Addressing Gender Differences in the Genetic and Environmental Contributions to Smoking During Adolescence

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Epidemiology of Cigarette Use

• Decrease in prevalence of cigarette use (42.4% to 19.3%)

• Less decline in smoking rates among (US) adolescents

• Prevalence of smoking in men greater than women
Genetic Epidemiology of Cigarette Use

- **Nicotine Dependence is highly heritable**
  - $h^2 = 30-75\%$

- **Smoking persistence**
  - $h^2$ (males) = 59%
  - $h^2$ (females) = 46%

- **Smoking Initiation less heritable**
  - $h^2 = 36-60\%$
  - May differ in males and females
  - Unclear how & whether heritability changes across adolescent development
Study Aims

• Identify developmental trends in smoking initiation among adolescents

• Determine the extent to which genetic and environmental effects play a role in the development of smoking initiation
# The Developmental Genetic Epidemiology of Smoking Study

<table>
<thead>
<tr>
<th>Study Abbreviation</th>
<th>Study Description</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABD</td>
<td>Virginia Twin Study of Adolescent and Behavioral Development</td>
<td>2819</td>
</tr>
<tr>
<td>MN</td>
<td>Minnesota Twin Family Study</td>
<td>4137</td>
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<tr>
<td>CO</td>
<td>Colorado Longitudinal &amp; Community Twin Studies</td>
<td>2804</td>
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<tr>
<td>AUS</td>
<td>Australian Adolescent and Young Adult Twin Study</td>
<td>2888</td>
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<td>MASAT</td>
<td>Mid-Atlantic School Age Twin Study</td>
<td>2210</td>
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<tr>
<td>BEL</td>
<td>Leuven Longitudinal Twin Study</td>
<td>220</td>
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<tr>
<td>NL</td>
<td>Netherlands Twin Register</td>
<td>5561</td>
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<tr>
<td>CVT</td>
<td>Cardiovascular Twin Study</td>
<td>1150</td>
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<tr>
<td>SWE</td>
<td>Swedish Twin Register</td>
<td>2593</td>
</tr>
<tr>
<td>FIN</td>
<td>Finnish Twin Register</td>
<td>6076</td>
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</tbody>
</table>
Measuring Smoking Initiation
<table>
<thead>
<tr>
<th>Study Name</th>
<th>Age Range</th>
<th>Study Design</th>
<th>Lifetime Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABD</td>
<td>8-17</td>
<td>PC- 3 Waves</td>
<td>Have you ever smoked?</td>
</tr>
<tr>
<td>MN</td>
<td>8-24</td>
<td>PC- 6 Waves</td>
<td>&quot;Have you ever tried any form of tobacco in your lifetime?&quot; / “Have you ever used tobacco?”</td>
</tr>
<tr>
<td>CO</td>
<td>8-24</td>
<td>PC- 2 Waves</td>
<td>Have you ever used tobacco?</td>
</tr>
<tr>
<td>AUS</td>
<td>8-24</td>
<td>PC- 3 Waves</td>
<td>Have you ever smoked even part of a cigarette?</td>
</tr>
<tr>
<td>MASA T</td>
<td>11-18</td>
<td>Cross-Sectional</td>
<td>How old were you when you smoked your first cigarette?</td>
</tr>
<tr>
<td>BEL</td>
<td>10-18</td>
<td>Cross-Sectional</td>
<td>Have you smoked at least 100 cigarettes in your life?</td>
</tr>
<tr>
<td>NL</td>
<td>10-24</td>
<td>PC- 8 Waves</td>
<td>Have you ever smoked?</td>
</tr>
<tr>
<td>CVT</td>
<td>9-18</td>
<td>Cross-Sectional</td>
<td>Have you smoked at least 100 cigarettes in your life?</td>
</tr>
<tr>
<td>SWE</td>
<td>8-21</td>
<td>PC- 4 Waves</td>
<td>How frequently have you smoked in the past 12 months? / Do you smoke?</td>
</tr>
<tr>
<td>FIN</td>
<td>16-24</td>
<td>PC- 4 Waves</td>
<td>Have you ever tried smoking?</td>
</tr>
</tbody>
</table>

*PC – Prospective Cohort Study*
Prevalence of Smoking Initiation by Age & Gender

* Significant gender difference (p < 0.05)
What are the Genetic and Environmental Contributions to Smoking Initiation?

Do they Differ Across Adolescence?

Do they By Gender?
Study Population

- 17,324 twin pairs
  - 3047 MZM, 3854 DZM
  - 2323 MZF, 2620 DZF
  - 3922 Opposite Sex

- Smoking Initiation at ages 12-18
Twin Correlations of Smoking Initiation by Age

Both additive genetic and shared environmental effects are important in SI for boys and girls.
Additive genetic effects may also function differently across development by sex.
Are there differences in the sources influencing SI in males and females?

Are the contributions of genetic/env effects equal in males and females?

Are there different sets of genes in males and females for SI?
Models Tested - “Full”

\[ \text{MZM} = \frac{1}{DZM} = 0.5 \]

\[ \text{MZF} = \frac{1}{DZF} = 0.5 \]

\[ \text{DZO} = r_g \times 0.5 \]

\[ r_g \Rightarrow \text{correlation between set of genes that contributes to SI in males \& females is estimated} \]
Submodel 1, $r_g = 1$

$\text{MZM} = 1 / \text{DZM} = 0.5$

$\text{MZF} = 1 / \text{DFZ} = 0.5$

$r_g = 1 - \text{A set of common genetic effects are shared between males/females}$

$\text{Am/ Cm/ Em}$

$\text{Af/ Cf/ Ef}$
Submodel 2, $r_g = 1$ and
A/C/E Equal in Males and Females

$M_{ZM} = 1/ D_{ZM} = 0.5$  

$M_{ZF} = 1/ D_{ZF} = 0.5$

A/C/E- No specific genetic effects in males and females

$r_g = 1$- A set of common genetic effects are shared between males/females
Standardized Parameter Estimates for Males and Females

Variance Component Estimates

- A
- C
- E

Age of Smoking Initiation

Variance Component Estimates

0.0 0.2 0.4 0.6 0.8 1.0

12 13 14 15
Results- Early Adolescence (12-15)

• Moderate additive genetic effects (0.30-0.50) and shared environmental effects (0.43-0.60)

• Magnitude of genetic and environmental effects same in males and females

• Same sets of genes in males and females
Standardized Parameter Estimates

Males

Females

Age of Smoking Initiation

Variance Component Estimates

A  C  E

16  17  18
Results- Late Adolescence (16-18)

• Sex-specific genetic and environmental effects
  – A/C/E and \( r_g \)

• Increasing additive genetic effects in males and females
  – Males- 0.34-0.52
  – Females- 0.33-0.55

• Significant shared environmental effects
  – Males- 0.37-0.55
  – Females- 0.36-0.41

• Weak unique environmental effects
Limitations

• Western samples- Generalizability
  – Nicotine use in low/middle income countries

• Data are currently analyzed as discrete time points
  – Possibly no significant differences across ages

• Analyzed to address effects of shared environment ($r_c$) but difficult to resolve
Implications for Prevention/Education

• Timing of Different Types of Intervention

• General messages directed to both boys and girls may still be valuable in early adolescence

• Gender-specific, personalized messages in later adolescence
  – Including biological information such as genetics could be beneficial

• Adolescent smoking prevention geared towards parents who smoke may improve by including familial/genetic risk
Thank You!

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Prevalence of Smoking Initiation by Gender and Study

* Significant gender difference (p < 0.05)