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# Predicting Stage Transitions in the Development of Nicotine Dependence

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## Abstract

The current study used survival analysis to identify psychiatric and psychosocial predictors of rates of transition from first cigarette to weekly smoking and from weekly smoking to nicotine dependence. Participants were 1269 offspring of twins at varying degrees of genetic and environmental risk for alcohol dependence (AD). Data was collected via telephone interview of offspring and their parents. Externalizing disorders, depression, and other substance use predicted transitions to both stages. Age of first cigarette and parental nicotine dependence were uniquely associated with the transition to weekly smoking and physical abuse was linked only to progression to nicotine dependence. Findings highlight the continuity of risk associated with psychiatric disorders and substance use across stages, but the differential impact of other factors suggest distinctions between mechanisms underlying the two stage transitions examined.



# Background

- The progression of nicotine dependence has frequently been examined using a stage model.
- Empirical studies have produced evidence for risk factors that differentially impact outcomes across stages in addition to identifying a common set of factors that predict a variety of smoking outcomes. Little is known, however, about the role of these factors in modifying the rate of transition between stages of nicotine dependence.
- In the current study, psychiatric and psychosocial correlates of smoking outcomes were examined as potential predictors of transitions at two critical junctures in development of the disorder: first cigarette to weekly smoking and weekly smoking to nicotine dependence.



# Aims

- To identify risk factors associated with rate of transition from first cigarette to weekly smoking and from weekly smoking to nicotine dependence.
- To determine the degree of continuity in risk posed by correlates of smoking related outcomes in early versus late stages of nicotine dependence progression.



# Participants

1269 offspring of male twins from the Vietnam Era Twin Registry

Twins were recruited based on AD status and AD status of their co-twins. Participants were offspring of:

1. AD father (*High G/High E risk; n=587*)
2. MZ co-twin of AD twin (*High G/Low E risk; n=162* )
3. DZ co-twin of AD twin (*Moderate G/Low E risk; n=157*)
4. Unaffected father with unaffected co-twin (*Low G/Low E risk; n=363*)

Age range: 12-28 (mean = 20.1 years)

Gender: 51.5% male; 48.5% female

90% Caucasian



# Assessment Protocol

Telephone interviews conducted with parents and offspring used an adaptation of the SSAGA-II to assess:

## Smoking Milestones

Age of first cigarette

Age began smoking weekly (or more frequently)

Onset of nicotine dependence

## Risk Factors

Parental nicotine dependence

Parental psychiatric diagnoses

Parent-offspring conflict

Childhood abuse

Consistency in parenting

Parent-offspring closeness

Regular marijuana use (7+ times)

Regular alcohol use (weekly for 8 weeks or monthly for 6 months)

Alcohol Dependence

Conduct Disorder

Attention Deficit Hyperactivity Disorder

Oppositional Defiant Disorder

One or more major depressive episodes

Social Anxiety Disorder

Panic Disorder

Generalized Anxiety Disorder



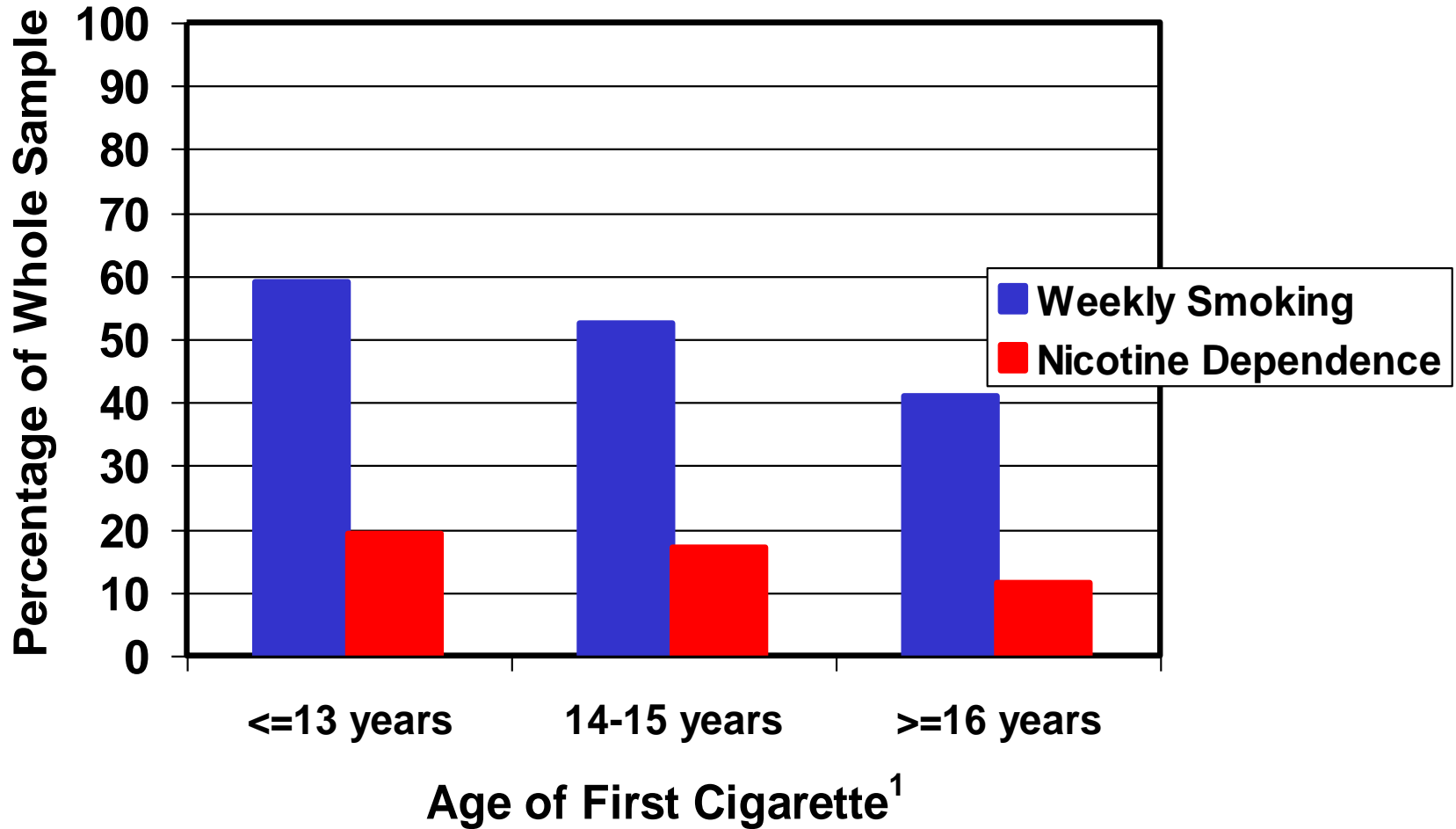


# Smoking Milestones and Stage Transitions

	N (% of whole sample)	Mean (S.D.)*
<b>Age of First Cigarette</b>	817 (64.4%)	14.17 (3.14)
<b>Age Began Smoking Weekly</b>	421 (33.2%)	15.90 (2.56)
<b><i>Years From First Cigarette to Weekly Smoking</i></b>		2.06 (2.09)
<b>Age Onset of Nicotine Dependence</b>	132 (10.4%)	18.40 (2.57)
<b><i>Years From Weekly Smoking to Nicotine Dependence</i></b>		2.87 (2.46)

\* Standard deviations adjusted for clustered data.

# Smoking Outcomes by Age of First Cigarette



<sup>1</sup>Group differences significant for both outcomes at  $p < .05$



# Survival Analysis

Cox proportional hazard regression analyses were conducted to predict rate of transition from:

- a) First cigarette to weekly smoking
  - b) Weekly smoking to nicotine dependence
- Analyses controlled for AD risk status and parental nicotine dependence.
  - Time-varying covariates were created using person-year data to more accurately model risk factors whose onset varied in relation to age smoking milestones were reached.
  - Proportional hazard assumptions were tested in both models. Addition of the interaction between early age of first cigarette (at age 13 or earlier) and the first two years of smoking adjusted for violations in the first cigarette to weekly smoking model. No violations were found in the nicotine dependence model.



# First Cigarette to Weekly Smoking

	Hazard Ratio (95% CI)
Regular Marijuana Use	2.69 (2.15 – 3.37)
Depression	1.95 (1.35 – 2.81)
Oppositional Defiant Disorder	1.73 (1.20 – 2.50)
Regular Alcohol Use	1.57 (1.15 – 2.13)
Conduct Disorder	1.40 (1.06 – 1.84)
Age 1 <sup>st</sup> Cigarette	
Early (<= 13 years)	0.52 (0.38 – 0.72)
Late (>= 16 years)	0.74 ( 0.55 – 0.99)
Early Age 1 <sup>st</sup> Cigarette X 1 <sup>st</sup> 2 Years Smoking	3.26 (2.10 – 5.06)
Paternal Nicotine Dependence	1.27 (1.01 – 1.60)
Maternal Nicotine Dependence	1.07 (1.00 – 1.15)
AD Risk Status	
Group 1: High G/High E*	0.98 (0.74 – 1.30)
Group 2: High G/Low E*	1.03 (0.72 – 1.49)
Group 3: Moderate G/Low E*	0.99 (0.65 – 1.50)

\* Not significant



# Weekly Smoking to Nicotine Dependence

	Hazard Ratio (95% CI)
<b>Depression</b>	<b>2.64 (1.76 – 3.95)</b>
<b>Alcohol Dependence</b>	<b>2.60 (1.50 – 4.48)</b>
<b>Conduct Disorder</b>	<b>2.51 (1.64 – 3.85)</b>
<b>Physical Abuse</b>	<b>2.40 (1.47 – 3.91)</b>
<b>Paternal Nicotine Dependence*</b>	<b>1.18 (0.77 – 1.82)</b>
<b>Maternal Nicotine Dependence*</b>	<b>0.98 (0.86 – 1.12)</b>
<b>AD Risk Status</b>	
<b>Group 1: High G/High E*</b>	<b>0.78 (0.46 – 1.29)</b>
<b>Group 2: High G/Low E*</b>	<b>1.36 (0.69 – 2.67)</b>
<b>Group 3: Moderate G/Low E*</b>	<b>1.66 (0.90 – 3.08)</b>

\* Not significant



# Conclusions

- Transitions both to weekly smoking and to nicotine dependence were associated with externalizing disorders, depression, and other substance use.
- In contrast, parental nicotine dependence status and age of first cigarette were uniquely associated with progression to weekly smoking and physical abuse did not emerge as a risk factor until the transition from weekly smoking to nicotine dependence.
- Despite evidence in the larger literature for common genetic factors linking AD and nicotine dependence, AD risk status did not predict rate of transition between stages of nicotine dependence after controlling for parental nicotine dependence and offspring alcohol use.



## Future Directions

- Further exploration of distinctions in the potency of risk factors at different stages of development of nicotine dependence is merited, as it may lead to greater precision in the timing and nature of intervention efforts.
- Replication with a larger sample would allow for clearer distinctions to be drawn regarding the lack of differences between AD risk groups; that is, whether they reflect reduced power to detect differences, absence of an association, or mediation of risk via more proximal risk factors, such as other substance use.
- Assessment of smoking behaviors into middle adulthood would allow for the study of later stage transitions as well, including cessation attempts and remission of nicotine dependence.