <i>r</i> (SE)	Australia (1980–81) <i>r</i> (SE)	Sweden (1973) <i>r</i> (SE)	Finland (1975) <i>r</i> (SE)	Australia (1980–81) <i>r</i> (SE)
Lifetime Regular Smoking						
Youngest Age Group (18–25 Yrs)						
MZ Twins	.91 (0.02)	.92 (0.02)	.86 (0.03)	.91 (0.02)	.87 (0.03)	.81 (0.06)
DZ Twins	.67 (0.03)	.72 (0.03)	.65 (0.07)	.58 (0.04)	.66 (0.03)	.61 (0.09)
Intermediate Age Group (26–35 Yrs)						
MZ Twins	.80 (0.03)	.79 (0.04)	.86 (0.03)	.85 (0.02)	.90 (0.02)	.66 (0.08)
DZ Twins	.58 (0.03)	.63 (0.04)	.40 (0.09)	.52 (0.04)	.54 (0.04)	.41 (0.14)
Oldest Age Group (36–46 Yrs)						
MZ Twins	.75 (0.03)	.79 (0.06)	.72 (0.06)	.72 (0.04)	.78 (0.05)	.63 (0.12)
DZ Twins	.43 (0.04)	.53 (0.06)	.40 (0.13)	.45 (0.05)	.57 (0.05)	.56 (0.19)
Persistent Smoking^a						
Youngest Age Group (18–25 Yrs)						
MZ Twins	.47 (0.09)	.53 (0.09)	.44 (0.15)	.62 (0.08)	.60 (0.08)	.46 (0.20)
DZ Twins	.40 (0.07)	.24 (0.08)	.52 (0.20)	.25 (0.08)	.41 (0.07)	.22 (0.25)
Intermediate Age Group (26–35 Yrs)						
MZ Twins	.67 (0.06)	.66 (0.09)	.37 (0.13)	.44 (0.08)	.54 (0.09)	.51 (0.16)
DZ Twins	.32 (0.07)	.36 (0.10)	.44 (0.17)	.08 (0.07)	.09 (0.07)	.39 (0.25)
Oldest Age Group (36–46 Yrs)						
MZ Twins	.49 (0.10)	.44 (0.22)	.43 (0.18)	.45 (0.09)	.53 (0.11)	.80 (0.14)
DZ Twins	.19 (0.11)	.10 (0.19)	.11 (0.30)	.26 (0.08)	.28 (0.08)	-.22 (0.37)

Note:^a Among lifetime smokers.

environmental estimates that varied by AG but otherwise were the same in women from Sweden, Finland and Australia ($\chi^2 = 32.86, df = 32, p = .43$). Under the best model a substantial proportion of the variance in risk of becoming a regular smoker in women from all countries was determined by additive genetic influences (46%, see Table 4). Familial influence due to environmental circumstances shared by a female and her co-twin also played an important role in the onset of regular smoking (from the youngest to the oldest AG: 45%, 35%, and 26%). The importance of shared environmental influences on becoming a regular smoker increased from the oldest to the youngest AG; that is, the effect of experiences shared by twin and co-twin was found to be larger in those who responded to the questionnaire surveys at younger ages, who also reported earlier ages-of-onset for regular smoking.

In men, the results were not as straightforward. Both the model with additive genetic estimates constrained across country and AG, and the model with shared environmental estimates constrained in the same way, provided good fits to the data compared to the full model where these parameters were estimated separately in Swedish, Finnish and Australian men by AG (additive genetic model: $\chi^2 = 11.86, df = 8, p = .16$; shared environmental model: $\chi^2 = 11.86, df = 8, p = 0.16$). However, constraining additive genetic and shared environmental parameter estimates across country and AG together in the same model provided a significant deterioration in fit (vs. full model: $\chi^2 = 64.04, df = 16, p < .001$). Therefore, in men, two models were found to be equally parsimonious and consistent with the data. One model allowed for additive genetic estimates that were equivalent for all three countries and AGs, and shared environmental estimates that varied by AG and estimated separately for men from the Scandinavian countries (Sweden and Finland) and from Australia (vs. the full model: $\chi^2 = 16.54, df = 11, p = .12$); and another model with the expectations for the genetic and shared environmental influences reversed, so that shared environmental estimates were constrained across all countries and AGs, and the genetic parameters estimated separately by AG in the Scandinavian and

Australian men (vs. the full model: $\chi^2 = 16.08, df = 11, p = .14$). Because there is no reason to expect that sources of genetic variation for smoking behavior differ more in men than women, the former model was chosen to represent the determinants of smoking in men.

In men, findings under the best model suggest that a substantial proportion of the variance in risk of becoming a regular smoker in the Swedish, Finnish, and the Australian twins was determined by additive genetic influences (57%, see Table 4). Familial influence due to environmental experiences shared by a male and his co-twin also played an important role in the onset of regular smoking (Australian men, from the youngest to the oldest AG: 26%, 9%, and 11%; Scandinavian men: 33%, 29%, and 19%). As in the women, the importance of shared environmental influences on becoming a regular smoker increased in the twins from the oldest to the youngest AG.

A joint analysis of data from men and women was conducted to determine whether the magnitude of estimated additive and shared environmental effects differed significantly by sex. The model with genetic estimates constrained across sex, country and AG was found to provide a significantly worse fit to these data than did the model where these parameters were estimated separately by sex ($\chi^2 = 4.29, df = 1, p = .04$). Similarly, the model with shared environmental parameter estimates constrained to be equivalent across sexes by AG provided a significant worsening of fit to the data compared to the full model where parameters were estimated separately for men and women ($\chi^2 = 9.93, df = 3, p = .02$), and this remained true when the magnitude of the shared environmental influences were estimated separately in the Scandinavian and the Australian twins ($\chi^2 = 13.46, df = 6, p = .04$).

Genetic Influences on Persistent Smoking

Twin tetrachoric correlations for persistent smoking are presented on the bottom half of Table 3. The standard errors on the twin correlations are quite large, especially those in the Australian samples and in the oldest age group (across country and gender) which

Table 4

Estimates (and 95% Confidence Intervals) of the Genetic and Environmental Variance Components for Lifetime Regular Smoking by Gender, Age Group, and Country

	Additive Genetic Variance	Shared Environmental Variance		
	(18–46 yrs) % (95% CI)	(18–25 yrs) % (95% CI)	(26–35 yrs) % (95% CI)	(36–45 yrs) % (95% CI)
Women				
All three countries	46 (40–53)	45 (40–53)	35 (29–41)	26 (19–32)
Men				
Australia	57 (49–64)	26 (14–36)	9 (0–23)	11 (0–28)
Scandinavia	57 (49–64)	33 (26–40)	29 (22–35)	19 (12–27)

have substantially smaller numbers of smokers compared with the other samples.

Despite large differences in rates of continued smoking among lifetime smokers, model-fitting analyses determined that the magnitude of estimated genetic or environmental effects did not differ by country, AG, or by sex. Models with all parameters constrained to be equivalent did not provide a significantly worse fit compared to the full model where parameters were estimated separately in Swedish, Finnish, and Australian men and women by AG. This was true under a model that specified additive and non-additive genetic and unshared environmental influences ($\chi^2 = 34.08$, $df = 34$, $p = .46$), and under a model that assumed additive genetic, shared and unshared environmental effects ($\chi^2 = 31.82$, $df = 34$, $p = .57$). Dropping the shared environmental parameter ($\chi^2 = 0.00$, $df = 1$, $p = 1.00$), or the non-additive genetic parameter ($\chi^2 = 0.42$, $df = 1$, $p = .52$) from these models did not produce a significant change in fit, while a model that only allowed for environmental influences, gave a significantly worse fit to these data ($\chi^2 = 66.12$, $df = 1$, $p < .001$). A substantial proportion of the variance in persistent smoking in both men and women was determined by additive genetic influences (52%, 95% CI: 47–56%) and the rest by environmental influences that were not shared by co-twins (48%, 95% CI: 44–53%).

Effects of Childhood and Adult Environments

The percentage of female Australian pairs who endorsed having the same childhood experiences was observed to range from 48 to 89% among the identical twins, with lower estimates, 19 to 83%, found among the fraternal twins (no comparable data were available for the Scandinavian pairs). A similar trend was observed in the Australian males (MZ: 29 to 84%; DZ: 8 to 75%). A significant association was found only between concordance for becoming a smoker and the degree to which female (but not male) twins reported sharing peers as children by likelihood-ratio Chi-square tests of heterogeneity

($\chi^2 = 10.16$, $df = 4$, $p = .04$). Table 5 displays the tetrachoric correlations for female twins by exposure condition with respect to shared peers. As shown, in contrast with the DZ correlation for twins with “different peers”, the DZ correlation for twins with “same peers” was notably more than one half of the MZ correlation, suggesting a larger role for shared environmental influences for twins with similar experiences. When genetic models were fitted to these data by maximum likelihood (Neale & Cardon, 1992) a nonsignificant reduction of the estimate of the genetic contribution to smoking initiation was found in female twins reporting to have shared the “same peers” as children (same peers: 41%, 95% CI: 14–72% vs. different peers: 59%, 95% CI: 16–81%). Estimates of the proportion of the variance in the initiation of regular smoking due to shared environmental influences was observed to increase (same peers, in the oldest to the youngest AG respectively: 32%, 49%, 48% versus different peers: 0%, 8%, 24%), with this increase significant in the 25–36 AG (same peers: 49%, 95% CI: 18–73% versus different peers: 8%, 95% CI: 0–44%). These results raise the question of whether higher correlations for lifetime smoking in MZ twin pairs is partially the consequence of influence from shared peers on smoking behavior, or alternatively, that choice of peer is partly influenced by genetic factors. Evidence for a genetic influence on smoking initiation remained even when the similarity of early experiences between twins was controlled for.

Although twins who were smoking at the time of survey reported spending more time in the company of their co-twin than did the ex-smokers (women: 65% vs. 35%, men: 56% vs. 45%, respectively), a significant association was not found between persistence in smoking and closeness with co-twin as an adult ($p > .05$). This finding is consistent with model-fitting results for persistence in smoking, where little evidence was found for an important role for environmental influences shared by co-twins.

Table 5

Twin Pair Tetrachoric Correlations (SE) for Lifetime Smoking in Australian Twins Conditional on Shared Peers as Children

	Youngest Age Group (18–25 yrs) <i>r</i> (95% CI)	Intermediate Age Group (26–35 yrs) <i>r</i> (95% CI)	Oldest Age Group (36–46 yrs) <i>r</i> (95% CI)
Same Peers			
MZ	.86 (0.77–0.93)	.90 (0.83–0.95)	.73 (0.56–0.85)
DZ	.81 (0.61–0.93)	.57 (0.29–0.77)	.47 (0.07–0.76)
Different Peers			
MZ	.83 (0.58–0.95)	.67 (0.36–0.86)	.65 (0.15–0.91)
DZ	.54 (0.24–0.76)	.38 (0.10–0.62)	.17 (–0.32–0.60)

Discussion

The purpose of this study was to examine the extent to which differences by culture, age and sex may modify risk of becoming a smoker and of smoking persistence. Genetic analyses were conducted on mailed questionnaire data obtained from surveys of large numbers of Swedish, Finnish and Australian same-sex adult male and female twins 18 and 46 years of age.

Despite substantial differences in prevalence, we found the magnitude of the genetic influence on lifetime regular smoking to be consistent across country and age group, although there was a small but significant difference in women and men (for women: 46%, 95% CI: 40–53%; and for men: 57%, 95% CI: 49–64%). The contribution to risk of becoming a regular smoker from shared environmental experiences that vary between families within a society (which would include exposure to familial smoking behaviors and attitudes) was found to increase from the oldest to the youngest age groups, to play a larger role in the onset of regular smoking in women (26%, 35%, and 45%; from oldest to youngest AG, respectively) than men; and in men to be greater in the Scandinavian (19%, 29%, and 33%) than the Australian (11%, 9%, and 26%) twins. Since younger age groups also on average reported earlier onset of regular smoking, our findings suggest that the importance of shared environmental influences on becoming a smoker is greater for those with an earlier age-of-onset for regular smoking.

A critical assumption in twin studies is that MZ twins are no more likely to share environmental experiences than are DZ twins. Consistent with the findings of Kendler and Gardner (1998) in a sample of US adult female twins, a strong association was found between twin concordance for becoming a smoker and the degree to which Australian twins reported sharing peers as children. These findings might imply that genetic influences are overestimated in analyses where the confounding effects of peer exposure remain unaccounted for. On the other hand, the influence of peers may play a smaller role in causing the onset of regular smoking than might be inferred by these results if peers are selected in part because of their predisposition to substance use. A strong resemblance among peers for substance use behavior has been supported by epidemiologic data. Kandel (1978, 1985) has noted that aside from sociodemographics (e.g., sex, age, etc.), adolescent peers are more similar with respect to drug use behaviors than on most other attributes, including self-report values (e.g., political or academic), and psychological traits (e.g., depressed mood). Results of longitudinal research on the similarity of peers for smoking behavior suggests an important role for selective friendship (i.e., peer relations are a consequence of behavioral likeness). Compatible with these findings, controlling for the influence of shared peers,

we found that a substantial genetic influence on becoming a smoker remained, indicating that exposure to cigarette use in peers cannot entirely explain the higher MZ than DZ twin pair concordances for the onset of regular smoking observed in these Australian female twins. However, a study of families ascertained from the general population that includes pairs of adolescent siblings and information on their peers is needed to properly evaluate the extent to which the initiation of substance use is due to socializing with peers outside of the family versus within-individual causes (Madden et al., 1999).

Unlike Heath et al. (1993), we did not find significant crosscultural differences in the magnitude of genetic influences on risk of becoming a smoker. However, their report focused on similarities in the Australian versus the US twins, instead of twins from Scandinavian countries, and their US sample included a large proportion of older twins (who were recruited from the American Association of Retired Persons). We found sex differences in the estimate of genetic influence for onset of regular smoking. However, given the large sample sizes and a borderline *p*-value of .04, our conclusion that genetic influences are less important in women than men must be considered tentative. The inconsistencies between these two studies may be an artifact of sampling and of differences in approach to data analysis. We separated our samples into three groups of twins by age cohorts (18–25, 26–35, and 36–45 years of age) and tested for group heterogeneity by combining data obtained from all three countries; while, Heath et al. (1993) used birth cohorts that only partially overlapped by country, and cohort differences were tested separately by country and sex using smaller subsamples of twins.

Persistence in smoking was found to run in families, and our results suggest that familial transmission was primarily due to biological predisposition, with up to 52% (95% CI: 47–56%) of the variance in smoking persistence in both women and men from all countries and AGs due to additive genetic influences. This is consistent with previous reports of high heritability of smoking persistence in most (though not all) major twin studies (Heath & Madden, 1995; Heath et al., 1998). The absence of heterogeneity in the magnitude of genetic influence for persistent smoking is notable given the widely differing rates, by country and by sex, of two indicators of nicotine dependence, heavy smoking (i.e., 20 or more cigarettes per day) and number of years smoked. In epidemiologic analyses of these data, no evidence was found to suggest that either a lifetime history of heavy smoking or age-of-onset of regular smoking accounted for differences in rates of quitting cigarettes by country, or by age group. Differences in lifetime patterns of cigarette use were only important predictors of discrepancies in rates of continued smoking between men and women in the youngest aged group, among Finns, and in the oldest aged group among Australians.

In contrast with the initiation of regular smoking, there was little evidence that environmental experiences shared by co-twins as adults played an important role in the maintenance of cigarette use (the upper limit to the 95% Confidence Interval for the estimate of the variance in smoking cessation due to shared environmental experiences was only 7%)! Despite higher rates of social contact as adults between Australian twins concordant for continued smoking versus other pairs of twins (women: 65% vs. 35%; men: 56% vs. 45%), a significant association was not found between concordance for persistent smoking and frequency with which co-twins spent time in one another's company.

When interpreting the results of this study, several potential limitations should be borne in mind. The assessments of smoking behavior were obtained by retrospective self-report, and our findings are limited by the accuracy of these data, which may be affected by the subject's ability to recall past events. Second, across all three societies the prevalence of lifetime and persistent smoking in men and women was higher in twins whose co-twin chose not to participate than in pairs where both twins responded to the questionnaire survey. Since smoking is familial, the non-responding co-twins were more likely to have a history of smoking than the randomly chosen twin, indicating that smokers may have been undersampled. Third, we have ignored the issue of censored data for smoking persistence, which would be most relevant in the youngest group of twins (18–25 years of age), who on average had smoked for fewer years than twins from the 26–35 or the 36–46 AGs. Advanced statistical methods can be implemented for the genetic analysis of censored data (e.g., Meyer et al., 1991), but these are beyond the scope of the present paper. Fourth, we did not examine the effects of assortative mating on the genetic and environmental estimates derived from these data. If smokers in the parental generation were more likely to marry smokers than non-smokers, as suggested in the work led by Kaprio (1995), and that by Boomsma (1994), the estimated contribution of familial influences from environmental effects shared between family members would be over-estimated and the genetic influences underestimated in twin data (see Neale & Cardon, 1992). This is less of a concern for persistence in smoking, where little evidence was found to suggest an important role for environmental experiences shared by family members. However, in the case of lifetime smoking, we cannot exclude the possibility that the importance of assortative mating by parents for smoking behavior has increased over the birth cohorts examined in this study, and thus is contributing to the apparent increase in the importance of shared environmental effects in more recent cohorts. Last, in the analyses reported in this paper, we used the simplifying assumption of independence of genetic and environmental effects on smoking initiation versus persistence. In a separate

paper (Madden et al., 1999), we allow for correlated genetic and environmental influences on smoking initiation and persistence.

In summary, consistent with most reports on the genetics of cigarette use, we found smoking behavior to run in families. Interestingly, comparably strong genetic contributions to risk of becoming a smoker were observed across country and age group, even in twins born nearly 30 years apart. Contrary to expectation, we did not find a decreased prevalence of smoking to be associated with either increased or decreased genetic contribution to either the onset or persistence of smoking in men or women. The stability of estimates for the genetic contribution to both onset and persistence of smoking suggests that, despite differences in overall rates of smoking, the transmission of smoking behavior in men and women is in large part due to genetic factors that, for the birth cohorts and societies studied here, have not been modified by culture or by societal forces influencing the availability or the allure of cigarettes. However, to further test this hypothesis, it would be informative to study data on smoking behavior obtained from samples of twins from the same country assessed at similar ages in the 1970s (or 1980s) and again in the 1990s (i.e., over a period when tobacco control policies; restrictions on advertising, health warnings on the hazards of smoking, etc.) have become increasingly employed in many countries (WHO, 1996).

Acknowledgments

Supported by NIH Grants DA00272, DA12854, and DA12540 (to PAFM), CA75581, AA07535, and AA07728, by grants from the Alcohol Beverage and Medical Research Foundation (to PAFM), the Swedish Council for Planning and Coordination of Research 970763:4 (to NLP), the Australian NH & MRC 941177 (to NGM), and support from the Academy of Finland (to JK and MJK).

The authors would like to acknowledge the support of the Australian, the Finnish, and the Swedish Twin Registries, and to thank Andrew Heath, D.Phil, and Kathleen K. Bucholz, PhD, for statistical advice and helpful comments.

References

- Boomsma, D. I., Koopmans, J. R., Van Doornen, L. J. P., & Orlebeke, J. F. (1994). Genetic and social influences on starting to smoke: A study of Dutch adolescent twins and their parents. *Addiction*, 89, 219–226.
- Carmelli, D., Swan, G. E., Robinette, D., & Fabsitz, R. R. (1990). Heritability of substance use in the NAS-NRC twin registry. *Acta Geneticae Medicae et Gemellologiae*, 39, 91–98.
- Carmelli, D., Swan, G. E., Robinette, D., & Fabsitz, R. (1992). Genetic influence on smoking — A study of

- male twins. *The New England Journal of Medicine*, 327, 829–883.
- Cederöf, R., Friberg, L., Jonsson, E., & Kaij, L. (1961). Studies on similarity diagnosis in twins with the aid of mailed questionnaire. *Acta Genetica et Statistica Medica*, 1, 338–362.
- Crumpacker, D. W., Cederlöf, R., Friberg, L., Kimberling, W. J., Sorensen, S., Vandenberg, S. G., et al. (1979). A twin methodology for the study of genetic and environmental control of variation in human smoking behavior. *Acta Geneticae Medicae et Gemellologiae*, 28, 173–195.
- Doll, R., Gray, R., Hafner, B., & Peto, R. (1980). Mortality in relation to smoking: 20 years' observations in female British doctors. *British Medical Journal*, 280, 967–971.
- Doll, R., & Peto, R. (1976). Mortality in relation to smoking: 20 years' observations on male British doctors. *British Medical Journal*, 2, 1525–1536.
- Eaves, L. J., & Eysenck, H. J. (1980). The genetics of smoking. In H. J. Eysenck (Ed.), *The causes and effects of smoking*. London: Temple-Smith.
- Eaves, L. J., Eysenck, H. J., & Martin, N. G. (1989). *Genes, culture and personality*. London: Academic Press.
- Edwards, K. L., Austin, M. A., & Jarvik, G. P. (1995). Evidence for genetic influences on smoking in adult women twins. *Clinical Genetics*, 47, 236–244.
- Grunberg, N. E., Winders, S. E., & Wewers, M. E. (1991). Gender differences in tobacco use. *Health Psychology*, 10, 143–153.
- Han, C., McGue, M. K., & Iacono, W. G. (1999). Lifetime tobacco, alcohol and other substance use in adolescent Minnesota twins: Univariate and multivariate behavioral genetic analyses. *Addiction*, 94, 981–993.
- Hannah, M. C., Hopper, J. L., & Mathews, J. D. (1985). Twin concordance for a binary trait. II. Nested analysis of ever-smoking and ex-smoking traits and unnested analysis of a “committed-smoking” trait. *American Journal of Human Genetics*, 37, 153–165.
- Heath, A. C. (1990). Persist or quit? Testing for a genetic contribution to smoking persistence. *Acta Geneticae Medicae et Gemellologiae*, 39, 447–458.
- Heath, A. C., Cates, R., Martin, N. G., Meyer, J., Hewitt, J. K., Neale, M. C., et al. (1993). Genetic contribution to risk of smoking initiation: Comparisons across birth cohorts and across cultures. *Journal of Substance Abuse*, 5, 221–246.
- Heath, A. C., & Madden, P. A. F. (1995). Genetic influences on smoking behavior. In J. R. Turner, L. R. Cardon, & J. K. Hewitt (Eds.), *Behavior genetic approaches in behavioral medicine* (pp. 45–66). New York, NY: Plenum Publishing Corporation.
- Heath, A. C., Madden, P. A. F., & Martin, N. G. (1998). Statistical methods in genetic research on smoking. *Statistical Methods in Medical Research*, 7, 165–186.
- Heath, A. C., Madden, P. A. F., Slutske, W. S., & Martin, N. G. (1995). Personality and the inheritance of smoking behavior: A genetic perspective. *Behavior Genetics*, 25, 103–117.
- Heath, A. C., & Martin, N. G. (1993). Genetic models for the natural history of smoking: Evidence for a genetic influences on smoking persistence. *Addictive Behaviors*, 18, 19–34.
- Heath, A. C., Neale, M. C., Hewitt, J. K., Eaves, L. J., & Fulker, D. W. (1989). Testing structural equation models for twin data using LISREL. *Behavior Genetics*, 19, 9–35.
- Hettema, J. M., Corey, L. A., & Kendler, K. S. (1999). A multivariate genetic analysis of the use of tobacco, alcohol, and caffeine in a population based sample of male and female twins. *Drug and Alcohol Dependence*, 57, 69–78.
- Hughes, J. R. (1986). Genetics of smoking: A brief review. *Behavior Therapy*, 17, 335–345.
- Jardine, R., & Martin, N. G. (1984). Causes of variation in drinking habits in a large twin sample. *Acta Geneticae Medicae et Gemellologiae*, 33, 435–450.
- Jöreskog, K. G., & Sörbom, D. (1993). *PRELIS 2 User's Reference Guide*. Chicago, IL: Scientific Software International, Inc.
- Kandel, D. B. (1978). Homophily, selection, and socialization in adolescent friendships. *American Journal of Sociology*, 84, 427–436.
- Kandel, D. B. (1985). On processes and peer influences in adolescent drug use: A developmental perspective. *Advances in Alcohol and Substance Abuse*, 4, 139–163.
- Kaprio, J., Boomsma, D. I., Heikkilä, K., Koskenvuo, M., Romanov, K., Rose, R. J., Viken, R. J., & Winter, T. (1995). Genetic variation in behavior risk factors for atherosclerosis: Twin-family study of smoking and cynical hostility. In F. P. Woodford, J. Davignon, & A. Sniderman (Eds.), *Atherosclerosis X (Proceedings of the Xth International Symposium on Atherosclerosis, Montreal, 1994)*. *Excerpta Medica International Congress Series #1066*. pp. 634–637.
- Kaprio, J., Hammer, N., Koskenvuo, M., Floderus-Myrhed, B., Langinvainio, H., & Sarna, S. (1982). Cigarette smoking and alcohol use in Finland and Sweden: A cross-national twin study. *International Journal of Epidemiology*, 11, 378–386.
- Kaprio, J., & Koskenvuo, M. (1988). A prospective study of psychological and socioeconomic characteristics, health behavior and morbidity in cigarette smokers prior to quitting compared to persistent smokers and non-smokers. *Journal of Clinical Epidemiology*, 41, 139–150.

- Kaprio, J., Koskenvuo, M., & Langinvainio, H. (1984). Finnish twins reared apart. IV: Smoking and drinking habits. A preliminary analysis of the effect of heredity and environment. *Acta Geneticae Medicae et Gemellologiae*, 33, 425–433.
- Kaprio, J., Sarna, S., Koskenvuo, M. & Rantasalo, I. (1978). The Finnish twin registry: Baseline characteristics, Section II. Helsinki: University of Helsinki Press.
- Kendler, K. S., Heath, A. C., Martin, N. G., & Eaves, L. J. (1986). Symptoms of anxiety and depression in a volunteer twin population: The etiologic role of genetic and environmental factors. *Archives General Psychiatry*, 43, 213–221.
- Kendler, K. S., & Gardner, C. O. (1998). Twin studies of adult psychiatric and substance dependence disorders: Are they biased by differences in the environmental experiences of monozygotic and dizygotic twins in childhood and adolescence? *Psychological Medicine*, 28, 625–633.
- Kendler, K. S., Neale, M. C., Sullivan, P., Corey, L. A., Gardner, C. O., & Prescott, C. A. (1999). A population-based twin study in women of smoking initiation and nicotine dependence. *Psychological Medicine*, 29, 299–308.
- Kendler, K. S., Thornton, L. M., & Pedersen, N. L. (2000). Tobacco consumption in Swedish twins reared apart and reared together. *Archives of General Psychiatry*, 57, 886–892.
- Lykken, D. T., McGue, M., & Tellegen, A. (1987). Recruitment bias in twin research: The rule of two-thirds reconsidered. *Behavior Genetics*, 17(4), 343–362.
- Madden, P. A. F., Heath, A. C., Pedersen, N. L., Kaprio, J., Koskenvuo, M. J., & Martin, N. G. (1999). The genetics of smoking persistence in men and women: A multicultural study. *Behavior Genetics*, 29, 423–431.
- Madden, P. A. F., Bucholz, K. K., Todorov, A. A., Grant, J. D., & Heath, A. C. (2002). The assessment of peer selection and peer environmental influences on behavior using pairs of siblings. *Twin Research*, 5, 38–43.
- Maes, H. H., Woodard, C. E., Murrelle, L., Meyer, J. M., Silberg, J. L., Hewitt, J. K., et al. (1999). Tobacco, alcohol and drug use in eight- to sixteen-year-old twins: The Virginia Twin Study of Adolescent Behavioral Development. *Journal on Studies in Alcohol*, 60, 293–305.
- Medlund, P., Cederlof, R., Floderus-Myrhed, R., Friberg, L., & Sorensen, S. (1977). A new Swedish Twin Registry. *Acta Medicae Scandinavica Supplementum* 600.
- Meyer, J. M., Eaves, L. J., Heath, A. C., & Martin, N.G. (1991). Estimating genetic influences on the age-at-menarche: A survival analysis approach. *American Journal of Medical Genetics*, 39, 148–154.
- Neale, M. C. (1994). *MX: Statistical modeling*. Department of Psychiatry, Virginia Commonwealth University.
- Neale, M. C., & Cardon, L. R. (1992). *Methodology for genetic studies of twins and families*, NATO ASI Series. Dordrecht, The Netherlands: Kluwer.
- Pedersen, N. (1981). Twin similarity for usage of common drugs. In L. Gedda, P. Parise, & W. E. Nance (Eds.), *Twin Research* (Vol. 3: Part C; Epidemiology and Clinical Studies; pp. 53–59). New York: Alan R. Liss.
- Peto, R., Lopez, A. D., Boreham, J., Thun, M., & Heath, C. (1992). Mortality from tobacco in developed countries: Indirect estimation from national vital statistics. *The Lancet*, 339, 1268–1278.
- Raascho-Nielsen, E. (1960). Smoking habits in twins. *Danish Medical Bulletin*, 7, 82–88.
- Risch, H. A., Howe, G. R., Jain, M., Burch, D., Holowaty, E. J., & Miller, A. B. (1993). Are female smokers at higher risk for lung cancer than male smokers? A case-control analysis by histologic type. *American Journal of Epidemiology*, 138, 282–293.
- Sarna, S., Kaprio, J., Sistonen, P., & Koskenvuo, M. (1978). Diagnosis of twin zygosity by mailed questionnaire. *Human Heredity*, 28, 241–254.
- SAS Institute (1990). *SAS/STAT User's Guide* (Version 6; 4th ed.). Cary, NC: SAS Institute.
- Swan, G. E., Carmelli, P., Rosenman, R. H., Fabsitz, R. R., & Christian, J. C. (1990). Smoking and alcohol consumption in adult male twins: Genetic heritability and shared environmental influences. *Journal of Substance Abuse*, 2, 39–50.
- True, W. R., Heath, A. C., Scherrer, J. F., Waterman, B., Goldberg, J., Lin, N., et al. (1997). Genetic and environmental contributions to smoking. *Addiction*, 92, 1277–1287.
- US Department of Health and Human Services (1989). *The health consequences of smoking: 25 years of progress*. Report of the Surgeon General. Rockville, MD: Public Health Service, Centers for Disease Control Office on Smoking and Health, DHHS Publication No. 89–8411.
- World Health Organization (1997). *Tobacco or health: A global status report*. Geneva: World Health Organization