# Changes in the genetic influences on smoking over a fifty year period*

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**Abstract**

We describe trends in the genetic influences on regular smoking across multiple cohorts of U.S. adults born between 1925 and 1970. Using a sample of identical and same-sex fraternal twin pairs from the National Survey of Midlife Development in the United States, we estimate that 36% of the variance in regular is due to additive genetic influences. Using a rolling sample we also show that the timing of the first Surgeon General's Report coincides with an increase in the genetic influences on regular smoking, but subsequent legislation prohibiting smoking in public places caused a significant reduction in the genetic causes for regular smoking. We argue that systematic variation in genetic influences across periods makes it difficult to estimate genetic effects on health behaviors from data obtained from a single point in time. Without properly describing the location of the sample within the larger epidemiological trend, the results from genetic studies are difficult to interpret and may lead to erroneous conclusions about the genetic and social factors that may underlie complex behaviors like smoking.

## Introduction

In this paper we use a nationally representative sample of same-sex adult twin pairs born between 1925 and 1970 to model variation in the genetic influences on regular smoking across five decades. We argue that genetic influences on smoking are part of a dynamic system that changes and evolves over time. We further argue that these changes are not random, and we illustrate this point by examining the genetic influences on of smoking before and after the Surgeon General's Report in 1964. This single event allows us to test several hypotheses regarding the causes of cigarette smoking and illustrates the importance of considering the historical context of genetic studies.

## Gene-environment interplay and smoking

Based on studies that compare the concordance of smoking among identical twin pairs to that of fraternal twin pairs, researchers estimate that roughly 50 to 60 percent of the variance of regular smoking is due to genetic factors (Carmelli et al. 1992; Sullivan and Kendler 1999; Hall, Madden, and Lynskey 2002; Li et al. 2003). However, by comparing reported tobacco use among same-sex twin pairs across three birth cohorts (1910-1924, 1925-1939, and 1940-1958), Kendler et al. (2000) demonstrate that heritability estimates are subject to change over time. Among the first cohort of women, none of the variance in tobacco use was due to genetic factors but by the third cohort, the heritability for regular tobacco use was nearly 60%. These results are consistent with the *social control* gene-environment interaction (GxE) model (Shanahan and Hofer 2005) which posits that "norms and other social forces that 'canalize' (i.e., restrict variability in the phenotype of) genetically diverse people. As these canalization forces increase (i.e., norms are more effective and choices are minimal), genetic differences are of

diminishing consequence." (pp. 69). The same understanding is applicable to studies showing that genetic influences on the use of tobacco and alcohol are either muted or non-existent among those who are raised with a strong religious upbringing with clear norms against the use of different substances (Koopmans et al. 1999; Timberlake et al. 2006).

The social control model assumes that there are shared behavioral expectations and corresponding sanctions that influence genetic associations. In other words, the social environment *causes* genes to operate differently. However, it is also possible that the contribution of genetic factors to overall variance of a behavior will vary across social contexts but the environment is *not causing* the genes to operate differently. Instead, the environment simply clarifies or obscures the role of genes. If the composition of smokers changes because more people (regardless of genetic makeup) begin smoking, then there will be a point in the distribution of smoking environments that entrée into smoking is primarily a socially oriented phenomenon; genetically vulnerable persons are no more likely to begin smoking than genetically resilient persons simply because of the predominant social influences on smoking. This process can be characterized by a tipping point in which, prior to this point time, there are *active* social forces that are shaping the understandings and expectations of smoking; however, at some point after norms have been established, smoking prevalence becomes the dominant causal factor and, despite the fact that genotypes may differentiate individuals from one another, the contribution of genes is relatively less important. As a result, in socially dominant contexts, the genetic influences on of smoking will decrease in salience.

Alternatively, it is also possible that changes in the social norms regarding smoking will lead to an *increase* in the relevance of genetic factors. Raine (2002) calls this the "social push perspective" and suggests that we should examine genetic associations in *benign* environments or those that lack social factors that encourage smoking. Under this perspective, if an individual with genetic tendencies to smoke cigarettes lacks social factors that "push" them to smoke, then biological factors may better explain their smoking. As Raine makes clear, this perspective does not mean that the environment causes genes to operate differently, rather it simply minimizes the "noise" in the study which allows for "biology to shine through" (Raine 2002:14).

**Smoking Trends and the Surgeon General's Report**

National trends in cigarette consumption are presented in Figure 1. Cigarette consumption increased more than five-fold from 1920 to 1960, reached a plateau between 1965 and 1975, and has declined consistently since this time. By some estimates, roughly one-half of men and one-third of women in the United States smoked regularly in 1966 (Forey et al. 2007). Two important changes took place during the 1960s and 1970s that had important implications for smoking. The first event occurred in 1964 when the Surgeon General released the first of a number of reports with clear warnings about the dangers of smoking. This led to the *Federal Cigarette Labeling and Advertising Act* which required the Surgeon General's Warning on all cigarette packages that read: "Caution: Cigarette Smoking May Be Hazardous to Your Health." The first report focused on the link between smoking and lung cancer and was followed by a series of reports linking smoking to heart disease (USDHEW 1967) and low birth weight (USDHEW 1969) and making a case for the risks of second hand smoke for vulnerable

populations (USDHEW 1973). These efforts led to the 1971 Public Health Cigarette Smoking Act which banned the advertising of cigarettes on both television and radio.

The second series of events occurred in the mid 1970s. In 1973, Arizona passed a comprehensive law that limited smoking in public places which was the first effort to formally control public smoking behaviors. This was followed by a more restrictive set of laws including the 1975 Minnesota Clean Indoor Air Act which required restaurants to have non-smoking sections in their restaurants; another twelve years would pass until Aspen, CO became the first city to formally ban all cigarette smoking in restaurants. The push for bans in all restaurants was bolstered by the 19th Surgeon General's Report, which argued that the "simple separation of smokers and nonsmokers within the same airspace may reduce but cannot eliminate nonsmoker exposure to environmental tobacco smoke." (USDHHS 1986).

The time-lag between scientific findings about the health risks of smoking and legislation designed to limit smoking is important because the former may influence the social component of smoking behaviors but the later may be particularly effective in influencing the genetic component of smoking. That is, norms about smoking were starting to change in the 1960s because of the shared understanding of regarding the health risks of cigarette smoking, but it wasn't until the 1970s, in which institutional controls were formalized, that the environment had a causal influence on genetic influences.

This historical backdrop provides an unusual opportunity to examine both causal and non-causal GxE and the timing of the first Surgeon General's Report serves as an experimental design to test the relevance of considering the smoking population as a

socio-genetic composition which changes over time. Using the causal/non-causal GxE distinction in combination with the changing social and institutional forces with respect to smoking, we hypothesize that genetic influences on smoking will change as follows (these hypotheses are indicated in Figure 1 by the direction of the arrows corresponding to each period):

Period 1 (1945-1965): This period was characterized by the low cost and ubiquitous availability of cigarettes in conjunction with regular images of cultural icons smoking. The socio-genetic composition of smokers is dominated by social entrée into smoking and during this period, *the genetic influences on smoking will decrease*.

Period 2 (1965-1975): During this period, the clear evidence provided by the scientific community lead many to stop smoking. This change should be the least evident among those for whom smoking is genetically oriented and *the genetic influences on smoking will increase.*

Period 3 (1975-1995): Local, state, and federal lawmakers enact and enforce policies aimed to reduced cigarette consumption. These social controls will causally influence the degree to which genetic characteristics differentiate between individuals. Thus, during this period, *the genetic influences on smoking will decrease*.

## METHODS

### Data

This study uses data from the 1995 National Survey of Midlife Development in the United States (MIDUS) (Brim et al. 1996). MIDUS is a nationally representative survey designed to study the effects of midlife development on the self-reported physical health, psychological well-being, and social consciousness of adults aged 25 to 75. Data

in the survey were collected through the use of a telephone interview and a mailed questionnaire to nearly 7,000 respondents. The MIDUS Twin Screening Project was used to identify 998 adult twin pairs to participate in the study. After a screening of roughly 50,000 households via a telephone interview, MIDUS interviewers contacted the respondent who was then asked to contact their twin to participate in the study. Of the 998 pairs, 1914 individuals completed at least some portion of the telephone survey with an overall response rate 96%. We use only same-sex monozygotic (MZ) and dizygotic (DZ); dropping twins whose co-twins did not participate in the survey, we have 350 pairs of MZ twins and 322 pairs of same-sex DZ twins. Questions used in this study come from the telephone interview and the extent of missing data is minimal. Of these, one pair of MZ twins was dropped due to missing smoking data and two pairs were dropped due to differing birth dates. The remaining sample used in the study included 348 MZ pairs and 321 same-sex DZ pairs.[1]

Regular smoking was assessed through two questions. Respondents were asked, "Have you ever smoked cigarettes regularly - that is, at least a few cigarettes every day?" Those responding "yes" were then asked, "On average, about how many cigarettes did you smoke per day during the one year in your life when you smoked most heavily?" Respondents indicating that they smoked less than three cigarettes per day during the time of heaviest smoking were considered to have never been a regular smoker. Respondents indicating that they have smoked regularly were also asked "At what age did you begin smoking regularly?"

To establish the genetic influences on smoking we use a variance decomposition method using the Mx software (Neale et al. 2004). We estimate a basic model with three

parameter estimates: a) additive genetic variance; b) shared environmental variance; and c) non-shared environmental variance. We estimate this model using the full sample to decompose phenotypic variance into genetic and environmental components. The purpose of this model is to establish an average heritability measure for this trait. We then build on this basic parameter estimate by modeling similarities in the timing of smoking onset among twin pairs by using a multivariate survival model with shared frailty among twin pairs by zygosity. The frailty variance is similar to a random intercept in a multilevel model and large estimates similarity in the timing of smoking among pairs of twins. By comparing the frailty estimate between the MZ and DZ twin pairs, it is possible to infer genetic influence on the timing of a particular behavior (Guo and Tong 2006). This model is specified in equation 1. The values for *T* are random variables capturing the survival times (the age of onset for regular smoking) for the *j*th sibling in the *i*th pair of twins. Thus, the survival function is conditional on this cluster-specific error term *Wi,* and the resulting hazard functions $h(t_{ij} \mid w_i)$ are multiplicative frailty models with a baseline hazard $\lambda_0(t_0)$.

$$h(t_{ij} \mid w_i) = w_i \lambda_0(t_{ij}) \exp\{(\beta(t_{ij})' x_{ij}(t_{ij})\} \quad (1)$$

Our model assumes that *Wi* has a gamma distribution indexed by α with the following density: $f(w_i) = w_i^{\alpha-1} e^{-\alpha W_i} \alpha^{\alpha} / \Gamma(\alpha)$. The distributional parameters for this density are mean = 1 and a variance of φ. The latent random effects of φ are assumed to affect the hazard multiplicatively. We assume the presence of genetic influences when the estimate of φ is significantly higher for MZ compared to DZ pairs and we calculate the ratio of φ for the pair types for the full sample. These estimates are shown in Table 3.

To address our primary research question, we then estimate similar models by the year of birth of the sibling pairs. This provides a trend for the genetic influences on of smoking for those born in the 1920s through the 1960s. Because of small sample sizes for each birth year in our study, time specific estimates are calculated for a rolling sample with a window of 4 years. For example, an estimate for 1925 includes individuals born in 1925 and those born within the four years before and after 1925. We do this for each year between 1925 and 1970. These models are summarized in Table 4 and they include controls for gender and the equal environments assumption.[2]

**Results**

[Table 1 about here]

[Table 2 about here]

Table 1 presents descriptive statistics for pairs of twins in our study. Of the 348 MZ twin pairs, only 19.5% were discordant for regular smoking status. Among DZ pairs, 28% gave discordant reports of their lifetime regular smoking. These same numbers are used in conjunction with traditional behavioral genetic models to quantify the proportion of regular smoking that may due to genetic influences and these estimates are provided in Table 2. According to these results, narrow heritability for regular smoking is estimated to be .36. That is, we estimate that over one-third of the variance in regular smoking may be due to additive genetic influences. We also show a very large influence of the social environment that is shared by both members of the twin pair. That is, forty-five percent of the variance in regular smoking is due to environmental factors of the home, the neighborhood, the schools, or the geographic regions that siblings shared in common with one another.

[Table 3 about here]

Survival models with shared frailty provide an alternative method to decompose variance into shared and unshared components. These methods are also more sensitive to the duration of exposure and the timing of smoking onset compared to a binary outcome that indicates whether the individual ever smoked regularly while also taking into account individuals who never smoked regularly (right censored). The baseline model is presented in Table 3. For the full sample the hazard function is significantly improved when the shared frailty among pairs is considered for both MZ ($\chi^2 = 110.79$, $p<.001$) and DZ ($\chi^2 = 40.54$, $p<.001$) pairs. This estimate ($\varphi_{mz} = 2.59$) for MZ pairs is more than twice that of DZ pairs ($\varphi_{dz} = 1.16$) which provides additional evidence for the genetic influences on regular smoking. This model can also be used to provide a rough indicator of heritability for the full sample. That is, the ratio of $\varphi/(2+\varphi)$ is equivalent to Kendall's (Kendall 1962) coefficient of intra-cluster rank correlation (see Guo and Rodriguez, 1992 for a detailed discussion). Accordingly, the intra-class correlation for MZ pairs is .56 (e.g., 2.59/[2+2.59]) and this estimate is .37 for DZ pairs (e.g., 1.16/[2+1.16]). Using a relatively crude measure of heritability as twice the difference of the correlations between MZ and DZ pairs, these initial survival models provide a heritability estimate of .38 (e.g., 2*[.56-.37]). This estimate is quite similar to quantitative genetic estimate provided in Table 2.

[Table 4 about here]

To address the primary aim of this study, this same model was repeated 46 times spanning the birth years of 1925 to 1970. The results from these analyses are summarized in Table 4. For each zygosity type, the first column presents the observed number of pairs

for each year of birth and the second column describes the number of pairs that were used in the rolling sample to estimate the survival model for that year. The shared frailty variance estimate and the significance of this estimate are also provided. The final column provides ratio of the shared frailty estimate of MZ pairs compared to DZ pairs for each birth year and these results denote the primary contribution of this paper. As a benchmark, the ratio for the full sample is 2.23 ($\varphi_{mz}/ \varphi_{dz}$ = 2.59/1.16 = 2.23) and is roughly equivalent to the average heritability estimate presented in Table 2.

Although the genetic influences presented Tables 2 and 3 ($h^2$ = *.36-.38*) summarizes the entire sample, these estimates should be understood as averages; at times genetic influences are much higher and much lower than this value. As shown graphically in Figure 2 (the estimates from Table 4 are adjusted by 20 years reflecting the peak of smoking onset for this sample) the genetic influences on regular smoking appear to be pronounced during the 1940s and early 1950s but decline steadily until the mid 1960s. The first minimum in this figure (1963-1965) corresponds with the hypothesized transition between the social and genetic composition of smokers following the Surgeon General's Report. However, following this first transition there is a persistent and steady increase in the genetic influences on regular smoking until the middle of the 1970s. We argue that this increase captures a non-causal form of gene-environment interactions where the socio-genetic composition of smokers is changing over time; those for whom quitting smoking is relatively easy may be the first to give up their smoking status in light of the evidence about the health risks. Because smoking desistence is the most highly heritable smoking phenotype (Vink, Willemsen, and Boomsma 2005), those who have the hardest time quitting, may also be those who have a stronger physiologic dependence

on nicotine. Therefore, as non-dependent individuals are removed from the smoking population, it causes genetic factors responsible for nicotine dependence to become relatively more important.

The first legislative efforts to limit or ban smoking in public places occurred during the end of this period. According to our hypotheses, the genetic contributions to regular smoking will decrease under non-causal social compositional changes *or* if there are social forces (normative, institutional, or both) that act on the behaviors of individuals as a source of control. As described earlier, this period extends until the mid 1990s and is characterized by an increasing number of federal, state, and local laws that controlled the sale, distribution, advertisement, and smoking of tobacco. In other words, changes in the social orientation of smoking did not *causally* influence genetic factors related to smoking onset or persistence until laws were developed and enforced that placed physical limits on this behavior. These legislative efforts reflect the forces described by Shanahan and Hofer (2005) that restrict the variation of genetic factors and the steep drop in the genetic influences on of regular smoking corresponds with the social control perspective of gene-environment interactions.

**Discussion**

The findings presented in this paper speak to an increasing body of work that quantifies genetic and environmental contributions to smoking in the population. As we have argued elsewhere, heritability estimates should be considered averages, and we should anticipate dispersion about this average. The context for this dispersion may be discrete social settings like schools (Boardman et al. 2008) or states (Boardman 2009) but, as we

show here, it may also be a social historical trend. This point is made nicely by Rutter (2006) who argues that:

> There is not, and cannot be, any absolute value for the strength of genetic influences on a trait, no matter how accurately the trait is measures or how carefully the genetic effect is assessed. As behavioral genetics have long recognized, and emphasized, heritability figures are necessarily specific to populations and to *time periods*. (pp. 60, *emphasis added*).

Despite the general acceptance of this perspective, little work has emphasized variation in heritability estimates over time. Our paper is one of few papers to use a nationally representative sample of twins to examine quantitative genetic estimates of regular smoking and the only known paper to show the trends in the genetic influences on estimate across this important period in US history.

This perspective is particularly relevant in the recent push to find specific genes that predict smoking (Li 2008) because the effectiveness of methods to identify single-nucleotide polymorphisms across the entire human genome may be subject to periodic highs and lows in the genetic influences on a particular trait. The current methods certainly consider this factor (e.g., the population prevalence is a key component of the estimation techniques), but they do not necessarily consider that their sample is drawn from a specific historical moment in a larger cycle with predictable ebbs and flows. The consideration of epidemiologic trends of cigarette use as causal and non-causal forms of gene-by-environment interactions in conjunction with quantitative genetic or genetic association methods to identify heritability forms a complicated picture of smoking. Out of this complexity, however, we argue that there may be relatively simple ways of considering which genetic and environmental effects change over time. Focusing on genetic influences on estimates as part of a larger trend is particularly important to the

study of epidemiology because it suggests that health-related policies should consider the timing of the policy implementation as a function of this larger trend.

**NOTES**

1. Date of birth was assumed for 29 individuals based on their co-twin's reported date of birth. 4 pairs reported different birth dates. Two of these pairs were dropped because their birth dates differed by several years – probably due to coding error. The other two pairs had birth dates differing by one year; for these twins, we used the earliest reported birth date. The date of birth for 8 pairs were imputed from their age (based on the oldest age reported) because both twins were missing a date of birth. In addition, because of the limited sample sizes and a failure of convergence at this time, we generated two pseudo observations of male DZ pairs for the year 1929. One pair was concordant for smoking and the other was discordant.

2. Violations to the equal environments assumption, resulting from MZ twins being treated more similarly than DZ twins can increase concordance among MZ twins and overestimate heritability estimates. The MIDUS twin data includes three questions assessing how often twins were dressed alike, placed in the same classrooms, and had the same playmates. These measures have been used to gauge and correct EEA violations (Kessler et al. 2004). We create a composite EEA score using a polychoric principle components analysis of the pair's mean response on the three items and include this estimate as a control in all models. We do not expect twin pairs who are treated more similarly to one another to be more likely to smoke, rather they will be more alike one another. Thus, if MZ pairs are like one another because they are more likely to share environments, then this control should reduce the frailty variance estimate for MZ pairs more so than DZ pairs.

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**Table 1.** Smoking concordance among identical and same-sex fraternal twin pairs.

| | Identical Twins (MZ) | | Fraternal Twins (DZ) | |
|---|---|---|---|---|
| | N | % | N | % |
| Both non-smokers | 165 | 47.4 | 115 | 35.8 |
| Both smokers | 115 | 33.0 | 116 | 36.1 |
| Discordant | 68 | 19.5 | 90 | 28.0 |
| Total | 348 | 100.0 | 321 | 100.0 |

(Chi-square = 10.9, df= 2, $p < .004$)

Note: All data come from the 1995 National Survey of Midlife Development in the United States (MIDUS) [Brim et al. 1996].

**Table 2.** Quantitative genetic parameter estimates for regular smoking

| | Estimate | 95% C.I. |
|---|---|---|
| Additive Genetic Variance | 0.36 | (.07, .65) |
| Shared Environmental Variance | 0.45 | (.19, .69) |
| Non-shared Environmental Variance | 0.19 | (.12, .28) |

Note: all data come from the 1995 National Survey of Midlife Development in the United States (MIDUS) [Brim et al. 1996]. Heritability estimates and confidence intervals (in parentheses) are calculated using Mx (Neale 2004). This freely available structural equation modeling package contains a number of standard procedures to decompose phenotypic variance into genetic and environmental components. The ctVCut2c.mx script developed by the GenomeUTwin group was used to calculate these estimates; this and other scripts are freely available at http://www.psy.vu.nl/mxbib/.

**Table 3.** Survival models for MZ and DZ with shared frailty.

| | Identical twins (MZ) | | Fraternal twins (DZ) | |
|---|---|---|---|---|
| | Hazard ratio | 95% CI | Hazard ratio | 95% CI |
| Year of birth | 0.98 | (.96, 1.00) | 0.99 | (.98, 1.01) |
| Gender | 0.71 | (.45, 1.13) | 0.72 | (.51, 1.02) |
| Equal environments | 1.06 | (.84, 1.34) | 1.15 | (.97,1.44) |
| Theta | 2.59 | | 1.16 | |
| $\chi^2$ | 110.79 | | 40.59 | |
| p < | .001 | | .001 | |

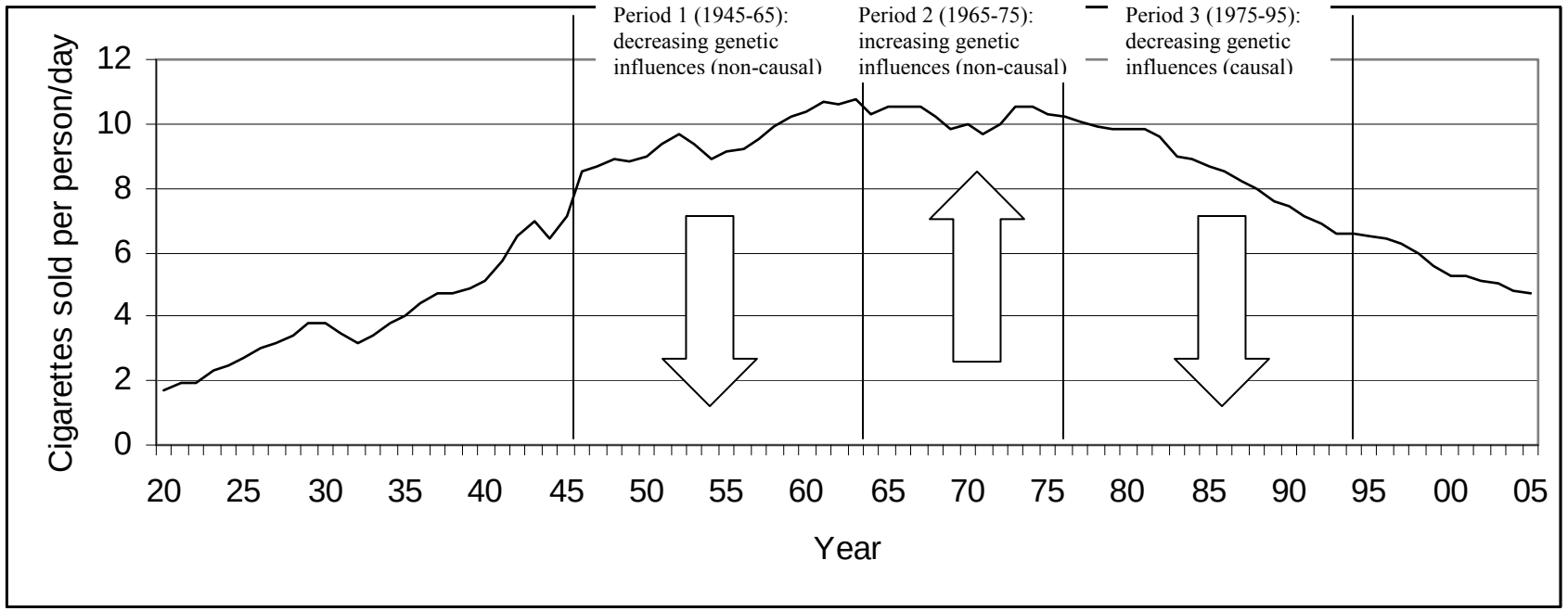
Note: all data come from the 1995 National Survey of Midlife Development in the United States (MIDUS) [Brim et al. 1996]. Cell entries represent parameter estimates and 95% confidence intervals from two survival models (for MZ and DZ twins separately) with shared frailty estimates capturing similarity in survival functions among twin pairs.

**Table 4.** Frailty estimates by birth year for the onset of regular smoking by zygosity.

| | MZ | | | | | DZ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Birth | N | Nm | φ | $\chi 2_{\varphi}$ | p< | N | Nm | φ | $\chi 2_{\varphi}$ | p< | $\varphi_{MZ}/\varphi_{DZ}$ |
| 25 | 1 | 19 | 1.76 | 4.21 | 0.02 | 1 | 30 | 0.24 | 0.12 | 0.36 | 7.44 |
| 26 | 5 | 22 | 3.10 | 8.11 | 0.00 | 5 | 33 | 0.42 | 0.45 | 0.25 | 7.43 |
| 27 | 2 | 25 | 2.47 | 8.81 | 0.00 | 2 | 34 | 0.53 | 0.93 | 0.17 | 4.69 |
| 28 | 3 | 26 | 1.94 | 7.87 | 0.00 | 1 | 36 | 0.44 | 0.82 | 0.18 | 4.41 |
| 29 | 0 | 27 | 1.51 | 6.59 | 0.01 | 9 | 34 | 0.21 | 0.23 | 0.32 | 7.34 |
| 30 | 4 | 31 | 1.84 | 7.67 | 0.00 | 4 | 35 | 0.32 | 0.62 | 0.22 | 5.70 |
| 31 | 4 | 36 | 1.29 | 6.23 | 0.01 | 5 | 33 | 0.29 | 0.56 | 0.23 | 4.42 |
| 32 | 5 | 37 | 1.24 | 5.53 | 0.01 | 4 | 35 | 0.52 | 1.89 | 0.08 | 2.37 |
| 33 | 3 | 45 | 1.40 | 8.89 | 0.00 | 3 | 37 | 0.51 | 1.79 | 0.09 | 2.73 |
| 34 | 5 | 47 | 1.50 | 10.42 | 0.00 | 2 | 34 | 0.52 | 1.68 | 0.10 | 2.86 |
| 35 | 10 | 47 | 1.53 | 10.40 | 0.00 | 3 | 38 | 0.44 | 1.59 | 0.10 | 3.48 |
| 36 | 3 | 47 | 1.25 | 7.53 | 0.00 | 4 | 37 | 0.23 | 0.49 | 0.24 | 5.36 |
| 37 | 11 | 46 | 1.21 | 7.12 | 0.00 | 3 | 44 | 0.57 | 2.53 | 0.06 | 2.13 |
| 38 | 2 | 49 | 1.39 | 8.57 | 0.00 | 6 | 48 | 0.78 | 4.64 | 0.02 | 1.79 |
| 39 | 4 | 51 | 1.27 | 9.66 | 0.00 | 8 | 57 | 0.72 | 4.51 | 0.02 | 1.75 |
| 40 | 4 | 50 | 1.53 | 9.66 | 0.00 | 4 | 61 | 0.85 | 6.20 | 0.01 | 1.80 |
| 41 | 4 | 53 | 1.98 | 13.38 | 0.00 | 11 | 68 | 0.92 | 6.73 | 0.00 | 2.15 |
| 42 | 6 | 52 | 1.57 | 11.22 | 0.00 | 7 | 75 | 1.08 | 9.43 | 0.00 | 1.45 |
| 43 | 7 | 61 | 1.65 | 13.80 | 0.00 | 11 | 74 | 1.29 | 11.96 | 0.00 | 1.28 |
| 44 | 9 | 72 | 1.64 | 15.66 | 0.00 | 7 | 73 | 1.40 | 12.77 | 0.00 | 1.17 |
| 45 | 6 | 80 | 2.04 | 23.71 | 0.00 | 11 | 81 | 1.46 | 16.55 | 0.00 | 1.39 |
| 46 | 10 | 89 | 2.18 | 27.94 | 0.00 | 10 | 80 | 1.15 | 12.21 | 0.00 | 1.90 |
| 47 | 11 | 86 | 2.43 | 30.00 | 0.00 | 5 | 76 | 1.09 | 10.28 | 0.00 | 2.22 |
| 48 | 15 | 87 | 3.02 | 34.01 | 0.00 | 7 | 70 | 1.17 | 11.06 | 0.00 | 2.58 |
| 49 | 12 | 90 | 3.90 | 48.27 | 0.00 | 12 | 71 | 1.22 | 10.90 | 0.00 | 3.21 |
| 50 | 13 | 97 | 3.41 | 46.38 | 0.00 | 10 | 71 | 0.81 | 6.65 | 0.00 | 4.20 |
| 51 | 3 | 95 | 3.62 | 43.99 | 0.00 | 3 | 75 | 0.56 | 4.63 | 0.02 | 6.49 |
| 52 | 8 | 102 | 4.10 | 48.23 | 0.00 | 5 | 78 | 0.46 | 3.55 | 0.03 | 8.95 |
| 53 | 12 | 95 | 4.65 | 50.44 | 0.00 | 8 | 80 | 0.52 | 4.16 | 0.02 | 8.91 |
| 54 | 13 | 94 | 3.99 | 40.04 | 0.00 | 11 | 75 | 0.46 | 3.00 | 0.04 | 8.69 |
| 55 | 8 | 94 | 4.66 | 41.32 | 0.00 | 14 | 77 | 0.66 | 5.19 | 0.01 | 7.11 |
| 56 | 18 | 102 | 4.42 | 47.17 | 0.00 | 8 | 85 | 0.73 | 6.97 | 0.00 | 6.04 |
| 57 | 8 | 100 | 3.93 | 41.55 | 0.00 | 9 | 89 | 0.99 | 10.47 | 0.00 | 3.95 |
| 58 | 11 | 98 | 3.34 | 33.18 | 0.00 | 7 | 96 | 1.11 | 13.03 | 0.00 | 3.01 |
| 59 | 13 | 97 | 3.67 | 33.58 | 0.00 | 12 | 92 | 1.52 | 18.29 | 0.00 | 2.42 |
| 60 | 11 | 94 | 3.02 | 26.13 | 0.00 | 11 | 84 | 1.77 | 18.84 | 0.00 | 1.71 |
| 61 | 6 | 81 | 2.52 | 19.39 | 0.00 | 9 | 80 | 1.83 | 18.21 | 0.00 | 1.38 |
| 62 | 10 | 82 | 2.49 | 20.21 | 0.00 | 15 | 76 | 2.12 | 21.08 | 0.00 | 1.18 |
| 63 | 12 | 79 | 2.68 | 19.75 | 0.00 | 7 | 74 | 2.21 | 18.73 | 0.00 | 1.21 |
| 64 | 5 | 75 | 2.25 | 15.72 | 0.00 | 6 | 71 | 2.48 | 16.90 | 0.00 | 0.90 |
| 65 | 5 | 73 | 2.06 | 12.74 | 0.00 | 4 | 63 | 2.16 | 11.61 | 0.00 | 0.95 |
| 66 | 9 | 70 | 2.35 | 14.56 | 0.00 | 5 | 58 | 2.10 | 9.70 | 0.00 | 1.12 |
| 67 | 8 | 60 | 2.22 | 11.09 | 0.00 | 5 | 43 | 2.21 | 7.42 | 0.00 | 1.01 |
| 68 | 9 | 48 | 1.90 | 8.04 | 0.00 | 9 | 36 | 2.06 | 5.32 | 0.01 | 0.93 |
| 69 | 9 | 43 | 2.68 | 10.20 | 0.00 | 3 | 30 | 2.27 | 4.27 | 0.02 | 1.19 |
| 70 | 3 | 38 | 3.05 | 9.98 | 0.00 | 4 | 26 | 2.45 | 3.02 | 0.04 | 1.25 |

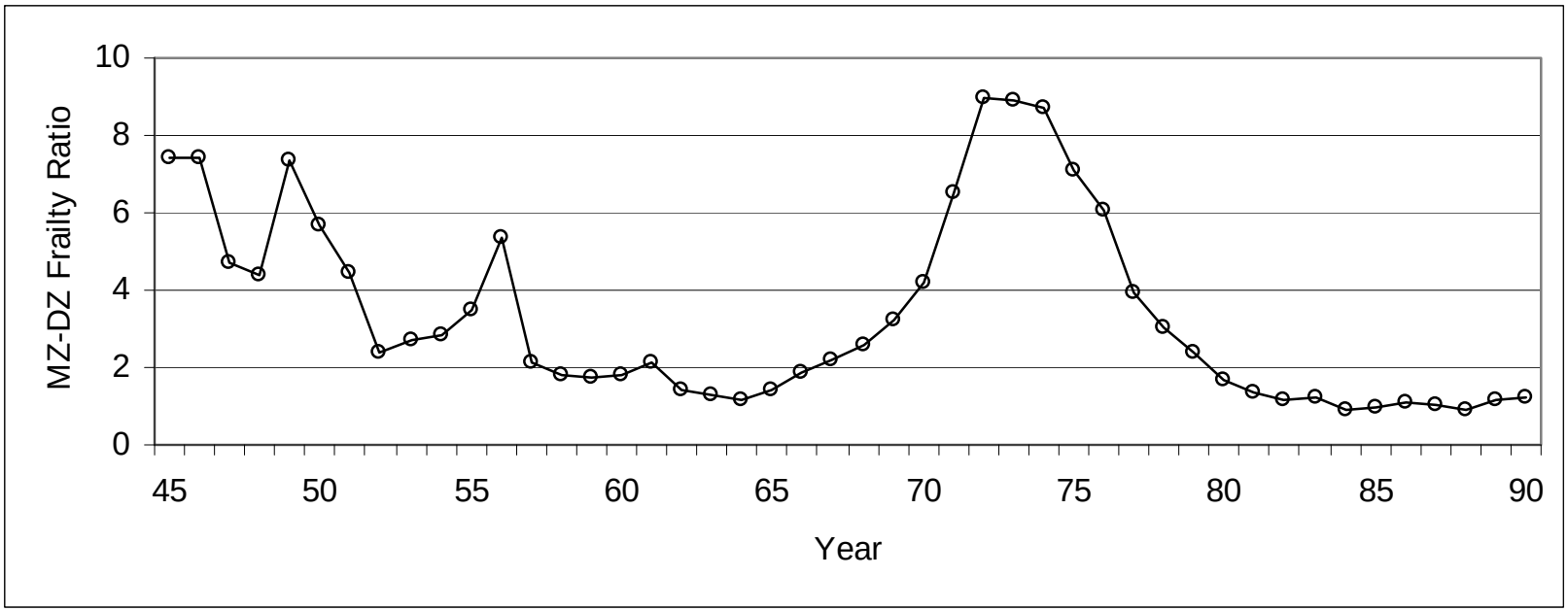
Note: all data come from the 1995 National Survey of Midlife Development in the United States (MIDUS) [Brim et al. 1996]. Cell entries represent parameter estimates obtained from 45 separate survival models (for MZ and DZ twins separately) by year of birth with shared frailty estimates capturing similarity in survival functions among twin pairs.

**Figure 1.** Trends in the sales of cigarettes in the United States: 1920-2005.




Note: Data obtained from Forey et al. (2007). Estimates describe the number of cigarettes sold in the United States per adult over the age of 15 per day. The arrows correspond with the hypothesized direction of the genetic influences on regular smoking during each of the three periods for which there are data in the MIDUS study.

**Figure 2.** Changes in the genetic influences on the timing of regular smoking over a 45 year period: comparing shared frailty estimates among MZ and DZ twin pairs.




Note: all data come from the 1995 National Survey of Midlife Development in the United States (MIDUS) [Brim et al. 1996]. Estimates obtained from the final column of Table 4. The value "year" is simply 20 years after the date of birth for each cohort corresponding with the peak in regular smoking onset.