

# **Rethinking and reframing research on tobacco use in youth: Reflections based on a longitudinal investigation of Quebec adolescents**

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## Abstract

*Cigarette use remains far too prevalent among Canadian youth – over 20% become and remain adult smokers, contributing a large preventable burden on health. Empirical research on tobacco use in youth began to be published in the 1950's and has grown exponentially since then, with hundreds of articles published in the health and social science literatures each year. While much has been learned about the determinants and consequences of tobacco use, as well as about tobacco control interventions for youth, we believe that there is a need to reflect on, rethink, and perhaps reframe youth tobacco use research, moving outside of paradigms and methods that have dominated the field. The purpose of this article is to critically reflect on results emerging from a 12-year longitudinal study of smoking onset in Quebec youth, to identify potential contributions of this work to new ways of conceptualising and framing research on tobacco use in youth. We discuss six issues: adopting a broad socio-ecological perspective in research on determinants; moving towards collaborative interdisciplinary research, moving beyond cross-sectional study designs, recognizing that youth and adult smoking differs, moving towards gender-specific research, and investigating multiple phenotypes.*

**Keywords:** *youth, tobacco, nicotine dependence, Quebec, NDIT Study, longitudinal cohort*

*Acknowledgements*

*This work was supported by an Interdisciplinary Capacity Enhancement (ICE) grant from the CTCRI, and by the National Cancer Institute of Canada with funds from the Canadian Cancer Society. The authors thank Michele Tremblay for her contributions.*

## **Introduction**

Despite recent declines, youth smoking remains a predominant public health issue, (Health Canada 2005). Indeed, it has been so in western countries for a very long time. An article published in the *Lancet* in 1863 (*Lancet* 1863), while claiming tobacco to be “*one of the least hurtful of luxuries*” also stated that “*youth of all countries should abandon it entirely*” (p. 73). A 1906 editorial (*Lancet* 1906) called for public policy action against “*the poisoning of the child with tobacco*”. A century later, cigarette use remains far too prevalent among Canadian youth – over 20% become and remain adult smokers (Statistic Canada, 2005), and collectively contribute a large preventable burden on health. While daily smoking is thought to begin at age 16, the average age at first puff is usually much earlier. Although there is a wide variability, many adolescents have already tried smoking by age 12 years, and in disadvantaged communities the average age of onset can be as young as age 8 years (O’Loughlin et al. 1998). It is known that early smokers consume greater quantities, smoke for longer, are less likely to quit and have a higher risk of premature death. Data from the most recent national Youth Smoking Survey (YSS 2002) indicate that today’s young smokers consume more cigarettes per day than they did eight years ago (8.1 cigarettes per day in 2002, compared to 7.4 cigarettes in 1994), and several recent reports suggest that there is increasing co-occurrence of tobacco

use and other unhealthy and addictive behaviours including alcohol abuse, use of marijuana, gambling, physical inactivity, and poor dietary habits (Audrain-McGovern et al. 2003, Scal et al. 2003, Dierker et al. 2004, De Bourdeaudhuij et al. 1999).

Empirical research on tobacco use in youth began to be published in the 1950s and has since grown exponentially, with hundreds of articles published in the health and social science literatures each year. While much has been learned about the determinants and consequences of youth smoking, as well as about the effectiveness of tobacco control interventions for youth, we believe that there may be a need to reflect, rethink, and perhaps reframe youth tobacco use research, moving outside of paradigms and methods that have dominated the field. To illustrate, an early study, published 50 years ago, entitled “*Smoking habits of schoolboys*” used several of the most common measures still in use today, including number of cigarettes smoked weekly, age at first cigarette, and age of onset. Among other findings, the author (Raven, 1957) reported associations between smoking and social class, low-self-esteem, delinquent behaviours, parental influence, and poorly enforced school policies on smoking – all findings replicated many times over, using essentially similar methods, over the last 50 years.

With a starting premise that fresh approaches to conceptualising and framing research on tobacco use in youth may be needed, the purpose of this article is to critically reflect on the utility of results emerging from the NDIT (Nicotine Dependence in Teens) Study (O’Loughlin et al. 2003a, O’Loughlin et al. 2003b, O’Loughlin et al. 2002a, O’Loughlin et al. 2002b, Karp et al. 2006, Karp et al. 2005) in reframing research on tobacco use in youth. The NDIT Study ([www.nditstudy.ca](http://www.nditstudy.ca)) is an ongoing (1999-2012) longitudinal investigation of adolescents in Montreal, Quebec funded by the National Cancer Institute of Canada. We would argue, based on NDIT work to date, that rethinking and reframing youth-focussed research on

tobacco use will require addressing at least six issues: adopting a broad socio-ecological perspective in research on determinants; moving towards interdisciplinary collaborative research, moving beyond cross-sectional study designs, recognizing that youth and adult smoking differs, moving towards gender-specific research, and investigating multiple phenotypes.

## **Adopting a broad socio-ecological perspective**

There are concerns that tobacco intervention research may have reached a plateau (Hebert 2003). For example, over the last 20 years prevention research has largely focused on testing interventions based on social learning theory, a perspective that may be too limited to result in the design of interventions that have strong and/or sustained impact. By investigating a relatively restricted set of time-bound determinants, risk factor research has likely contributed to the development of narrowly focussed prevention interventions. However it has become abundantly clear that the determinants of cigarette use in youth range from basic biological and physiological factors, to broad societal influences. In addition, and adding to the complexity of understanding youth smoking, researchers have recently begun to adopt the perspective that risk factors for smoking may change along the life course. The set of risk factors underlying cigarette use in childhood or early adolescence may differ from the set of factors that are important in mid- or late adolescence. Finally over and above issues related to research on youth smoking, tobacco as a public health and research issue is a moving target in terms of legislation, bans, policies, social norms and other factors that contribute to constant evolution of the problem and in turn, to its solutions.

Established risk factors for youth smoking to date include among others genotype, socio-demographic factors (age, sex,

family composition, socio-economic status), social environment (family, friends, teachers smoking), psychosocial factors (depression, stress, impulsivity, novelty-seeking, self-esteem, academic performance, weight concerns), perceived benefits of smoking (weight control, being cool, weight control), and the availability and access to cigarettes (school smoking bans, cost, advertising). This wide array of diverse determinants illustrates that investigation of the causes of cigarette use in youth truly warrants perspectives captured in broad socio-ecological models of health determinants. The Ecological Systems Theory (Bronfenbrenner, 1994) for example, posits that complex contextual layers of the environment, such as family, peers, school, neighborhood, and society, interact with individual-level determinants to shape the development of lifestyle behaviors. Below we discuss two determinants of youth smoking investigated in the NDIT Study, that argue the need for widening our perspective on possible determinants of youth smoking beyond the traditional socio-demographic, psychosocial, and social environmental determinants.

### **Nicotine dependence in novice smokers**

One of the most important contemporary research issues related to youth smoking is the question of when symptoms of nicotine dependence (ND) or addiction emerge after smoking onset, and if ND symptoms drive escalating cigarette use in novice smokers. In the 1994 Surgeon General's Report on Youth Smoking (U.S. Department of Health and Human Services, 1994), the natural history of cigarette use onset was described as progressing sequentially through five stages including preparation during which interest in smoking is established, trying, irregular use, regular use, and finally after two to three years, nicotine-dependent smoking in which there is a physiological need for nicotine. This model gained wide acceptance and for many years, the natural history of smoking onset in adolescence

has been conceptualized as progressing sequentially through these five stages (Mayhew et al. 2000, Flay et al. 1993, U.S. Department of Health and Human Services, 1994, Lerman et al. 2003). However work by Joseph DiFranza at the University of Massachusetts in the early 2000s (DiFranza et al. 2000, DiFranza et al. 2002, DiFranza et al. 2004) first raised concerns that symptoms of ND can in fact occur very early after cigarette use onset, raising questions about the validity of the 5-stage model. In more recent work, DiFranza et al contend that withdrawal symptoms in young smokers may appear at very low levels of smoking, they may be relieved for many days by one cigarette, and they may not be felt until days after the last cigarette (DiFranza et al., accepted; DiFranza et al., accepted).

Using data from the NDI Study, we characterized early onset according to the sequence and timing of milestones related to both cigarette use (first inhalation, first whole cigarette, monthly, weekly, daily smoking, lifetime consumption of 100cigarettes) and ND symptoms (physical addiction, mental addiction, tolerance, craving, withdrawal symptom, time of conversion to ICD-10 tobacco dependence) (Gervais et al. 2006). We found that many novice smokers progress quickly to inhalation after first puff, and that ND symptoms including cravings, develop rapidly thereafter, well before both weekly and daily smoking or a lifetime consumption of 100 cigarettes. Rather than being an innocuous event without serious consequences, first puff may represent the beginning of a process that leads rapidly to the development of ND symptoms and to escalating cigarette use in many youth.

In addition to supporting DiFranza's contentions, this description of the natural history of the onset of smoking and ND symptoms challenges long-held beliefs among researchers that smoking onset progresses sequentially through five stages (Flay et al. 1993, U.S. Department of Health and Human Services 1994, Fleming et al. 2002), that ND does not develop

until after two years of regular heavy smoking, and that a lifetime consumption of 100 cigarettes is a central marker of “becoming a smoker” in youth. It suggests that etiologic and prevention research as well as surveillance should incorporate the notion of early onset of ND after first puff. It may well be for example, that cessation interventions are needed by some young people soon after first puff to manage symptoms of ND that occur early on during the onset process, and to prevent escalation of cigarette use.

### **Genetic risk factors**

There is growing interest in whether or not individuals with specific genotypes are at greater risk of tobacco use uptake and ND, and more specifically whether genes interact with the environment or with other genes to increase risk. Evidence from twin, adoption, and linkage studies in fact suggests a strong genetic component to tobacco use initiation, persistence, dependence, and cessation, with 28-85% of the variation in smoking related to inherited factors Tyndale 2003). Similar to other complex health outcomes, tobacco use uptake and ND are likely to be polygenic, caused by many DNA variations, each one of which has only a small effect on phenotype. Interest in genetic factors to date has focused primarily on neurotransmitter pathways (i.e., dopaminergic and serotonergic neurotransmitter and receptor systems), nicotine metabolizing enzymes (i.e., *CYP2A6*, *CYP2D6*, *CYP2E1*), and neuronal nicotinic receptors (i.e., *CHRNA4*, *CHRNA7*, *CHRNA2*), although evidence for a contribution of specific genes to smoking behavior remains modest (Munafò and Flint 2004).

NDIT data on genetic risk provide information on mechanisms underlying the acquisition of smoking in youth that may eventually be useful in conceptualizing tobacco control programs (O’Loughlin et al. 2004). In contrast to case control



studies in adults suggesting that inactive alleles in the gene that codes for the hepatic cytochrome P450 2A6 (*CYP2A6*) protect against ND and higher levels of cigarette consumption, we found that adolescents in the NDIT Study with 1-2 copies of *CYP2A6*\*2 or \*4 (i.e., slow nicotine metabolizers) are at substantially increased risk of becoming ND, but smoke less once dependent (O'Loughlin et al. 2004). We have also genotyped *CYP2B6*, another cytochrome P450 enzyme that metabolizes nicotine, although with less efficiency than *CYP2A6*. In preliminary analyses using NDIT data, *CYP2B6* variants were associated with increased rates of conversion to dependence, and the effect was larger in *CYP2A6* slow metabolizers, suggesting a possible gene-gene interaction. These gene-level factors, in interaction with other risk factors may play a role in determining or modulating cigarette use or ND trajectories.

## Moving toward interdisciplinary research

Increased appreciation of the complex, multidimensional nature of tobacco use behaviour has encouraged researchers to consider a new research paradigm in tobacco control research. While distinctions are made between multi-, inter-, and trans-disciplinary research (Stokals et al. 2003), the basic premise is that, rather than working in disciplinary and institutional silos, researchers should work jointly using shared conceptual frameworks that draw together discipline-specific theories, methods and measures (Rosenfield 1992; Kahn and Prager 1994). Input from many varied disciplines including genetics, neurology, psychology, pharmacology, population health, epidemiology, health policy, medicine, marketing, gender-based research, anthropology, political science, ethnography, and economics is needed. Interdisciplinary scientists should have a solid scientific foundation with excellent conceptual, methodological, and research design skills; a predisposition to cross-analytic and

disciplinary boundaries; acceptance and respect for different disciplines, excellent interpersonal and communication skills; and a willingness to collaborate rather than compete (Hebert 2003). While bringing researchers together from disciplines as divergent as genetics and evaluation of public policy is challenging, the premise is that interdisciplinary melding of research paradigms, knowledge, and methods will permit deeper understanding of tobacco use, prevention, and cessation, and in turn development of more relevant, effective programs and policies that will reduce the burden of tobacco use.

The NDIT Study underscores the potential contribution of increased interdisciplinarity in tobacco control research, through linking the epidemiology of youth smoking to the basic science of genetics, to the developmental psychological concept of the life course, and to public health. Methodologically NDIT work has used both quantitative and qualitative methods such as focus groups, to provide insight from the perspectives of young people on their experiences with tobacco. This work has helped sharpen and refine quantitative measures – for example, by showing that some ND symptoms measured using common ND tools are not experienced by youth, or are experienced differently than among adults (O’Loughlin et al 2003).

## **Moving beyond cross-sectional study designs**

Whereas hundreds of studies that investigate the determinants of youth smoking have relied on cross-sectional research designs, in the last 10 years longitudinal studies have begun to proliferate in the literature, with at least 45 such studies published in the last five years. Longitudinal designs are necessary to address research questions about the natural history of smoking behaviors, cigarette use onset trajectories, the predictive validation of measurement tools, and time-dependent

risks and outcomes. They permit incorporating the notion that the context or environment of youth smoking is constantly changing, as the world changes around them and as their own physical and psychological development shapes their changing interactions with their environments. Finally longitudinal designs are useful in understanding the long-term outcomes of intervention trials, notably demonstrating long-term failure of preventive intervention such as in the Hutchinson trial (Peterson et al. 2000). Overall we could adopt the view that, except in the context of public health surveillance, the age of cross-sectional inquiry into the determinants of youth smoking is drawing to a close. It will be a challenge to ensure that funding agencies recognize the importance of this shift, and to develop funding mechanisms that support complex, large scale longitudinal research in youth.

There is increasing interest in characterizing developmental trajectories of cigarette use and ND by quantitatively modelling developmental pathways over time using longitudinal databases. Our work and that of others have begun to find consistent patterns in cigarette use onset trajectories. Chassin et al. (Chassin et al. 2000) identified six trajectory patterns in participants aged 11-31 years, including stable abstainers, erratic smokers, early stable and late stable smokers, quitters and experimenters. Colder et al. (Colder 2001 et al.) identified five patterns in adolescents aged 11-16 years, including early rapid escalators, late moderate escalators, late slow escalators, stable light smokers, and stable puffers. Audrain-McGovern et al. (Audrain-McGovern et al. 2004) identified four patterns among youth in grade 9 to 12 including never smokers, experimenters, earlier/faster adopters, and later/slower adopters.

In the NDIT study, although individual trajectories were highly heterogeneous, we identified four classes of smoking intensity trajectories in 369 subjects (mean age 13 years) who initiated cigarette use during follow-up, including low-intensity,

non-progressing smokers (72% of initiators), and slow, moderate, and rapid escalators (11%, 12%, and 6% of initiators, respectively) (Karp et al. 2005). Participants who escalated cigarette use were at increasingly high risk of becoming tobacco dependent over time. Many rapid escalators for example converted to tobacco dependence soon after first puff and after about one year, 90% had done so.

Importantly risk factors associated with specific trajectory patterns can be identified. Gender, poor academic performance, and having more than half of friends who smoke at smoking onset independently predicted development of trajectory pattern in the NDIT Study (Karp et al. 2005). Not surprisingly, persons with a greater number of risk factors escalate cigarette use more quickly, and those with fewer risk factors tend to maintain lower levels of smoking (Chassin et al. 2000, Audrain-McGovern et al. 2004).

## **Recognizing that youth and adult smoking differ**

One pitfall that may impede rapid progress in youth-focussed tobacco control research is the assumption that the models applied to, and the learnings from, adult-based research are fully applicable to youth. A striking example is that, while cigarette use patterns in adults usually vary little from day-to-day, youth, and especially novice smokers, often have sporadic and irregular patterns of cigarette use. Young smokers share cigarettes with their friends, not necessarily smoking a whole cigarette. They have more environmental constraints than adults, both at home and at school. Especially during early onset, novice smokers may not recognize ND symptoms as such, and they may experience and/or report ND symptoms differently than adults. Finally although youth begin smoking for a variety of specific reasons, these can change over time as ND symptoms emerge

for example. However, although exposure in novice smokers tends to be lower than in adults and the patterns of cigarette use differ, there is evidence that the physiological effects of nicotine may not be all that different. Youth inhale and absorb as much nicotine per cigarette as adults, even with first few cigarettes (McNeill et al, 1987). These kinds of findings suggest a need for development of literature that recognizes how youth smoking mirrors but also differs from that of adults, and how the youth smoking evolves into adult smoking. In particular they call into question notions such as defining an adolescent smoker as one who has consumed  $\geq 100$  cigarettes in their lifetime (a relatively late milestone in the natural history on cigarette use onset (Gervais et al. 2006), but one that is commonly used in surveillance and in studies on cessation) and suggests that surveillance and research in adolescents should include smokers in the earliest stages of smoking onset and nicotine dependence.

## **Moving towards gender-specific research**

NDIT data point to gender differences in smoking acquisition. While boys were at higher risk for the rapid escalation trajectory, girls were at higher risk for the slow and moderate escalating patterns (Karp et al. 2005). The incidence rates for several early cigarette use and for most ND milestones were higher in girls (Gervais et al, 2006). These data support those of DiFranza et al. (DiFranza et al. 2002) who showed that the median latency from monthly smoking to one or more symptom on the Hooked on Nicotine Checklist, was 21 days for girls and 183 days for boys. However, the NDIT study found little difference by sex in late cigarette use milestones and perhaps more importantly, in attainment of tobacco dependence.

There are several plausible explanations for early gender-related differences in smoking acquisition and nicotine dependence. First, earlier reporting of ND symptoms in girls may

relate to higher levels of cigarette use early in the onset process. Indeed, NDIT data suggest higher incidence rates of inhalation, smoking a whole cigarette, and monthly smoking among girls compared to boys. Second, girls may be more sensitive to the effects of nicotine than boys. Fallon et al. (2005) showed that nicotine patch administration affected brain metabolism differently in women than in men. Women had higher brain metabolism than males and the nicotine patch decreased these gender differences. Third, it may be that girls are more sensitive or attuned to body signs and symptoms and because they are more attuned, they may be more likely to recognize, articulate, and report ND symptoms they experience as related to their cigarette smoking. Whatever the explanation, gender differences early on in the smoking onset process warrant attention so that prevention and cessation interventions can take important differences into account.

## **Moving towards investigating multiple phenotypes**

NDIT data suggest that research on youth smoking may benefit from investigating outcomes beyond those focussed on cigarette use, to aim for increased understanding of other cigarette-related phenomena such as ND symptoms, cravings, tolerance, withdrawal, and self-medication through cigarette use. Future longitudinal studies will be key to increasing understanding of the trajectories of co-occurrence and interactions between cigarette use and other substances or behaviours. We know little for example about how ND trajectories are influenced by cannabis use trajectories, an area of considerable concern because of the growing mixed use of tobacco and cannabis (YSS 2002). Finally there may be opportunities for cross-learning between tobacco research and research into other public health priority areas such as physical inactivity and obesity.

## Conclusion

This article argues for new approaches to research on tobacco use among youth. The issues we have discussed in this article could be viewed as beginning to deconstruct and reframe our understanding of the determinants and consequences of tobacco use, and may lead toward new implications for public health policy and intervention. Over and above the promising research directions highlighted above, we argue that the key to advancing knowledge about youth tobacco use, will be our enthusiastic submission to strong criticism, from within and outside our disciplinary boundaries. Interestingly, the concluding line of Dr. Raven's 1957 article was about smoking by girls: "*Replies from the headmistresses of 3 public (girls') schools suggested that the problem does not exist in these schools. As one said, "it is no longer considered clever to smoke."*" (p. 1141). Fifty years later, it is clear that Dr. Raven – who was shown, over the subsequent five decades of research, to have been right about so much – was wrong about this, or at least is no longer right. Instead of congratulating ourselves on gains in knowledge, we should perhaps ask ourselves: what else have we been wrong about over the last 50 years?

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