

The Science and Ethics of Research on Smoking Behavior

NWABR EDUCATION PROGRAM

NORTHWEST ASSOCIATION FOR BIOMEDICAL RESEARCH

GENOME SCIENCES EDUCATION OUTREACH

UNIVERSITY OF WASHINGTON

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This Project was supported by Science Education Drug Abuse Partnership Award R25 DA013180 from the National Institute on Drug Abuse (NIDA), National Institutes of Health (NIH) and a Science Education Partnership Award from the National Center for Research Resources (NCRR), National Institutes of Health, 1R25RR016284-01A2. Its content is solely the responsibility of the authors and does not necessarily represent the official views of NIDA, the NCRR, or the NIH.

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Forward

This unit was developed through the collaboration of two Seattle-based science education groups, the Northwest Association for Biomedical Research (NWABR) and Genome Sciences Education Outreach (GSEO) at the University of Washington (UW). Funding for NWABR was provided by a Science Education Partnership Award from the National Center for Research Resources, National Institutes of Health, 1R25RR016284-01A2. GSEO was funded by a Science Education on Drug Abuse Partnership Award from the National Institute on Drug Abuse, National Institutes of Health, R25DA013180.

NWABR has a long history of promoting the teaching of bioethics in secondary science classes through the development of curricula and teacher professional development. Their module, *An Ethics Primer*, is a centerpiece of their teacher workshops and a definitive resource for teaching this topic. GSEO involves secondary teachers and students in doing authentic research in their classrooms and discussing related bioethical issues. Their curriculum, *Investigating the Effects of Genes and the Environment on Smoking Behavior*, involves students in designing and implementing a research investigation of factors that influence whether people become highly addicted smokers. The collaborative efforts of NWABR and GSEO have resulted in an ethics unit that explores the biology of smoking behavior and many of the societal and ethical issues related to carrying out research on this topic. This unit can be used in a variety of classes and contexts, including science, health, or social studies classes. In addition, several of the lessons from this unit are integrated into the *Investigating Smoking Behavior* curriculum so students can consider the societal and ethical issues associated with the research they are doing.

Introduction

Overview of Unit

What are the benefits of doing research on smoking behavior? What are the drawbacks? Who benefits from such research? Why is research on smoking and other addictive behaviors so often controversial? Can we hope to resolve these issues and move forward with the research? This unit addresses these and other questions.

The Science and Ethics of Research on Smoking Behavior has three main objectives:

1. to teach students about the many factors, both environmental and genetic, that contribute to a complex trait like smoking behavior
2. to help students understand the potential benefits and risks of research on smoking behavior
3. to challenge students to consider the ethical issues associated with this research.

Teaching ethics to high school students within the context of science is engaging for students and helps motivate them to learn complex scientific concepts. Learning about ethics helps students develop critical thinking and decision-making skills that they can apply in many real world situations. This unit helps students understand the need to critically evaluate research based not only on its scientific merit but also in light of the ethical issues involved. This unit consists of five lessons:

F1: Weyco Tobacco-Free Policy: Can Doing Good Cause Harm? Estimated time: 50 minutes	Students analyze the true case of a company that adopted a mandatory tobacco-free policy for all its employees. Students learn about ethical principles and are able to identify the ethical questions raised by this case.
F2: Why Do Research on Smoking Behavior? Estimated time: 20 minutes	By assembling a jigsaw puzzle, students learn the main reasons scientists conduct research on smoking behavior, examples of how such research has been used, and ethical issues related to the research.
F3: The Science of Nicotine Addiction Estimated time: 100 minutes	Students learn about the physiological effects of nicotine on the body and brain, neurotransmission basics, the stages of smoking behavior, why it is so difficult to quit smoking, and currently available smoking cessation treatments.
F4: Multifactorial Traits Estimated time: 75 minutes	Students learn that many genes and environmental factors contribute to complex behaviors like smoking. They look at smoking behavior in a pair of identical twins and play a game that introduces them to the concept of risk.
F5: What is a Useful Genetic Test? Estimated time: 100 minutes	Students investigate one application of research on smoking behavior--genetic testing to match people to the cessation treatment most likely to succeed for them. They identify and explore the ethical issues related to testing for complex behavioral traits.

Background on Smoking Behavior and its Societal Impact

Smoking is a Societal and Public Health Issue

Tobacco kills almost 440,000 people in the U.S. each year. The death toll includes users of tobacco, people who are exposed to secondhand smoke, and victims of fires started by burning cigarettes. Smoking during pregnancy can lead to miscarriage, premature delivery, low birth weight, and developmental delays during childhood. Secondhand smoke in the home can lead to or aggravate asthma in children and may contribute to sudden infant death syndrome. In the U.S. over \$138 billion/year is spent on health care for smoking-related ailments (NIDA, 2006).

In 1964, the Surgeon General's report on the health risks of tobacco was published (National Library of Medicine, 2008). It implicated cigarette smoking in increased lung cancer, chronic bronchitis, emphysema, and coronary heart disease in smokers compared to non-smokers, as well as decreased birth weight of babies born to people who smoke. Data collected by the Center for Disease Control (CDC) showed a dramatic decline in the number of adult smokers in the United States following release of the report, from 41.9% in 1965 to 20.8% in 2004 (CDC, 2007, see Figure 1).

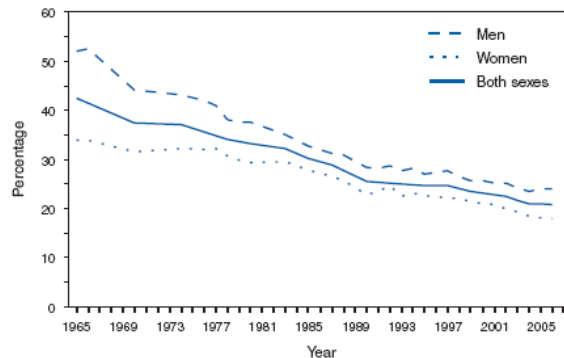
Several policies contributed to the decline in smoking between 1965 and 2004, including increased taxation on tobacco products, a ban on smoking in public places, and anti-smoking advertising. However, since 2004, the rate of decline has leveled. This leveling has been attributed to several factors. The most effective deterrent to smoking cigarettes is their price, which has remained stable since about 2002. To counteract increased federal taxes on tobacco, cigarette companies lowered their prices. In recent years there has been no increase in federal tax to counterbalance pricing changes by tobacco companies. In addition, there has been a dramatic cut in federal funding to states for programs to keep children from starting smoking and to help people quit (Kaufman, 2007). Thus, current federal policies need to be restructured if the decline in national smoking rate is to continue.

Smoking is a Complex Trait

The term, "smoking behavior," covers the gamut of tobacco-related behaviors, including early experiences when people are experimenting with smoking; when, where, and how much a person smokes; their level of addiction to nicotine; whether a person is able to quit; whether they experience relapse after quitting; etc. Because of its detrimental impact on health, smoking has been the subject of extensive research for decades. In tackling this complex topic, researchers must consider the wide variation in people's smoking behavior in order to address the following kinds of questions: Why do some people become addicted to nicotine almost immediately following initiation (trying it out) while others smoke for several months or years and then stop without difficulty? Why do certain cessation programs work for some people and not others?

Smoking behavior is so variable because it is a multifactorial trait, determined by many genes and environmental factors. Studies that compare smoking in monozygotic and fraternal twins allow scientists to estimate the genetic contribution to becoming a regular smoker, which is about 56%, while the contribution of environmental influences is 44%. Many different genes contribute to inter-individual variation in smoking behavior, and the contribution of most genes is bound to be small. Thus, we are unlikely to find a single gene variant that accounts for a person becoming highly addicted to nicotine, but rather will identify variants in many different genes that all have a small effect on smoking behavior.

FIGURE. Estimated percentage of persons aged ≥ 18 years who were current smokers,* by sex — National Health Interview Survey, United States, 1965–2006



*During 1965–1991, current smokers were defined as persons who reported smoking at least 100 cigarettes during their lifetimes and who, at the time of interview, reported smoking (“Have you smoked at least 100 cigarettes in your entire life?” and “Do you smoke cigarettes now?”). In 1992, the definition changed to more accurately assess intermittent smoking (i.e., smoking on some days) and included persons who reported they smoked either every day or some days (“Do you now smoke cigarettes every day, some days, or not at all?”)

Figure 1. Reprinted in its entirety from Morbidity and Mortality Weekly Report (MMWR) Weekly, November 9, 2007

Environmental factors, such as whether a person’s parents or peers smoke, the cost of cigarettes, and establishment of smoke-free areas also make a significant contribution to whether people smoke.

How do scientists determine which genes affect smoking? The traditional approach is to propose candidate genes based on our understanding of how nicotine interacts with the body, and then investigate whether these genes are actually involved. Like other addictive drugs, nicotine interacts with a neural pathway in the brain called the reward pathway, which is important for reinforcing behaviors that are necessary for survival. Nicotine binds to receptors on neurons of the reward pathway, resulting in the release of the neurotransmitter, dopamine, by these neurons. Dopamine, in turn, binds to receptors on other neurons, which ultimately leads to the rewarding effects of smoking often reported by smokers, such as relaxation or an increased ability to focus. Possible candidate genes for modifying smoking behavior include those that code for nicotine receptors, dopamine receptors, enzymes involved in dopamine synthesis and breakdown, and the enzymes that break down nicotine.

In a candidate gene study, scientists test whether a variant in a candidate gene is associated with a particular trait by comparing the prevalence of the variant in experimental research subjects who have that trait and control subjects who do not. This approach has been used extensively to identify associations of candidate genes with different aspects of smoking and is also used to study other addictive drugs and behaviors. Although some studies have shown a small effect of certain alleles, these results have not always been reproducible.

The whole genome approach is another method that can be used to identify genes associated with a particular trait. Using this method, genomic DNA samples from case and control subjects are surveyed for genetic variants throughout the genome using microarray technology. The data from the two groups are compared to look for genetic variation that is more strongly associated with cases or controls. This method has been applied in smoking-related studies, including studies with highly addicted smokers, smoking-associated diseases, and the effectiveness of different cessation programs (Thorgeirsson et al,

2008). This approach may ultimately be more successful than candidate gene studies because it does not depend on assumptions made at the start of the study about which genes may be involved.

Potential Benefits of Genetic Studies on Smoking Behavior

Learning about genetic variations that influence smoking behavior will deepen our understanding of the many effects of nicotine on the body, including addiction. One application of this knowledge is the development of a genetic test. In the case of smoking, genetic testing might be helpful for two applications (from Fullerton, 2008):

1. identifying people whose genotype makes them more susceptible to becoming addicted to nicotine, so they can avoid ever starting to smoke
2. determining which cessation program would be most appropriate for an individual, based on genotype

Understanding why people become addicted to nicotine might be useful in developing cessation methods. However, some applications of this knowledge raise strong ethical concerns. For example, suppose that we routinely tested children for their susceptibility to nicotine addiction. Would children who don't have the susceptibility variants then believe they are less likely to become addicted, so it's OK for them to smoke? The health risks of cigarettes affect all smokers, whether or not they are addicted to nicotine, so the only effective way to avoid these risks is not to smoke. In contrast, using genetic testing to select appropriate cessation methods seems less problematic. The challenge for this application lies in whether we will understand the genetic factors related to cessation well enough to develop reliable genetic tests.

Potential Risks of Genetic Studies on Smoking Behavior

Applications of research on the genetics of smoking behavior could lead to stigmatization of and discrimination against individuals and groups. In our anti-tobacco society, being a smoker carries many stigmas—being perceived as uneducated, weak-willed, indifferent to your own or other people's health, etc. Imagine what the stigma might be for someone who is genetically predisposed to becoming a highly-addicted smoker! Even for people who are not smokers, such a diagnosis could result in discrimination. Here are some possible scenarios:

- Discrimination in the workplace or in obtaining health or life insurance. Historically, people have been denied jobs, health insurance, and life insurance coverage because of pre-existing conditions, including genetic conditions (e.g. Huntington's Disease). The Genetic Information Nondiscrimination Act (GINA), recently passed by Congress and the Senate and signed by President Bush in 2008, is intended to prevent discrimination based on genetics in the workplace and in obtaining health insurance (but does not cover life insurance, long-term care insurance, or disability insurance). It is still too early to assess the impact of this act.
- Assumptions about inherited risks for other stigmatizing conditions based on genes for nicotine susceptibility. Many of the genes that are candidates for nicotine addiction, such as genes coding for proteins in the reward pathway, are also potential candidates for addiction to other drugs, as well as schizophrenia, compulsive gambling, alcoholism, sexual promiscuity, etc.

(Genes that affect more than one phenotype are said to be pleiotropic). A genetic variant associated with smoking behavior might also be associated with these other behaviors. Genetic testing for nicotine susceptibility could therefore reveal a predisposition for other behaviors, which could lead to stigmatization, even if a person did not have those behaviors.

- Stigmatization of a group based on prevalence of a nicotine susceptibility gene. Genetic variants can differ in prevalence among different ethnic and racial groups. If a particular variant associated with smoking behavior is more common in a particular group, this could lead to stereotyping of that group as being more prone to nicotine addiction (or other behaviors associated with that variant).

Applying Ethical Principles to Resolve Complex Issues

Principles that Guide Biomedical Research

Discussion and evaluation of ethical issues are woven into each of the lessons in *The Science and Ethics of Research on Smoking Behavior*. Although there are many different approaches for consideration of ethical issues, this unit focuses on principle-based ethics because it is readily applied in a high school classroom and is the approach most frequently used in medicine. NWABR's *An Ethics Primer*, discussed earlier, provides a comprehensive discussion of ethical perspectives, ways to integrate ethical discussions into a science classroom, and sample lessons. This free resource can be downloaded at <http://www.nwabr.org/education/ethicslessons.html>.

Principle-based ethics was originally defined by two philosophers, Tom Beauchamp and Jim Childress, who identified four principles that guide moral conduct. These four principles—autonomy, justice, non-maleficence, and beneficence—have been widely adopted in medical practice to guide decision-making regarding patient care. They are also the basis of the Belmont Report, a report published in 1979 by a team of doctors, scientists, bioethicists, and lawyers to guide the treatment of human subjects in research. These four principles, as applied to human subject research, are defined below.

- **Autonomy** refers to a person's right to make decisions regarding his/her own health and future. This principle is the basis of informed consent, the process of informing potential research subjects about a study so they can decide whether or not to participate in the study.
- **Justice** refers to equitable distribution of both the benefits and the costs of a research study. For example, it would violate the principle of justice to gather data on one socioeconomic group in order to benefit a different socioeconomic group.
- **Beneficence** literally means "to give benefit." This principle guides researchers to develop studies that promote the welfare of individuals and society.
- **Non-maleficence** means to do no harm. The Belmont Report discusses non-maleficence as an aspect of beneficence. This principle provides guidance to researchers on different levels, such as designing research studies so there is minimal harm to the research subjects and considering potential outcomes of a line of research to avoid negative consequences.

Introducing Ethical Principles in a High School Classroom

One approach for involving students in ethical discussions is to present them with a case study that invokes an ethical dilemma. A case study can consist of a short fictional scenario, a newspaper article, or a classic case from the scientific literature (such as the Tuskegee Syphilis Study). Lesson 1 in this unit is based on an actual event involving Weyco, Inc., a health insurance company that instituted a tobacco-free policy for its employees.

Analyzing the ethical issues in a case study requires careful consideration of the different aspects of the case. The following steps are often used to guide students' analysis:

- defining the ethical question(s)
- identifying relevant facts
- identifying stakeholders
- considering stakeholders' values as they pertain to the case.

Depending on the goal of the assignment, students may then identify possible solutions to the case and analyze the solutions in the context of the four ethical principles to determine the best solution(s). In the Weyco case, students discuss one ethical question related to the case in terms of the four ethical principles.

Application of the ethical principles to a complex dilemma models how ethical issues are resolved in the medical community. Students' participation in ethical discussions helps them develop respect for alternative views of the world and other people's values. It teaches students to use critical thinking to resolve complex decisions, and to weigh consequences and make reasoned judgments based on what they have learned.

This unit exposes students to many of the scientific and ethical issues related to carrying out research on smoking behavior. It helps them to understand that these issues are not always clear cut and may be viewed differently by different people, depending on their culture, beliefs, education, and level of involvement in a situation. As society moves toward the notion of the "personal genome" it becomes increasingly important that people understand that complex diseases or behaviors are affected by multiple genes and environmental factors. Throughout the unit, students learn important features of complex traits, including the contribution of both genetic and environmental factors, the pleiotropic nature of many genes, and the potential impact of genetic information on individuals, families, and groups of people. Students develop skills in analyzing related ethical issues and applying their understanding of the science and ethics to resolve these issues. These activities are not merely academic exercises—for many students they are lessons that they will one day apply in their own lives.

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ACTIVITY F1

Weyco Tobacco-Free Policy: Can Doing Good Cause Harm?

OVERVIEW

In this lesson, students consider the ethical issues related to an actual event, in which a health insurance company, Weyco, Inc. adopted a tobacco-free policy for all its employees. This lesson introduces or reinforces students' understanding of concepts and terms in ethics, including values, morals, ethics, ethical questions, stakeholders, and principle-based ethics.

Time

70 minutes.

Learning Objectives

Students will learn:

- about concepts and terms in ethics, including values, morals, ethics, ethical questions, stakeholders, and ethical perspectives
- about ethical principles: autonomy, beneficence, non-maleficence, and justice
- how to analyze the interplay of these principles, as they apply to the Weyco case study
- how the rights and needs of a community and an individual may sometimes conflict
- that quitting smoking can be very difficult for some people, even when the consequences of not quitting are profound

Materials

for each student

- Transcript of *Whose Life Is It Anyway?*
- Stakeholder Role description cards (equal numbers of the 7 stakeholder cards, one card per student.)
- Student Sheets F1.1 and F1.2
- Copies of *Tobacco Fact Sheet* and *A Summary of Ethics*

for the class

- Transparencies of Overhead Masters F1.1, F1.2, and F1.3
- Computer and projector

Tips & Tricks

- Be sure to check that you can stream the video before class.

Getting Ready

- 1** Download *An Ethics Primer* at <http://nwabr.org/education/ethicslessons.html>
- 2** Review the chapter, *Ethics Background* in the primer.
- 3** Photocopy materials for students.
- 4** Prepare transparencies of Overhead Masters F1.1, F1.2, and F1.3.
- 5** Access Morley Safer's report on the Weyco story, *Whose Life Is It Anyway?* This video can be streamed, but not downloaded. http://www.cbsnews.com/sections/i_video/main500251.shtml?id=994270n
- 6** If unable to access the video, you can access a transcript by clicking on the "Whose Life is it Anyway?" link below the video window (the url for the transcript link is given in the references section below). Page 1 of the transcript has the same information as the video.

Presenting the Activity

Day 1

- 1** To engage the class, ask: "How many of you are employed or have applied for a job?" Use this question to prompt a discussion about what type of questions are asked by employers when considering job applicants and what behaviors are expected on the job. Further questions for students include:
 - a.** What are some general characteristics employers expect to see in their employees?
 - b.** How do you expect to be treated by your boss?
 - c.** How much control do you think your boss should have over your activities at work? Outside of work?
 - d.** Does your boss have the right to know how you spend your time off the job?
- 2** Show the video, *Whose Life Is It Anyway?*, or give students a copy of the first page of the transcript to read. Tell the students to think about how Weyco employees might feel about the no-smoking policy.
- 3** Use the overhead, *A Summary of Ethics Terms* to introduce the terms *values*, *morals*, *ethics*, and *stakeholders*. Use examples from the Weyco case to explain these terms.

Tips & Tricks

- Students may be confused by the difference between values, morals, and ethics. A more detailed discussion is provided on p. 27 of *An Ethics Primer*.
- A list of values and their definitions are provided on pp. 42-45 of *An Ethics Primer*. Review these qualities if your students are confused about what values are.

Presenting the Activity, Day 1, continued...

- **Values:** qualities that are important and worthwhile. For example, Howard Weyers values the productivity of his employees.
- **Morals:** codes of conduct that govern behavior. For example, Mr. Weyers' actions in part reflect the moral code of doing what is helpful to other people.
- **Ethics:** an approach that provides a systematic, rational way to work through dilemmas and come up with the best source of action.
- **Ethical questions:** questions that consider conflicting moral choices. In this case, one ethical question is whether a company should have a policy that prohibits all smoking by its employees.
- **Stakeholders:** individuals or groups who are affected by the outcome of an ethical question. The many employees of Weyco are stakeholders in this case.

4 Lead the class in making a list of all the individuals and groups who may have a concern or stake in the outcome of the Weyco policy. Write the word, "Stakeholder" on the board, and record student suggestions under this title. The student list should include individuals/groups that are either directly or indirectly impacted by this policy.

5 Tell students that they will now become stakeholder representatives. Put them in seven groups (one for each prepared stakeholder role). The prepared roles may not include all those listed on the board, but the student-generated list should include all of these:

- Employees and their families
- Weyco company representatives
- Medical professionals and research scientists
- Society
- Representatives of the state legislature or senate
- Tobacco company representatives
- Health insurance companies

6 Give each group the following materials:

- Set of identical stakeholder role description cards (one for every student in the group)
- Stakeholder Values and Concerns Summary Sheet (one for every student in the group).
- Tobacco Fact Sheet (one per group)

Tips & Tricks

- Ask students to suggest more familiar words for the four ethical principles. Some definitions are provided in *An Ethics Primer*. Your students may be more comfortable using these familiar words in place of the formal terms.

Presenting the Activity, Day 1, continued...

- 7 Ask the student groups to read the stakeholder role description and discuss the concerns and values that are important to the stakeholder. Then instruct them to complete the Stakeholder Values and Concerns Summary Sheet as a group (but each student needs to complete his/her own copy).

Day 2

- 1 Begin the class by grouping students as they were yesterday in like stakeholder groups to review their viewpoint and come to consensus.
- 2 Once the students have a clear understanding of the stakeholder viewpoint, redistribute them into mixed groups consisting of one student from each stakeholder group. There should be at least seven members in each of the new groups, with at least one representative for each stakeholder.
- 3 Pass out Student Sheet F1.2, *Weyco Tobacco-Free Policy Case Study Analysis*.
- 4 Ask the students to review the case in their new groups. Each stakeholder representative should share his concerns and values, using the summary sheet completed in the previous activity.
- 5 Introduce (or review) principle-based ethics to your students and discuss the four principles usually considered in a principles-based ethical perspective, autonomy, justice, beneficence, and non-maleficence.
- 6 Ask each group to complete Student Sheet F1.2 together. Each student should make a record on his/her own sheet. This sheet asks students to list the facts of the case, describe the concerns and values of each shareholder, identify three ethical questions related to the case, and discuss at least one of those questions from a principles-based ethical perspective. You may want to complete the table for one stakeholder and discuss one ethical question. If you prefer, you can substitute the "4-box" on page 63 of *An Ethics Primer* (2008) for the second page of Student Sheet F1.2.
- 7 Once the groups have completed their discussions and filled out Student Sheet F1.2, give them time to briefly discuss their group's work with the rest of the class. Have each group elect a spokesperson to share key points from the group discussion. The discussion should include:
 - a. What facts are presented in this case?
 - b. What are the values of the stakeholders? Why?
 - c. What ethical questions are presented in the case based on the Principles perspective? What makes them ethical questions?

Possible Student Responses to Student Sheet F1.1: Stakeholder Values and Concerns Summary Sheet

- 1** List the important values and concerns of your assigned stakeholder with regard to the tobacco-free policy. Express your answer in the 'voice' of the stakeholder.

Answers will vary. See possible responses to Question 2 of Student Sheet F1.2.

- 2** Describe how this stakeholder might benefit from the Weyco tobacco-free policy.

Answers will vary for each stakeholder. For example:

- *Employees and their families benefit from a policy that promotes improved health.*
- *Medical professionals and research scientists benefit from a policy that promotes better health for one sector of society, since this is a goal they share.*
- *Health insurance company representatives benefit from improved health of their customers, since this reduces their costs.*
- *Howard Weyers benefits from decreased health-related expenses to his company and increased productivity.*
- *Society benefits from increased productivity/decreased health care costs.*
- *Tobacco company representatives seem not to benefit from this policy, since it will result in fewer people smoking. However, the backlash to this policy may result in an increase in society's support for "smokers' rights."*
- *A state legislator might benefit because the policy raises issues regarding the balance between personal liberties and health care costs that are borne by all of society.*

- 3** Describe how this stakeholder might be harmed by the tobacco-free policy.

Answers will vary for each stakeholder. For example:

- *Employees and their families would be harmed if a family member lost his/her job.*
- *Medical professionals and research scientists might be harmed if such policies encouraged a "right to smoke" attitude among society, which could affect how their work is valued and funded.*
- *Health insurance company representatives and their companies might be harmed if their customers adopted a "right to smoke" attitude.*
- *Howard Weyers might be harmed if his company lost valuable employees because of the policy.*
- *Society might be harmed by the limitation to individuals' right to make choices for themselves.*
- *Tobacco company representatives might be harmed if such a policy caused a decrease in the number of cigarettes sold.*
- *A state legislator might be harmed by anger among his/her constituents as a result of the policy.*

- 4** What do you think are the motivations of Weyco to have only non-smoking employees?

The main motivation, expressed by Howard Weyers in the video, is to save business expenses, which might include the cost of absenteeism due to smoking-related illness and the cost of health care for employees.

Possible Student Responses to Student Sheet F1.2: Weyco Tobacco-Free Policy Case Study Analysis

1 What are the facts presented in this case study?

- *Weyco, a health insurance company, developed a tobacco-free policy for its employees that gave them two years to quit smoking completely, even when not at work.*
- *The company provided support to help its employees quit.*
- *If they didn't quit by January 1, 2005, they would lose their jobs.*
- *Of the 24 employees who were smokers, 20 quit smoking, but four did not.*

2 List the concerns and values important to each stakeholder.

Stakeholder	Key Concerns and Values
Employees and their families	<ul style="list-style-type: none"> - <i>Value good health, but also personal privacy and autonomy</i> - <i>Concerned that Weyco's anti-smoking policy will have an unfair impact on employees who can't quit smoking</i>
Medical professionals and research scientists	<ul style="list-style-type: none"> - <i>Value research and knowledge; and value their abilities to help society understand health issues related to smoking and second hand smoke</i> - <i>Concerned about the effect of smoking and second hand smoke on the health of individuals and the burden of health care costs due to smoking on society</i>
Health insurance company representatives	<ul style="list-style-type: none"> - <i>Value healthy population; also value having a profitable business</i> - <i>Concerned with the impact of smoking on health care and life insurance costs</i>
Howard Weyers, Weyco, Inc. President	<ul style="list-style-type: none"> - <i>Values good health for employees, productivity of employees, cost of health care for company, employees, and their families</i> - <i>Concerned about the impact of smoking on employee health, productivity, and health care costs</i>
Society	<ul style="list-style-type: none"> - <i>Values personal liberties</i> - <i>Concerned that policies like that of Weyco, once accepted, will lead to employers trying to control other activities of their employees.</i> - <i>Concerned with the health care impacts of smoking</i>
Tobacco company representative	<ul style="list-style-type: none"> - <i>Values the financial success of the tobacco industry</i> - <i>Concerned that publicity about secondhand smoke will lead to a decrease in smoking, so they counteract this publicity with other viewpoints suggesting that it is not a problem</i>
State legislator	<ul style="list-style-type: none"> - <i>Values rights of citizens and their need to make informed decisions, also values upholding the law (anti-discrimination) .</i> - <i>Concerned that Weyco policy should not conflict with discrimination laws</i> - <i>Concerned with balancing the anti-smoking policies with the income from tobacco sales</i>

Possible Student Responses to Student Sheet F1.2, *continued...***3** List at least three ethical questions that this case has raised in your group.

- *Should a company be allowed to dictate its employees' legal activities, like smoking, even when they are not at work?*
- *Should an employee be fired for smoking, even when he/she has made a substantial effort to quit smoking?*
- *Is it right that a company (or society) has to pay the health care costs for people who have an unhealthy habit like smoking?*

4 Choose one of your questions and discuss how each of the following ethical principles relates to it:

Autonomy: Respect an individual's right to make self-determining choices

The tobacco-free policy conflicts with individual's freedom to decide whether to smoke

Justice: Be Fair. Treat people equitably, distribute benefits/burden fairly

This policy has more impact on smokers than non-smokers. It especially impacts the smokers who have real difficulty quitting

In some ways the policy promotes justice because health care costs are shared by everyone in society, plus everyone is potentially affected by secondhand smoke.

Beneficence: Do good

The policy is intended to benefit employees by making them quit smoking. It will help the employees directly because they will be more healthy, and it will help employees, their families, and the company because there will be fewer health care costs due to smoking. It will also help to decrease smoking-related sickness and increase productivity.

Non-maleficence: Do no harm/Minimize harm

The policy can harm people who are unable to quit by causing them to lose their jobs. They may have difficulty finding another job or finding one with similar wages and benefits.

The policy can also lead to resentment among employees because it limits people's right to choose.

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Chang, C.F. Covering risk but not risky behavior: A critical review of the arguments for insurance coverage for smoking-cessation therapies. *Managed Care Magazine* [online] May 2001; Available at: http://www.managedcaremag.com/archives/0105/0105.peer_smoking.html (Accessed Aug 27, 2010)

Insurance.com. Life insurance rates for smokers. Available at: http://www.insurance.com/Article.aspx/Can_You_Hide_Smoking_From_Life_Insurance_Companies/artid/245 (Accessed Aug 27, 2010)

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Peters, J.W. Company's smoking ban means off-hours, too. *New York Times* [online] Feb 8, 2005. Available at <http://www.nytimes.com/2005/02/08/business/08smoking.html> (Accessed Aug 27, 2010)

Tobacco Fact Sheet

- Approximately 450,000 smoking related deaths occur in the United States each year (1 out of every 5 deaths) due to the adverse health effects from cigarette smoking.
- This is more than alcohol, AIDS, automobile accidents, illegal drugs, murders, and suicides combined.
- The Center for Disease Control estimates that each smoker in this country costs \$3,391 per year in healthcare costs and lost productivity, an annual national total cost of nearly \$160 billion.
- It is estimated that an employer's health insurance costs could be reduced by 20% if it employed only non-smokers.
- About 1 in 5 Americans, or 46 million people, smoke.
- The courts have repeatedly held that there is no constitutionally protected "right to smoke".
- Legislatures in 29 states have been persuaded to pass legislation either directly prohibiting discrimination against tobacco users ("smokers' rights" laws), or more indirectly prohibiting inquiry into employees' lawful private activities ("lifestyle" laws).
- 17 states have some form of smoking ban to protect the public from secondhand smoke.

A Summary of Ethics Terms

(Chowning, J. & Fraser, P. (2006). An Ethics Primer. Seattle WA:
Northwest Association of Biomedical Research)

Values, Morals, and Ethics

These terms have different but related meanings.

Values

- Qualities that represent what is important and worthwhile
- An individual's values are influenced by many factors, including family, peers, religion, social background, culture, ethnicity, etc.

Morals

- Codes of conduct governing behavior
- They are an expression of values reflected in actions and practices

Ethics

- An approach that provides a systematic, rational way to work through dilemmas and determine the best course of action in the face of conflicting choices.

Ethical Questions and Stakeholders

(Chowning, J. & Fraser, P. (2006). An Ethics Primer. Seattle WA:
Northwest Association of Biomedical Research)

Ethical questions

- Use the words 'should' or 'ought'
- Involve conflicting moral choices or dilemmas
- Several alternate solutions
- Often involve the conflicting values or needs of two or more people, organizations, or entities

Stakeholders

- Are individuals or groups of individuals who are affected by (have a stake in) the outcome of an ethical question.

Principle-based ethics

- Is widely used in biomedical ethics
- Considers an action in the context of four principles:
 - Autonomy: Respect an individual's right to make self-determining choices
 - Beneficence: Do good
 - Non-maleficence: Do no harm or minimize harm
 - Justice: Be fair. Treat people equitably and distribute benefits and burdens fairly

Stakeholder Role Description Cards

Role: Weyco Employees and their families

Weyco has been supporting healthy lifestyles for its employees and their families for several years now by offering incentives to exercise, classes in eating well, and by providing walking trails throughout the Weyco campus. As an employee of the company you have taken advantage of these programs, but the announcement of the policy to eliminate employees that smoke has given you something to think about. You are concerned about your company's attempt to control an individual's lawful, off-the-job behavior. Some employees welcome company support of their smoke-free lifestyle and appreciate working in a healthy environment. However, a few of your smoking co-workers are finding it difficult to stop smoking, and you wonder if Weyco is asking too much of them. The incentive to stay employed is strong, but so is their nicotine addiction. Some employees have chosen to find work elsewhere, since they see this policy as a violation of their privacy and freedom to choose how they live their lives. They have lost income, family medical coverage, and satisfying careers due to this policy. In addition, Weyco plans to charge employees a \$1000 penalty if their spouses smoke. This \$1000 penalty is also seen as interference in the private relationships of employees.

Role: Medical Professionals and Research Scientists

As a member of the medical community, you have long recognized that tobacco use is strongly associated with increased risk of heart disease and cancer in both smokers and those who are exposed to secondhand smoke. In fact, recent studies have supported the hypothesis that secondhand smoking has a very heavy impact on the health of non-smokers and that reducing exposure can significantly reduce these impacts. Your research has been devoted to understanding the causes of nicotine addiction and developing smoking cessation treatments. This work will benefit both smokers and non-smokers. Because health problems related to smoking are so prevalent across the globe, many countries invest heavily in research and medical treatment related to tobacco use.

Role: State Legislator

As a government representative, you remind people that the government's responsibility is to protect citizens' civil rights and provide the information citizens need to make informed decisions. You inform others that state and federal civil rights laws prevent discrimination based on age, race, color, gender, marital status, national origin, weight, height, and religion. An employer is free to hire on the basis of what it considers are desirable traits, skills, and characteristics, provided they don't violate the law. You know that the Department of Health discourages smoking and that there are currently tobacco regulations in place prohibiting smoking in public buildings to protect citizens. Yet, at the same time, the state uses taxes collected from tobacco sales and subsidizes tobacco farmers.

Stakeholder Role Description Cards

Role: Health Insurance Companies

Smoking is a leading cause of mortality in the U.S. Diseases and deaths caused by smoking also exact a heavy financial toll on society. In 1992, the U.S. Surgeon General reported that the "... estimated average lifetime medical costs for a smoker exceed those for a nonsmoker by more than \$6,000." Health insurance companies exist to offset the financial burden of medical care in our society. But these companies are also commercial businesses motivated by profit and economic growth. To be financially stable, health and life insurance companies generally support the healthy life choices of their customers to reduce the need of high medical payouts to cover debilitating diseases. Since smokers statistically have higher medical costs, health insurance companies often charge them higher premiums than non-smokers. The average premiums for smokers are 38% higher than for non-smokers in the 35-year-old category, and 122% higher in the 55-year-old category. In addition to health and life insurance, smokers generally pay higher home owners insurance since smokers are more likely to cause a house fire than a non-smoker.

Role: Weyco President

As the president of Weyco, Inc. you are in business to help other companies save money and improve employee health through innovative benefit plans. It is natural that you would establish a policy of promoting healthier lifestyles through a Lifestyles Challenge Program with the goal of encouraging your employees to become healthier. As part of this program, you have designed a tobacco-free employee policy with smoking cessation support. Tobacco use has devastating effects on our society because it is a major killer and a drain on health care resources. Costs related to smoking include loss of employee productivity due to tobacco-related illnesses and the increased health care costs to employers, employees, and their families. These issues concern you immensely, and you think your business has the right to protect itself from the enormous financial harm that smokers inflict on society. But it's not just about saving money, it's about saving lives. Since you began this program your company has helped the majority of your smoking employees stop using tobacco.

Stakeholder Role Description Cards

Role: Society Representative

You cherish your personal liberties and recognize that once you yield even the slightest bit, you can expect your liberties to be reduced little by little; therefore, you make sure you are an informed citizen. Only California, Colorado, New York, and North Dakota have worker privacy laws that prohibit employers from regulating most legal activities when their workers are off the job. You read an article by Lewis Maltby, president of the National Workrights Institute, an employees' rights organization, in which he said, "Once you cross the line and allow employers to control any type of behavior that's not related to job performance, there's no limit to the harm that can and will be done." However, you have also seen the data from the Center for Disease Control's 2002 study, indicating our nation's cost of smoking is \$3,391 a year per smoker—\$1,760 in lost productivity and \$1,623 in excess medical expenditures. The economic burden of smokers is more than \$75 billion per year in medical expenditures and \$80 billion a year from lost productivity. You know that the reasons people smoke are complex and that nicotine addiction must be very strong since many people continue to smoke despite the known economic and health effects.

Role: Tobacco Company Representative

As a representative of the tobacco industry, you strongly oppose those who provide organizational and financial support for smoke-free environments in restaurants and bars. You often also support the opposition to smoke-free environments in other workplaces. As part of these efforts, your industry distributes "educational material" to employers and employees containing information about the risks of secondhand smoke and about the economic impact of smoke free environments. The tobacco industry argues that restaurants, bars, and related businesses will lose money from smoke-free policies. Your industry also suggests that secondhand smoke can be controlled with ventilation systems and with designated areas for smokers. This would protect the non-smoker without violating the rights of the smoker. In addition, you support physicians or scientists who testify that exposure to secondhand smoke is not harmful.

Name: _____ Date: _____ Period: _____

STUDENT SHEET F1.2:

Stakeholder Values and Concerns Summary Sheet

With your group, read the description of your stakeholder and answer the questions listed below. You will share this information in the next activity, so make sure you fully understand the perspective of your stakeholder.

- 1 List the important values and concerns of your assigned stakeholder with regard to the tobacco-free policy. Express your answer in the 'voice' of the stakeholder.

- 2 Describe how this stakeholder might benefit from the Weyco tobacco-free policy.

- 3 Describe how this stakeholder might be harmed by the tobacco-free policy.

- 4 What do you think are the motivations of Weyco to have only non-smoking employees?

Name: _____ Date: _____ Period: _____

STUDENT SHEET F1.1:

Weyco Tobacco-Free Policy Case Study Analysis

1 What are the facts presented in this case study?

2 List the concerns and values important to each stakeholder.

Stakeholder	Key Concerns and Values
Employees and their families	
Medical professionals and research scientists	
Health insurance company representatives	
Howard Weyers, Weyco, Inc. President	
Society	
Tobacco company representative	
State legislator	

STUDENT SHEET F1.1 *continued...*

3 List at least three ethical questions that this case has raised in your group.

4 Choose one of your questions and discuss how each of the following ethical principles relates to it:

Autonomy: Respect an individual's right to make self-determining choices

Justice: Be Fair. Treat people equitably, distribute benefits/burden fairly

Beneficence: Do good

Non-maleficence: Do no harm/Minimize harm

STUDENT SHEET F1.1 *continued...*

Homework

Write a reflection on the following questions:

- 1** Do you believe it is ethical for an employer to monitor its employees' lifestyle choices? Explain, using ethical principles in your argument.
- 2** Why do you think that it is so difficult for Weyco employee, Anita, to quit smoking, when there is so much at stake if she doesn't? Why is it harder for her to quit than for other Weyco employees who were smokers?
- 3** What ethical perspective best describes Howard Weyers' decision to enforce his tobacco-free policy for his company? Use evidence from the video clip and the stakeholder role description card for the Weyco President.

ACTIVITY F2

Why Do Research on Smoking Behavior?

OVERVIEW

This activity exposes students to some of the reasons that smoking behavior research is carried out and how the results of that research can be used. This helps establish a “why?” for students as they proceed through the curriculum. By assembling a jigsaw puzzle, students will match up reasons for doing smoking behavior research with examples of the results and applications of that research.

Time

20 minutes (may be combined with another activity or part of an activity.)

Materials

for each student

- Student Sheet F2.1

for each pair of students

- Envelope containing jigsaw puzzle pieces

Learning Objectives

Students will learn:

- the reasons for doing research on smoking behavior
- applications of the results of this research
- benefits and drawbacks of such research

Getting Ready

- 1** Do double-sided photocopying of the jigsaw piece page and picture page onto cardstock. Cut out the pieces such that the reasons, all on the left side of the page, remain together in one large piece. (This is essential and keeps the puzzle in the correct order, such that when it is turned over, the correct picture has been formed on the back.) Cut the examples, on the right of the page, into individual pieces. Laminating the pieces may help preserve them for future years.
- 2** Put a set of jigsaw pieces in an envelope for each pair of students.
- 3** Make copies of the student summary handout for each student.

Tips & Tricks

- Students may be interested in discussing other areas of research that have a strong impact on human health and public policies.
- As an extension, students might collect newspaper articles that discuss areas of research that interest them and how research findings are applied to develop public policies, improve human health, or develop commercial products.

Presenting the Activity

- 1** Explain to students that the jigsaw puzzle will help them identify several reasons that research scientists, policy makers, and manufacturers are interested in studying smoking behavior. Encourage them to think about how the information scientists gain from smoking behavior research may be used, or even *misused*.
- 2** Hand out an envelope to each pair of students and instruct them to assemble the puzzle, making sure to match the reasons for doing research with the correct example. All the puzzle pieces with reasons are the same shape, and all the pieces with the examples are the same shape, so students need to be sure that the reason and the example match.
- 3** When students have completed the puzzle, they can perform a self-check of their work by taping the pieces together and flipping over the page to see the correctly assembled picture. They will be able to see at a glance if they have made any errors and go back and correct them. Give students the handout to complete for their lab books. (This can be done as homework).
- 4** When students return to class with the handout completed, be sure to discuss some of the benefits and drawbacks associated with this type of research (questions 3 and 4).

Teacher Background: Information on Benefits and Drawbacks of Research on Smoking Behavior

In addition to the information provided in the introduction to the Ethics Unit, the notes below will help you guide discussion of questions 3 and 4 in Student Sheet F2.1

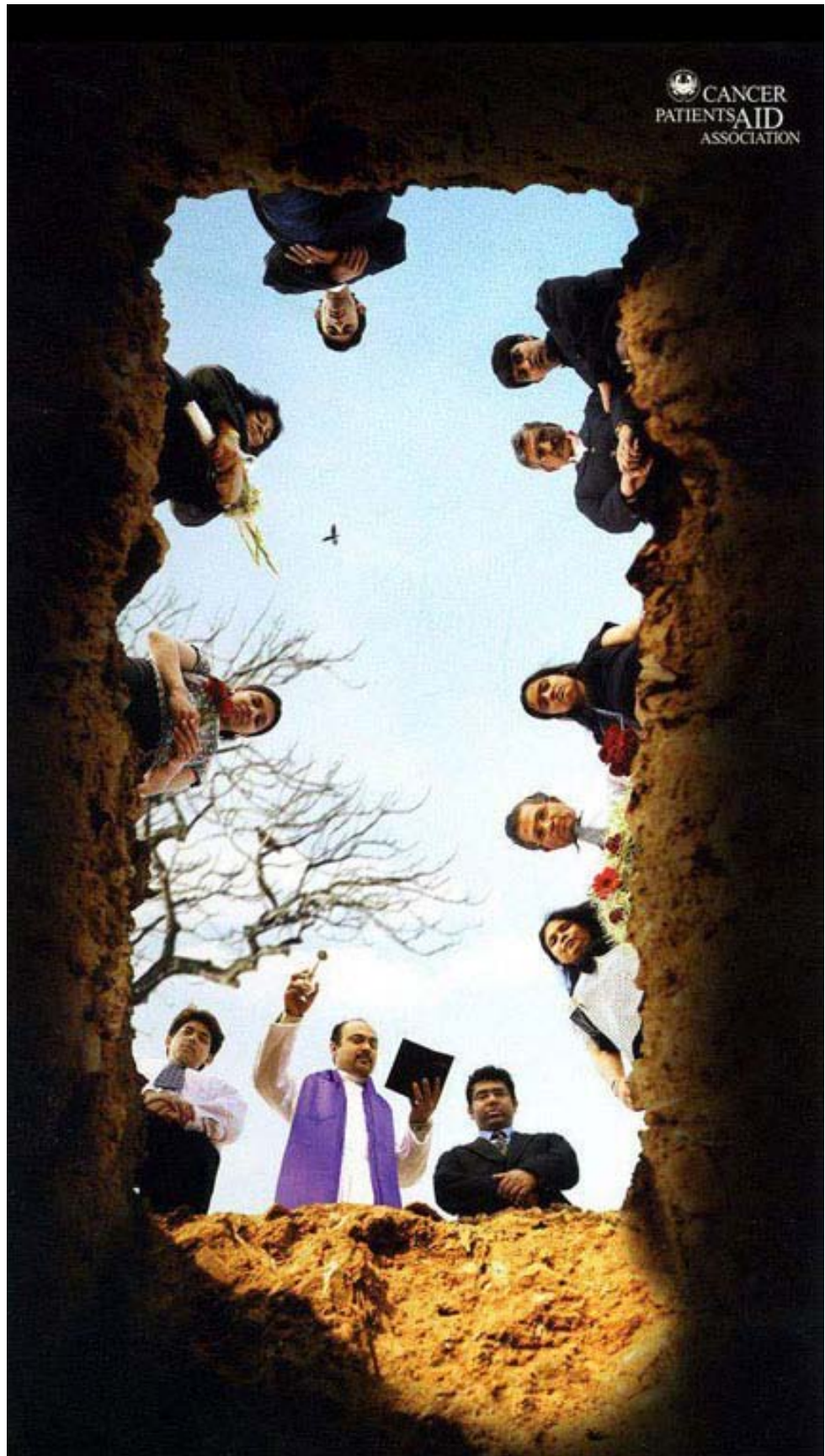
Question 3: Drawbacks. There are a number of possibilities.

- information about their “smoking behavior genes” could give people unwanted information about other phenotypes, such as how prone they are to other addictive behaviors like substance abuse and gambling
- information about their risk of strong addiction to nicotine might discourage smokers from even trying to quit, by promoting a fatalistic attitude, “I can’t change my genes”
- even if they are non-smokers, people might become discriminated against by their health insurer or employer if they were found to have genetic variants that increase their risk for being highly addicted to nicotine
- research on smoking behavior can lead to restrictions on personal liberties and autonomy

Question 4: Benefits. Some of the examples listed on the right of the puzzle are benefits. Students may come up with others, which can be evaluated as they are suggested. For example, more knowledge of smoking behavior could lead to more effective counseling of smokers by physicians and addiction counselors.

Learn more about how our brain works	The brain's reward pathway and neurotransmission will be better understood. The applications of basic research are wide-ranging and cannot always be predicted.
Develop new cessation methods	Nicotine replacement therapy (nicotine patch, gum), bupropion (Zyban), and Chantix are several examples that each use a different mechanism.
Develop new nicotine products	Snus, a tobacco product popular in Sweden, fits under your lip and does not cause lung cancer. So people can enjoy nicotine's pleasurable effects and not worry about lung cancer or secondhand smoke. Snus is highly addictive and is linked to pancreatic and mouth/throat cancer.
Develop genetic tests for smoking behavior	This application might help people choose the best cessation method for themselves, help them understand their risk for becoming highly addicted to nicotine (and smoking), and help motivate them to quit smoking, or never to begin.
Inform public policy decisions	Examples include these regulations: no smoking within 25 feet of public doorways, no smoking on airplanes, no smoking in bars, and a high tax on cigarettes and other nicotine products.
Lead to further insights into the genetics of other types of addictive behaviors	Some genetic variations influence not only nicotine addiction but other addictive behaviors, such as gambling.

Ceiling of a smoker's room



Name: _____ Date: _____ Period: _____

STUDENT SHEET F2.1:

The Reasons for Researching Smoking Behavior

After completing the jigsaw puzzle, answer the following questions and be prepared to discuss them in class. Include this page in your notebook.

- 1** The puzzle pieces list several reasons for doing research on smoking behavior. Which reason seems most important to you? Explain your answer.

- 2** Are there any reasons that support the tobacco industry? If so, which ones?

- 3** One reason for doing research on smoking behavior is that it may lead to insights into the genetics of other types of addictive behaviors, such as drug use (e.g. cocaine, heroin) and gambling. Read the example for this reason from your jigsaw. What potential problems might result from this type of research?

- 4** There may be other benefits from this type of research as well. List two potential benefits that were not directly listed in this activity.

ACTIVITY F3

The Science of Nicotine Addiction

OVERVIEW

The purpose of Activity F3 is to provide relevant background on the biology of smoking so students can develop an understanding for the wide variation in the way people smoke (or don't smoke) and how genetic and environmental factors might contribute to this variation. This lesson introduces students to the stages of smoking, factors that affect smoking behavior, the physiological effects of nicotine, and the current treatments for smoking cessation.

<p>Time</p> <p>Two 50-minute class periods.</p> <p>Materials</p> <p><i>for each student</i></p> <ul style="list-style-type: none"> • Student Sheets F3.1, F3.2 F3.3, and F3.4 • One of four smoker profiles <p><i>for the class</i></p> <ul style="list-style-type: none"> • Chart F3.1 on poster paper or overhead transparency 	<p>Note to Teachers:</p> <p>Activity F3 covers much of the same material contained in Activities A2 and A3 from the <i>Investigating the Effects of Genes and Environment on Smoking Behavior</i> curriculum. If you have already done A2 and A3, you don't need to do F3, which is provided primarily for teachers who will be doing only the F activities in their classrooms.</p> <p>Learning Objectives</p> <p>Students will learn:</p> <ul style="list-style-type: none"> • The definition of terms like drug, drug abuse, drug addiction, nicotine, withdrawal • That smoking behavior has four stages: initiation, maintenance, cessation, and relapse • That both environmental and genetic factors affect smoking behavior • About basic neural transmission and the reward pathway • That many of the physiological effects of smoking and the difficulty of quitting smoking are caused by addiction to the drug, nicotine • About several methods for smoking cessation
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Tips & Tricks

- Students usually have many anecdotes about the smoking behavior of people they know. Depending on time, this is a good opportunity to elicit what students think about smoking behavior.

Getting Ready

- 1 Photocopy Student Sheets F3.1, F3.2, F3.3, F3.4, and the smoker profiles (one of each per student).
- 2 Prepare a packet of PowerPoint notes pages for each student. Follow the instructions below to print a master document you can photocopy:
 - a. With the PowerPoint presentation open on your computer, use the mouse to select “File / Print.”
 - b. Select “Handouts” in the “Print what” pull-down menu in the **Print** dialog box.
 - c. You can choose how many slides to print per page to the right of the **Print what** menu. Printing three slides on a page leaves room for students to take notes next to each slide.
- 3 For Day 1, prepare an overhead transparency or wall chart of Chart F3.1.
- 4 For Day 2, reserve a computer lab, or print and copy the following smoking cessation resources:
 - a. National Cancer Institute. “Quitting Smoking: Why To Quit and How To Get Help”
<http://www.cancer.gov/cancertopics/factsheet/Tobacco/cessation>
 - b. Centers for Disease Control and Prevention. “Smoking Cessation”
http://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/quitting/index.htm
 - c. Drug Digest. “Smoking Cessation” At the Drug Digest website, <http://www.drugdigest.org/wps/portal/ddigest>, click on the following links: Conditions & Treatments / Treatment Options / Smoking Cessation

Presenting the Activity, Part 1: Stages of smoking and factors that affect smoking behavior*Day 1*

- 1 Begin the class by explaining that, in order to consider ethical issues related to genetic testing for smoking behavior, students will need to learn more about what smoking behavior is and what factors affect people’s smoking behavior.
- 2 Ask students to think about people they know who have tried smoking, are currently smokers, or are former smokers. Spend about 5 minutes sharing anecdotes about the different smoking behaviors students have observed. Encourage them to share a range of smoking patterns, from people who try one or two cigarettes to people who light up within the first few minutes of getting out of bed.

Tips & Tricks

- Students may prefer using everyday language to discuss the stages of smoking: starting, continuing, quitting, and starting again.
- After analyzing the smoker profiles, students should recognize that there are a large number of factors, both environmental and genetic, that influence people's smoking behavior.

Presenting the Activity, Part 1, Day 1 continued...

- 3** Point out that there is a pattern to smoking behavior, and scientists often discuss smoking in terms of four stages. Relate the stages to the students' anecdotes.
- **Initiation (starting):** The process of trying and experimenting with smoking before becoming a regular smoker. Studies have shown that over half of the population tries at least one cigarette sometime in their lives. Most smokers try smoking in their teens.
 - **Maintenance (continuing):** Stage in which people become regular smokers. This stage is usually marked by complex physiological changes in the body that lead to addiction and nicotine cravings.
 - **Cessation (quitting):** The process of trying to quit smoking. Cessation generally follows a pattern of thinking about quitting, planning how to stay off cigarettes, decreasing consumption, and efforts to stop smoking.
 - **Relapse (starting again):** Starting up smoking again after quitting.
- 4** Give each student one of the four Smoker Profiles and Student Sheet F3.1. Divide the class into groups of four, each with a different smoker profile. Have students read their own smoker profile, and then as a group answer the questions on Student Sheet F3.1, using evidence from their smoker profiles to answer the questions. Make sure that each student records the answers on his own sheet.
- 5** As a class, fill in Chart F3.1 (on an overhead or large poster). Define the terms, nicotine, drug, addiction, drug abuse, and withdrawal as your students bring them up, and write them on the poster. Definitions for these terms are provided below.
- 6** As a class, discuss whether each of the reasons that people start smoking, continue to smoke, and have difficulty quitting is an environmental factor, a physiological factor, or both. On Chart F3.1, write E beside environmental factors, P beside physiological factors, and E & P beside those that are both.
- 7** Conclude the activity by discussing the large variation in the ways people smoke and the observation that both environmental and physiological factors contribute to smoking. Remind students that physiological factors are controlled by genes, so we usually refer to these as genetic factors. Environmental and genetic factors contribute to different stages of smoking to different extents. For example, initiation is believed to be more heavily influenced by environmental factors, while genetic factors may have a stronger effect on maintenance and quitting.
- 8** Keep the poster on your wall as you complete this unit so you can refer back to it in later discussions.

Tips & Tricks

- Students may be confused or overwhelmed by the physiological aspects of nicotine addiction. Focus on the important concepts—that nicotine interacts with the reward pathway in the brain and is broken down by enzymes in the liver—and do not worry about the details.
- Students should realize that there are many genes that may influence variation in people's smoking behavior.

Presenting the Activity, Part 2: The science of nicotine addiction

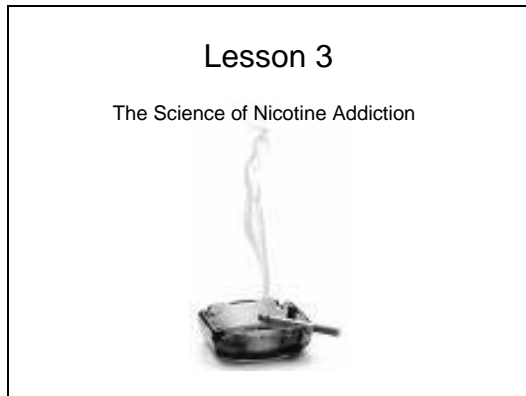
Start on Day 1, complete on Day 2

- 1** Provide each student with Student Sheets F3.2 and F3.3.
- 2** Present PowerPoint slides on the science of nicotine addiction. The notes provided below offer some discussion points you can share as you present the slides.

Second half of Day 2 (Completed in the computer lab)

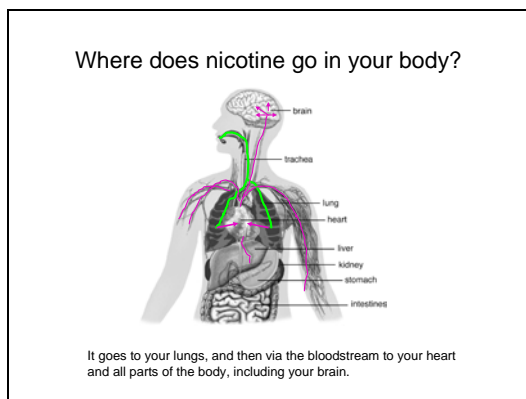
- 1** Refer the students to Student Sheet F3.4 - *Treatment Options for Smoking Cessation*
- 2** Direct students to the three websites listed on Student Sheet F3.4, and have them fill in the chart with information about smoking cessation.
- 3** Have students use the chart to complete the follow up questions in small groups. Their results should be archived in their lab notebooks.

PowerPoint Presentation and Teacher Notes



Slide 1. The Science of Nicotine Addiction

Explain to your class that they are going to learn about the biology of nicotine addiction at the molecular level so they can understand how genes might contribute to smoking behavior.



Slide 2. Where does nicotine go in your body?

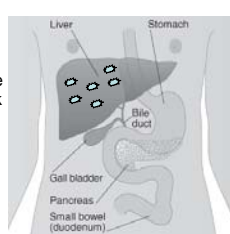
Ask students where nicotine goes in the body. Tell them to pair up and draw where it goes on Student Sheet F3.2. Then point out the pathway on the slide:

- From the mouth, down the trachea to the lungs
- From the lungs into the bloodstream to the heart
- From the heart to all parts of the body, including the brain

Make sure that students recognize that nicotine goes to the brain.

How does the body get rid of nicotine?

- Nicotine circulates throughout the body in the bloodstream.
- Eventually it is carried to the liver, where enzymes break it down into other compounds.
- These compounds are carried by the bloodstream to the kidneys and then excreted from the body in urine.



Slide 3. How does the body get rid of nicotine?

Explain that nicotine is carried in the bloodstream to the liver.

One of the functions of the liver is detoxifying the body.

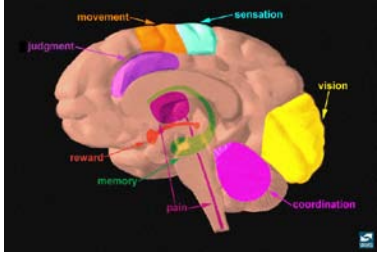
Enzymes in the liver convert nicotine to compounds that dissolve in water.

These compounds are carried by the bloodstream from the liver to the kidneys and are excreted as urine.

Ask students to correct their drawing on Student Sheet F3.2, if necessary.

A look at the brain

Different parts of the brain are involved in different functions, like vision, movement, thinking, memory.



Slide 4. A look at the brain

Tell students that in order to understand how nicotine interacts with the brain, they need to know more about brain structure and function.

Point out that different parts of the brain have different functions, like vision, movement, memory, thinking, etc.

Mention that there is a special region of the brain for “reward.”

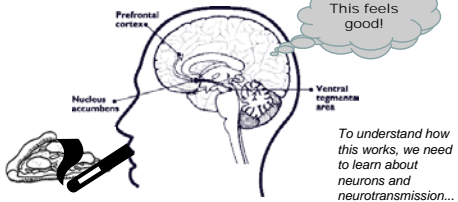
Ask students, “What effects does nicotine have in the brain?”

Students may say that nicotine gives some people a “buzz” or slight “high” or helps them relax or helps them focus.

The Reward Pathway

The reward pathway is a neural pathway used for reinforcing behaviors that are important for survival.

Nicotine also stimulates the reward pathway.



Slide 5. The Reward Pathway

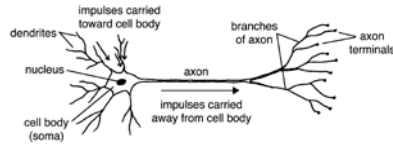
Tell students that the brain also has a region involved in reinforcing behaviors that are important for survival, called the reward pathway.

- It is a neural pathway in the brain
- It consists of specialized nerve cells that start in the ventral tegmental area and end in the nucleus accumbens (emotional center of the brain) and the prefrontal cortex (thinking area)
- It is activated by behaviors that are important for survival, such as eating
- Activation of the reward pathway leads to a feeling of pleasure, which reinforces these behaviors

As you point out the reward pathway, don’t worry about the names of the different brain regions.

Neurons

- Have a cell body, dendrites, and axon
- Use electrical impulses and chemical signals



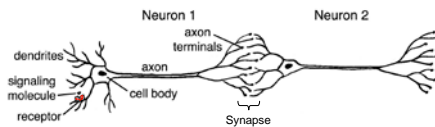
Slide 6. Neurons

Point out the different parts of a neuron (cell body, dendrites, axon, axon terminals).

Explain that neurons use two kinds of signals, electric impulses (action potentials) that travel down the axon from the cell body to the axon terminals and chemical signals (neurotransmitters), which carry signals from one neuron to the next.

Neurotransmission is...

The process of transferring messages between neurons. Its purpose is to carry signals from one part of the brain to another or to other parts of the body, like muscles.



Slide 7. Neurotransmission

Tell students:

- That neurons are arranged in networks, with the axon terminals of one neuron lying close to the dendrites and cell body of other neurons (only two neurons shown in the figure)
- Neurotransmission goes in one direction, from the dendrites to the cell body, along the axon to the axon terminals of the first neuron and then across a space to the dendrites of the second neuron.
- As mentioned earlier, neurons use 1) electrical signals to send a message from the cell body to the axon terminal and 2) chemical signals, called neurotransmitters to send messages to the next neuron.
- Each type of neuron uses a certain kind of neurotransmitter. Some examples are: acetylcholine, serotonin, and dopamine.

Dopamine is the neurotransmitter in the reward pathway

Stimulation of neurons in the VTA area results in release of dopamine in the NA (emotional center) and the prefrontal cortex (thinking).

Slide 8. Dopamine is the neurotransmitter in the reward pathway

Remind students that the reward pathway contains neurons that have their cell bodies in the VTA and their axon terminals in the NA and prefrontal cortex

Activation of neurons in the VTA results in release of the neurotransmitter dopamine in the NA and prefrontal cortex

How Does Nicotine Interact with Neurotransmission and the Reward Pathway?

Nicotine binds to receptors on neurons in the ventral tegmental area.

An electrical impulse travels down the neuron axon.

Dopamine is released at axon terminals in the nucleus accumbens and prefrontal cortex.

Dopamine binds to dopamine receptors on other neurons.

This leads to the rewarding effects of smoking, such as relaxation, a "buzz", or an increased ability to focus.

Slide 9. How does nicotine interact with the brain?

Nicotine binds to receptors in the VTA

An electric impulse travels down the neuron axon

Dopamine is released at the axon terminals in the NA and prefrontal cortex

Dopamine binds to dopamine receptors on other neurons

This activates the reward pathway, reinforcing the desire to smoke

What is the impact of nicotine interacting with the reward pathway?

Addiction!

Slide 10. What is the impact of nicotine interacting with the reward pathway?

Give students time to respond before advancing the slide to provide the answer.

Students should recognize that drugs that interact with the reward pathway have the potential to be addictive.

They should also recognize that the addictive properties of nicotine can lead to becoming a regular smoker and difficulty in quitting. The more people smoke, the greater their risk for smoking-related diseases.

What genes might be involved in differences in smoking behavior?

Nicotine receptors Dopamine receptors; enzymes that make or break down dopamine Enzymes involved in nicotine breakdown

Slide 11. What genes might be involved in differences in smoking behavior?

Ask students to look at Student Sheet F3.3 and answer questions 1-4 with a partner.

After students have had a chance to complete Student Sheet F3.3, click the mouse to show examples of genes that might affect smoking behavior.

The reward pathway is involved in other addictive behaviors

- Cocaine slows the re-uptake of dopamine in the nucleus accumbens.
- Methamphetamine results in increased dopamine release as well as blocking the re-uptake of dopamine in the nucleus accumbens.
- Other addictive behaviors, like gambling and risk taking involve the reward pathway.

Slide 12. The reward pathway is involved in other addictive behaviors

Cocaine slows the re-uptake of dopamine in the nucleus accumbens.

Methamphetamine results in increased dopamine release as well as blocking the re-uptake of dopamine in the nucleus accumbens.

Other addictive behaviors, like gambling and risk taking involve the reward pathway.

What are some benefits of identifying variants in genes associated with smoking behavior?

- Increasing our understanding for the addiction process
- Helping people understand their own risk for becoming addicted to nicotine or other addictive drugs or behaviors
- Helping to choose the best cessation program for an individual based on their genes

Slide 13. What are some benefits of identifying variants in genes associated with smoking behavior?

Discuss how knowledge about genetic variations associated with smoking behavior may be beneficial by:

- Increasing our understanding of the addiction process
- Helping people understand their own risk for becoming addicted to nicotine or other addictive drugs or behaviors
- Helping to choose the best cessation program for an individual based on their genes

What are some risks of identifying variants in genes associated with smoking behavior?

- The same gene variants may also be associated with the use of other addictive drugs or addictive behaviors. By learning about genes that affect smoking behavior, people also get information about other behaviors (which they may not want). A gene that affects different traits is called pleiotropic.
- People who carry a risk variant may face discrimination getting jobs, health insurance, or life insurance.
- The frequency of a risk variant may be higher in a certain group, leading to stigmatization of that group.

Slide 14. What are some risks of identifying variants in genes associated with smoking behavior?

Use the slide to discuss possible drawbacks and define the words, pleiotropy, discrimination, and stigmatization.

- **Pleiotropy:** The ability of a variant in a single gene to affect multiple traits. For example, *APOE* is the gene that codes for apolipoprotein E, a protein that binds fats and cholesterol and carries them to the liver for processing. One of the three common variants for this gene, *APOE4*, results in increased risk for atherosclerosis and Alzheimer's Disease.
- **Discrimination:** To treat a person differently (usually negatively) based on their membership to a particular group.
- **Stigmatization:** A negative label given to an individual or group based on a particular characteristic.

Teacher Keys

Key to Chart F3.1: Smoking Behavior

Why people start smoking

- people may start because their friends or family members smoke (E)
- young people may try smoking to look cool (E)
- some people think the cigarette tastes bad, while others do not mind, or even enjoy the taste (P)
- some people like the way smoking makes them feel, while others don't (P)

Why people continue to smoke after trying it

- people may smoke because their friends or family members smoke (E)
- smoking may be associated with other enjoyable past-times, like having a break at work, drinking coffee with friends, or going to a party on the weekend (E)
- frequency and number of cigarettes smoked each day vary among individuals (E and P)
- pleasurable feeling from smoking causes individuals to continue smoking (P)
- people may experience cravings and smoke to relieve the cravings (P)
- people may like the ritual of meeting with other smokers, getting out a cigarette, lighting up, and smoking (E)
- some people may smoke to control their hunger and therefore their weight, or they may not want to quit because of concern that they'll gain weight (E and P)

Why people have difficulty quitting smoking

- many people have difficulty quitting because they have strong cravings for cigarettes (P)
- some people get headaches when they try to stop smoking (P)
- for some people, smoking is a way to relieve stress, so if they become stressed while trying to quit, they start smoking again (E and P)
- they are worried about gaining weight (E and P)
- they hang out with people who smoke, so the temptation to smoke is always present (E)
- smoking is part of an enjoyable ritual, like taking a break with co-workers or meeting a friend for coffee (E)

Related terms

- Nicotine. The addictive drug in tobacco.
- Drug. A chemical compound or substance that can alter the structure and function of the body. Psychoactive drugs affect the function of the brain, and some of these may be illegal to use and possess.
- Addiction. A chronic, relapsing disease characterized by compulsive drug-seeking and abuse and by long-lasting chemical changes in the brain.
- Drug abuse. The use of illegal drugs or the inappropriate use of legal drugs. The repeated use of drugs to produce pleasure, to alleviate stress, or to alter or avoid reality (or all three).
- Withdrawal. Symptoms that occur after chronic use of a drug is reduced or stopped.

(Definitions from the National Institute on Drug Abuse: <http://teens.drugabuse.gov/utilities/glossary.asp>)

Key to Student Sheet F3.3: How might variation in genes lead to differences in smoking behavior?

- 1** What evidence do you have that genes contribute to variation in smoking behavior?

People have different physiological reactions to smoking. Some people get a “buzz” from smoking, while others don’t. People also react differently when quitting—some people get headaches and others don’t. Some people, but not all, get very strong cravings.

- 2** Think about how nicotine interacts with your brain. What proteins in your brain might vary among different people to account for differences in their smoking behavior?

Answers might include: nicotine receptors, dopamine receptors, enzymes involved in making or breaking down dopamine.

- 3** What proteins in your liver might vary among different people to account for differences in their smoking behavior?

People may vary in the enzymes that break down nicotine.

- 4** How might variations in the genes for these proteins affect smoking behavior, like how much or how little people smoke, whether they become addicted to nicotine, or whether it’s hard for them to quit smoking?

There is no “right answer” to this question, but students should show that they’re thinking about how a genetic change might affect a protein, which could affect how a person reacts to nicotine. For example, a smoker who makes more than the usual amount of the enzyme that breaks down nicotine would get rid of nicotine more quickly, so he might smoke more than other smokers. A variation in the nicotine receptor gene might result in a receptor that doesn’t bind nicotine as well, and this might lead to a person being less susceptible to nicotine addiction.

Key to Student Sheet F3.4: Treatment Options for Smoking Cessation

Treatment	Type	Common Brand Name	Action	Availability
Counseling	In person (individual or group), telephone	---	Helps motivate & encourage patient	Through medical clinics and smoking cessation programs
Educational Materials	Online, print	---	Helps educate patient	Through clinics, by mail, online
Bupropion	Pill, anti-depressant	Zyban, Wellbutrin	Non-nicotine medication that is thought to reduce the urge to smoke by affecting the same chemical messengers in the brain that are affected by nicotine Helps prevent cravings, reduces withdrawal symptoms	Prescription
Varenicline Tartrate	Pill, nicotine receptor agonist	Chantix	Nicotine receptor agonist Binds nicotine receptor and blocks nicotine binding	Prescription
Nicotine replacement therapy	Gum, patch, spray, inhaler, lozenge	Nicorette, Nicoderm, Nicotrol, etc.	Provides small doses of nicotine in a controlled way that separates nicotine intake from the act of smoking	OTC and prescription

1 What methods have been found to be effective in helping smokers to quit?

All of the above methods in the table work for at least some people. Least effective is educational materials on their own. Some methods are more effective in combination with another method.

2 What are the symptoms of nicotine withdrawal?

Irritability, anxiety, difficulty concentrating, increased appetite.

3 Why is it so difficult for people to quit smoking?

Some people are more motivated than others. Different people have different genetic make-ups, which can affect ability to quit. Some people have a harder time resisting the cravings and are overcome by the pains of withdrawal. Some people are afraid of gaining weight.

Resources

- Centers for Disease Control and Prevention: Smoking and Tobacco Use (<http://www.cdc.gov/tobacco/>).

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Why people start smoking

Why people continue to smoke after trying it

Why people have difficulty quitting smoking

Related terms

STUDENT SHEET

Smoker Profile 1

NAME: Barbara

AGE: 55

GENDER: Female

EDUCATION LEVEL: College graduate

JOB: Teacher

Barbara grew up in a culture where the dangers of smoking weren't on the public radar. "It wasn't that big of a deal," she says. Despite this, Barbara had almost no exposure to cigarettes or smoking as a young girl. "I'm the third of four daughters, and neither my parents nor my older sisters smoked. I guess smoking just never seemed like something I wanted to do."

As a teenager, however, her attitude changed. "I remember spending summer afternoons with my best friend on the porch of our cottage at the lake. We used to sit there and smoke these long, thin cigarettes. It just seemed cool." Barbara says this small act of rebellion made her feel grown up and somehow more chic. "I actually hated the smoking, but the idea of smoking I liked." Barbara's smoking didn't last for long. "I smoked a few packs over the course of a summer or two, but it never really caught on for me. It didn't make me feel particularly good, and eventually I just thought it was stupid. So I stopped, cold-turkey. I guess I never really got hooked."

During college, plenty of Barbara's friends and acquaintances smoked occasionally, but she never felt much peer pressure to join in. "I never started again. I was pretty busy with work, but I was very happy, and the idea of smoking never appealed to me again." As far as she can remember, what pleasure she got from smoking cigarettes came purely from the image. "I don't remember a buzz at all, really."

Now in her fifties and the mother of four, Barbara hasn't touched a cigarette since her teenage summers, nor has she felt the craving to do so. "My husband is a doctor now, so I hear all sorts of horror stories about the dangers of using cigarettes. It makes me very glad I didn't get addicted."

STUDENT SHEET

Smoker Profile 2

NAME: Mark

AGE: 50

GENDER: Male

EDUCATION LEVEL: Ph.D.

JOB: University Professor

Mark spent his youth surrounded by people who smoked. He doesn't remember exactly why he started: "Smoking was just ubiquitous in my family and social circles growing up. It was before everyone knew it was stupid." When he was 17, Mark took up smoking, just as most of his friends and relatives had. "I really don't remember exactly why I began, other than that it was all around me. I guess I smoked about a half a pack a day, usually later in the day." Mark doesn't remember any particularly strong physical effects. "I would just get a physical craving that made me want to have a cigarette. I don't remember much of a buzz."

He has struggled several times with trying to quit. "My experiences varied. The first couple of weeks are always hard." Powerful cravings made quitting extremely difficult, but Mark has found nicotine gum to be very helpful in controlling cravings and allowing him to taper off nicotine gradually. "My problem is always relapse behavior. I'll quit for six months or so, and then for no particular reason, start up again. It's not rational at all. It's a yearning you can't control." It's particularly dangerous, Mark says, to be in a situation where others are smoking. "Someone will offer me a cigarette, and I'll think 'Hey, it's just one,' and then I'm right back where I started." Quitting permanently has not been easy. "The cravings always return, but usually less frequently with time. I haven't smoked for 3 months now, and I've promised myself that I won't start again. The hard part is, the cravings never go away."

STUDENT SHEET

Smoker Profile 3

NAME: Donald

AGE: 83

GENDER: Male

EDUCATION LEVEL: 10th grade

JOB: Retired civil servant

As a boy in a small mining town, Donald started smoking at the age of twelve. He started mainly “because of peer pressure, to be a part of the crowd.” Donald’s mother was not a smoker, but his father smoked a pipe. “My parents weren’t aware of my smoking, or at least didn’t acknowledge it. I don’t think they would’ve condoned it, either.” Unaware of the health risks associated with smoking, he continued to smoke into his teens.

On his 17th birthday, Donald joined the army to fight in World War II and was sent to an army base in England. A government program allowed families to ship cigarettes inexpensively to their loved ones serving overseas. “They’d come a thousand at a time, sometimes once, sometimes twice a month,” Donald recalled. Cigarettes served as a form of currency. They could be used to pay for services or goods, and even “led to black market-type stuff. I’d smoke cigarettes when I had them, and worry when I didn’t. I can think of maybe one guy I knew at the time who didn’t smoke.” The soldiers must have had some idea that smoking was bad for their health, because the common saying on lighting up was “Put another nail in the coffin.”

Returning from England at the end of the war, Donald started smoking less, partly because of the high “sin tax” on cigarettes. He quit for a while, but then started again when he was offered a cigarette at a dance. Donald smoked about a pack a day and would usually have his first cigarette around breakfast time. “It was just the habit that kept me going, although it was relaxing, too. I just got into the pattern.”

At age 60, Donald finally managed to kick the habit, quitting outright. He thinks that making a personal decision to quit is the only way to stay off cigarettes, rather than doing it to please someone else. “I missed it at first, but I didn’t have any of the physical effects like headaches.”

STUDENT SHEET

Smoker Profile 4

NAME: Aaron

AGE: 18

GENDER: Male

EDUCATION LEVEL: In high school

JOB: Student

Aaron started smoking three years ago because he thought it would help him with schoolwork. "I was doing really bad in math, and I figured it would help me relax. Also, a couple of my friends were doing it, and I kinda did it just to blend in." Aaron found the taste of cigarettes somewhat unpleasant, so he smokes menthol cigarettes, going through a pack every couple of days. Aaron is eighteen and can legally buy his own cigarettes now. But for the three years he smoked as a minor, it was surprisingly easy for him to get cigarettes.

Smoking is something Aaron does "under the radar" of his parents, although he thinks they are aware that he smokes. Neither of his parents smoke, yet they haven't talked to him much about it either. During school, Aaron smokes between classes, during breaks, or at lunch. He says that his craving to smoke is so powerful that "there's no way I can quit." Cigarettes help Aaron focus and relax; without them he gets distracted, irritable, and fidgety. If he goes for more than a few hours without a cigarette, he gets an intense headache. "It doesn't go away, either, and all I can think about is having another cigarette." Aaron is trying to quit, "but these headaches are killing me."

Students in Group: _____

Date: _____ Period: _____

STUDENT SHEET F3.1:

Group Questions: Comparing Smoker Profiles

Stages of Smoking

- **Initiation (starting):** The process of trying and experimenting with smoking before becoming a regular smoker. Studies have shown that over half of the population tries at least one cigarette sometime in their lives. Most smokers try smoking in their teens.
- **Maintenance (continuing):** Stage in which people become regular smokers. This stage is usually marked by complex physiological changes in the body that lead to addiction and nicotine cravings.
- **Cessation (quitting):** The process of trying to quit smoking. Cessation generally follows a pattern of thinking about quitting, planning how to stay off cigarettes, decreasing consumption, and efforts to stop smoking.
- **Relapse (starting again):** Starting up smoking again after quitting.

Use what you and your group partners have learned from reading the smoker profiles to answer the following questions.

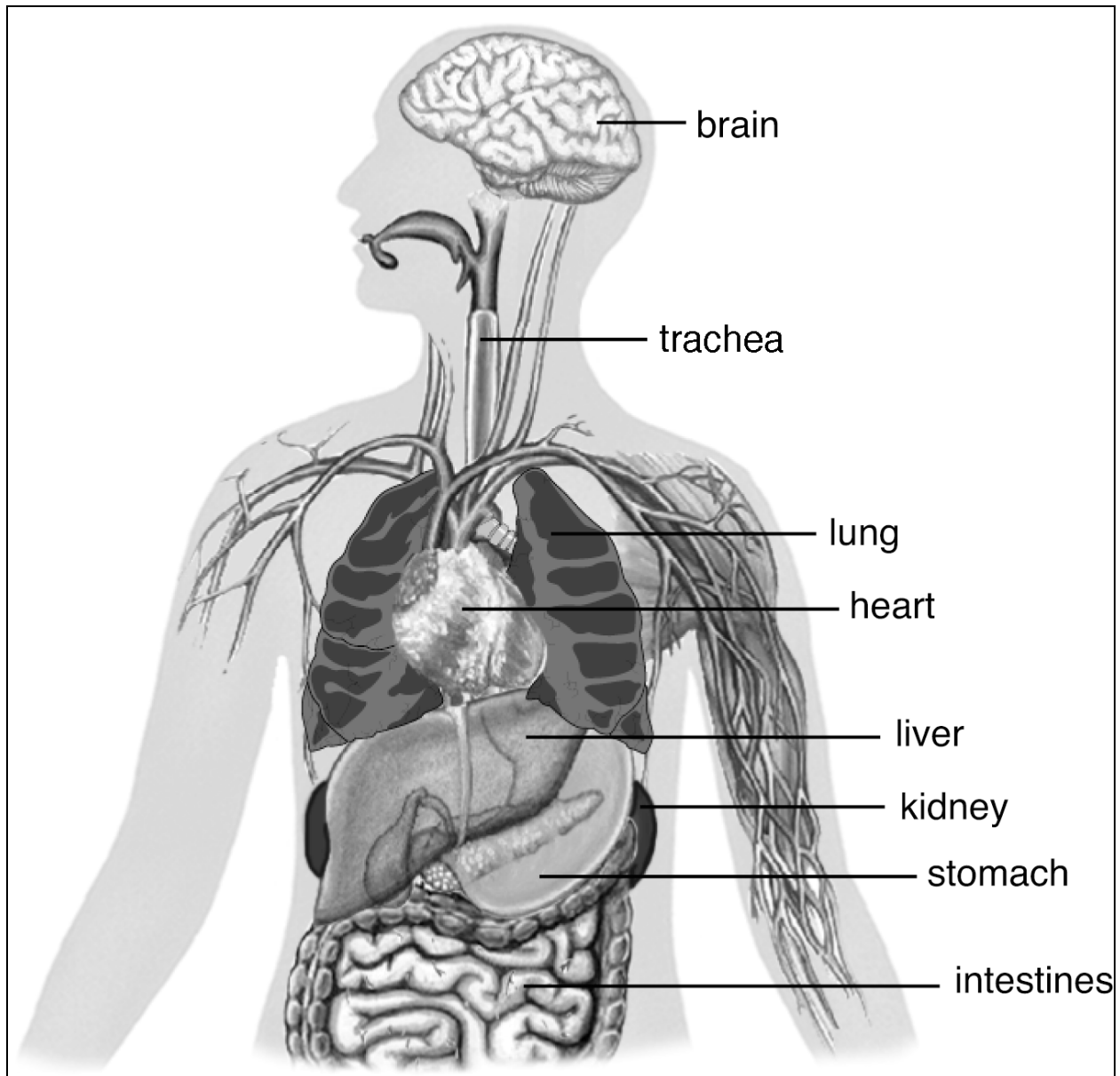
- 1 At what ages do people start smoking?
- 2 What factors influence people to start smoking?
- 3 What factors influence people to continue smoking after they have started?
- 4 What factors make it difficult for many people to quit smoking?
- 5 What methods do people use to help themselves quit smoking? Are these techniques effective?

Name: _____ Date: _____ Period: _____

STUDENT SHEET F3.2:

Where Does Nicotine Go?

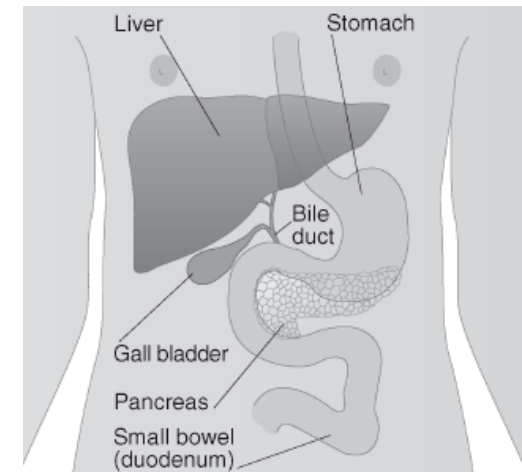
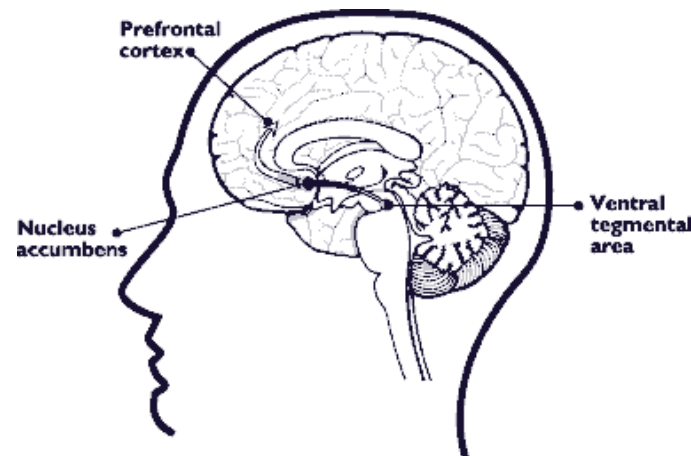
Think about where nicotine might go when it enters the body. Use a pen to trace the path that nicotine might follow beginning when a person inhales until it leaves the body.



Name: _____ Date: _____ Period: _____

STUDENT SHEET F3.3: How might genetic variation cause differences in smoking behavior?

- 1 What evidence do you have that genes contribute to variation in smoking behavior?
- 2 Think about how nicotine interacts with your brain. What proteins in your brain might vary among different people to account for differences in their smoking behavior?
- 3 What proteins in your liver might vary among different people to account for differences in their smoking behavior?
- 4 How might variations in the genes for these proteins affect smoking behavior, for example, how much or how little people smoke, whether they become addicted to nicotine, or whether it's hard for them to quit smoking?



Name: _____ Date: _____ Period: _____

STUDENT SHEET F3.4:

Treatment Options for Smoking Cessation

Several treatment options are available to help smokers quit. In this assignment, you will collect information on the available methods by visiting the following websites:

National Cancer Institute

<http://www.cancer.gov/cancertopics/factsheet/Tobacco/cessation>

Centers for Disease Control

http://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/quitting/index.htm

Drug Digest

<http://www.drugdigest.org> (Click on the following links for information on smoking cessation drugs: "Conditions & Treatments" / "Treatment Options" / "Smoking Cessation")

Complete the table, and then answer questions 1-3 on the next page.

Treatment	Type	Brand Name	Action	Availability
Counseling				
Educational Materials				
Bupropion				
Varenicline Tartrate				
Nicotine replacement therapy				

ACTIVITY F4

Multifactorial Traits

OVERVIEW

In this activity, students investigate multifactorial traits. First, students read a scenario about identical twins separated at birth and are asked to consider how environmental and genetic factors could influence the twins' smoking behavior. Students then play a game to further investigate the effect of environmental and genetic factors on the risk for becoming a smoker.

<p>Time</p> <p>75 minutes or less</p> <p>Materials</p> <p><i>for each student</i></p> <ul style="list-style-type: none"> • Student Sheets F4.1 and F4.2 • Dice (one die per student) <p><i>for the class</i></p> <ul style="list-style-type: none"> • Genetic Contribution Cards • Four containers for Genetic Contribution Cards marked with the Number Rolled: 1 or 2; 3; 4; 5 or 6 • Sticky notes (any color, 1" x 2") 	<p>Learning Objectives</p> <p>Students will learn:</p> <ul style="list-style-type: none"> • environmental and genetic factors both contribute to the expression of a multifactorial trait. • in multifactorial traits, the contribution from genetic factors is often due to more than one gene. • many traits are multifactorial, including many behavioral traits in humans. • smoking behavior is a multifactorial trait. <p>Getting Ready</p> <ol style="list-style-type: none"> 1 Photocopy Student Sheets F4.1 and F4.2. 2 Photocopy the Genetic Contribution Cards for the Smoking Risk Game. Cut out the cards and place in the four containers. Place the containers at the front of the room. 3 For the Smoking Risk Game, draw axes for student bar graph on the board (see #10, Presenting the Activity).
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Tips & Tricks

- Students may need to draw a Punnett square to recall how many phenotypes result from the crossing of two heterozygotes.
- To demonstrate a multifactorial trait, ask students in the class to line up from shortest to tallest. Ask them to suggest factors that might affect people's height.

Presenting the Activity*Introducing the Activity*

- 1** Ask students to volunteer some examples of single gene traits that have been studied in class. These might include any of Mendel's pea traits, cystic fibrosis, sickle cell anemia, etc.
- 2** Ask students to recall how single gene traits are inherited and how many phenotypes result (when two heterozygotes are crossed). The important point is that only two or three phenotypes will be produced (if the gene has only 2 alleles). For example, pea seeds will be either wrinkled or smooth due to their inheritance of the single gene for seed coat texture. You should be able to move through this quickly as this should be review for the students.
- 3** Ask students how a trait such as height is inherited and how many different phenotypes exist. Elicit responses that consider the effect of environment (e.g. nutrition) and heredity (multiple genes) and that indicate the wide range of phenotypes. Other examples of multifactorial traits include weight, skin color, and a number of human diseases, such as heart disease, cancer, and type 2 diabetes.
- 4** Use this example to develop a definition of multifactorial traits. Here is one possible definition:
Multifactorial traits are traits whose expression results from the interaction of genetic and environmental factors. The genetic contribution usually involves multiple genes.

Twin Scenario

- 5** Ask students to individually read Student Sheet F4.1 *If One Twin Smokes, Will the Other?* and answer the Analysis Questions in their notebook.
- 6** In small groups, ask students to make a list of all the reasons they think that Michael may or may not be a smoker, using specific information from the scenario. Each group should also indicate the chance of Michael being a smoker using a scale of 1 to 5, with 1 indicating he is unlikely to be a smoker and 5 indicating he is definitely a smoker.

Tips & Tricks

- Ask students to consider whether Michael is likely to even try a cigarette, given his adoptive family and involvement in athletics.

Presenting the Activity, continued...

7 In a class discussion, ask students to indicate, with a show of hands, which number their group chose.

- a.** Ask for groups to report their findings—list reasons they think that Michael may or may not be a smoker. Make a list of student responses on the board or an overhead. Some possible student responses are given below.

Michael is likely to be a smoker because:

- *Michael's biological parents are smokers and so would be a genetic influence.*
- *His identical twin is a highly addicted smoker and Michael has the same genetic information as his twin.*

Michael is not likely to be a smoker because:

- *His adoptive parents are not smokers and so their smoking is not an environmental influence. Their non-smoking behavior, in fact, may influence Michael not to smoke.*
- *His socioeconomic status is higher than Joe's.*
- *He is a serious athlete and would be interested in remaining healthy to pursue this interest.*

- b.** Ask students to hypothesize how smoking behavior is inherited and expressed. Students should propose that both genetics and the environment contribute to smoking behavior and that smoking behavior is a multifactorial trait.

- c.** Students often want to know the “answer”—is Michael a smoker or not? Use this opportunity to emphasize that there is no one right answer, that Michael could either be a smoker or not, depending on his genes and the environmental factors he has been exposed to. Refer to the Teacher Background material on twin studies of smoking behavior for information to support your discussion.

Smoking Risk Game

8 Review directions for the activity with the class. These are found on Student Sheet F4.2. **Emphasize to students that they cannot predict their own chance of being a smoker by playing this game.** The game is a simulation, not true to life. Several of the environmental factors have been shown to associate with a higher chance of smoking but not necessarily to cause a person to smoke. Refer to the teacher background information, if needed, to support your discussion. Alternatively, this topic can be explored in more depth after the game has been played. Students who have completed the case control curriculum will already be familiar with the difference between association and causality.

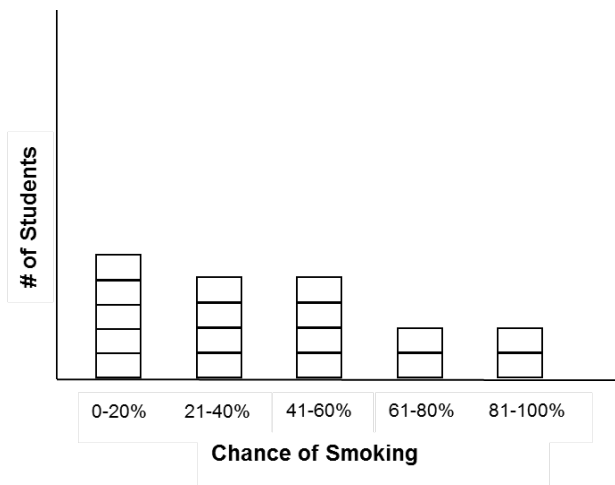
Tips & Tricks

- Make sure that students put on their sticky notes in neat columns so the number of students in each category is easy to see.
- Remind students that the smoking risk game is a simulation, and their chance of smoking from the game does not have anything to do with their personal risk.

Presenting the Activity, *continued*...

9 Each student, individually, should follow the directions to complete the activity. Alternatively, they can work in pairs, if desired, but they should then run through the activity twice, so that each pair generates two figures for risk (for the bar graph).

10 Prepare a set of axes on the board which will be used to create a bar graph of student data. Each student will plot his “chance of smoking” on the graph using a sticky note. The axes should be Number of Students (Y) versus Chance of Smoking (X). Divide the X axis into discrete categories and specify where each bar of the graph will be located: 0-20%, 21-40%, 41-60%, 61-80%, and 81-100%. A sample sticky note bar graph is shown below.



11 After the students have posted data to the graph, discuss the following points.

- Our scientific understanding of smoking is incomplete. The game includes factors that have been studied, and more research will likely uncover other factors.
- Make sure that students understand that not all of the environmental risk factors in the game have been shown to cause people to smoke. Rather, some factors are associated with people who smoke.
- Although research supports that the factors used in the game are associated with a person’s risk of smoking, the numbers assigned are arbitrary and not an actual probability. Some factors have been given a greater weight than others, but this is not necessarily based on actual research.
- The final numerical score obtained by each student is not a true risk or chance of becoming a smoker
- **Emphasize to students that they cannot predict their own chance of being a smoker by playing this game.**

Tips & Tricks

- Ask students to consider why the chance of smoking is never 0% in the game.

Presenting the Activity, *continued*...

12 Allow students time to work on Analysis Questions. If time permits, go over the questions in class, or discuss just a couple of the questions you wish to emphasize. This can also be done the next day at the beginning of the period, after you have had a chance to look at some of the student answers and see what they need clarification on. For example, you may want to discuss question 5, which asks about students' concept of Chance.

13 Assign the Reflection Questions as homework.

Extension Activity

In addition to the environmental factors mentioned in the Smoking Risk Game, a number of other factors may be associated with smoking. Ask students to research an environmental factor that influences smoking behavior and write up a summary of what they learn. The following list is a good starting point for student references on environmental factors.

Teacher Background

Twin Studies of Smoking Behavior

Many studies have examined the environmental and genetic contributions to various aspects of smoking behavior, for example, initiation, age of initiation, progression to regular smoking, length of time between initiation and regular smoking, daily number of cigarettes smoked, ease of cessation, etc. A twin study is common way of estimating the genetic and environmental contributions to a trait. In a large study population of twins, the degree of concordance (when both twins have the same trait) between identical twins is compared to the degree of concordance between fraternal twins. Using mathematical models, researchers use the concordance figures to predict the contributions of genes and environment to the trait. In studies on smoking behavior, one study of male twins showed that genetic factors made a stronger contribution to nicotine dependence than did environmental factors (61% genetic, 39% environmental). A study of female twins showed an even stronger genetic contribution to nicotine dependence (72% genetic, 28% environmental). The numbers vary in different studies, but it seems safe to conclude that there is a strong contribution of both genetic and environmental factors to some aspects of smoking behavior, such as nicotine dependence, whereas environmental factors contribute more to other aspects (e.g. smoking initiation).

Understanding the Difference between Causality and Association

As you introduce the Smoking Risk Game, briefly discuss the difference between **causality** and **association**. If you are doing the entire *StarNet* Smoking Behavior Curriculum, you can remind students about what they have already learned on this topic in Activity B1, Epidemiology and Case Control Studies.

Make sure that students understand that not all of the environmental risk factors in the game have been shown to *cause* people to smoke. Rather, some factors are *associated* with people who smoke. For example, people with less education are more likely to be smokers, but it doesn't mean that less education *causes* smoking. There could be a several different factors associated with less education that are causative, for example, higher stress due to lower income due to lower education (on average). But education alone is not the actual cause.

Emphasize to students that they cannot predict their own chance of being a smoker by playing this game. They cannot add up the five environmental risk factors for themselves, make some sort of guess at their genetic component, and arrive at a number that tells them how likely they are to be smokers. **The Smoking Risk Game is only a simulation** that allows students to see that many factors, both environmental and genetic, may contribute to whether one is a smoker or not. Through playing the game, they should observe that any one factor actually plays only a small role.

If students need more information, particularly those who haven't done entire *StarNet* curriculum, explain that in their human subjects research, scientists may detect associations between an event and an outcome, but proving that an event *causes* an outcome is another thing entirely. In experimental studies, which often aren't possible on humans for ethical and logistical reasons, it is easier to demonstrate that a treatment or event causes an outcome. For example, if a scientist feeds rats a high fat diet and they gain weight, but rats on a low fat diet do not gain weight, it is fairly straightforward to conclude that a high fat diet causes weight gain. Through statistical calculations, scientists may be able to show that an event and outcome are associated. For example, people with red hair often have freckles, so they are definitely associated. But red hair does not necessarily *cause* freckles.

Scientists who interpret studies on human populations apply a number of criteria to a detected association to help determine whether a certain factor is likely to have caused the outcome. The more criteria that are satisfied, the more likely the association is to be causal. Five commonly used criteria are given in the table below.

Criteria for causality

Strength of association. A strong association exists between the event and outcome. For example, if 70% of red haired people also have freckles, this would be a strong association. (In scientific studies looking for associations, the strength of an association is demonstrated by statistical methods.)

Dose-response relationship. An increased dose or amount of the event is associated with a greater risk for having the outcome. (Are people with more red pigment in their hair more likely to have freckles than people with less red pigment in their hair?)

Temporal sequence. The potentially causative event must occur before the outcome.

Consistency with other studies. The result should be mostly consistent with what is already known in the field. (If it is not, there is always the possibility that you have discovered something new and unexpected, but there is also the possibility that your study design or assumptions were in some way flawed.)

Biological plausibility. The result should make biological sense.

If you would like to share this table with your students to help them understand the difference between association and causality, an overhead master of a simplified table is included in this activity.

Reference List of Additional Environmental Factors

Note that in Activity C of the full StarNet Smoking Behavior curriculum, students do an exercise that covers similar ground, using the same reference list. All websites listed were accessed successfully on August 24, 2010.

Ethnicity, Gender and Risk Factors for Smoking Initiation

<http://archives.drugabuse.gov/Meetings/Nicotine/mermelstein.html>

<http://www.americanheart.org/presenter.jhtml?identifier=11226>

Access to Tobacco

<http://archives.drugabuse.gov/meetings/Nicotine/Rigotti.html>

Economics

<http://archives.drugabuse.gov/meetings/Nicotine/Chaloupka.html>

Advertising and Promotion

<http://archives.drugabuse.gov/Meetings/Nicotine/Pierce.html>

Education and Prevention Programs

<http://archives.drugabuse.gov/meetings/Nicotine/Pentz.html>

<http://www.fhcrc.org/about/ne/news/2000/12/19/HSPFinalfinal.html>

Parental and Family Influence

Modeling Anti-Smoking Behavior

http://www.fhcrc.org/about/pubs/center_news/2004/apr15/sart4.html

Quitting while Kids are Young

http://www.fhcrc.org/about/pubs/center_news/2003/may15/sart1.html

http://www.fhcrc.org/about/ne/news/2005/03/01/quit_smoking.html

Communication Styles

<http://atmizzou.missouri.edu/apr05/teensmoking.htm> *

Involvement in Athletics

<http://www.icsspe.org/documente//PhysicalActivity.pdf>

<http://www.menstuff.org/issues/byissue/sportsteensmoking.html> *

Diet

http://www.findarticles.com/p/articles/mi_m0887/is_n1_v11/ai_11971277 *

Peer Influence

<http://www.apa.org/news/press/releases/2002/08/teen-smoking.aspx>

* Denotes shorter articles. Additional reading materials suitable for students in lower grades can be found at the National Institute on Drug Abuse's Students and Young Adults web page (<http://www.drugabuse.gov/students.html>) and the Center for Disease Control's National Center for Chronic Disease Prevention and Health Promotion Tobacco Information and Prevention Source (<http://www.cdc.gov/tobacco/>)

Teacher Keys

Key to Student Sheet F4.1, Analysis Questions

- 1 Why do you think Joe is a smoker? List the reasons why and support each with evidence from the scenario.
 - *Joe's biological parents are smokers and so would be a genetic influence.*
 - *Joe also grew up around his parents and so has them as an environmental influence.*
 - *Joe's siblings also smoke and may influence him.*
 - *Joe is a longshoreman. Statistically, people in working-class occupations are more likely to be smokers.*

- 2 Do you think it is likely that Michael smokes? Why or why not? Use information from the scenario to support your answer.

Michael is likely to be a smoker because

 - *Michael's biological parents are smokers and so would be a genetic influence.*
 - *His identical twin is a highly addicted smoker and Michael has the same genetic information as his twin.*

Michael is not likely to be a smoker because

 - *His adoptive parents are not smokers and so their smoking is not an environmental influence. Their non-smoking behavior, in fact, may influence Michael not to smoke.*
 - *His socioeconomic status is higher than Joe's.*
 - *He is a serious athlete and would be interested in remaining healthy to pursue this interest.*

- 3 If Michael had remained in the Jeffreys family, do you think he would have been a smoker?
 - *Michael would likely have been a smoker because of the influence of environmental factors (parental and sibling smokers) in addition to the genetic factors he may have inherited from his parents. In addition, he may have ended up in a different job and may have had a different socioeconomic status if he grew up in the Jeffreys family, and so may have had these additional factors that predisposed him to smoking.*
 - *Michael would likely not have been a smoker because the fact that he does not currently smoke suggests he may not have inherited genetic factors that predispose him to smoking.*

Key to Student Sheet F4.2, Analysis Questions

- 1 What does the graph tell you?

There is a wide range of results for the class showing that multifactorial inheritance of a trait results in a variety of phenotypes in a population.

- 2 What would the graph look like if smoking behavior was determined by a single gene with little or no environmental contribution (e.g. pea seed coat color, cystic fibrosis)

There would be only two or three (or a few) phenotypes depending on the type of inheritance.

Teacher background: *for example, a trait determined by a single gene with only two alleles and that is inherited as a complete dominant would give rise to two phenotypes. A trait determined by a single gene with two alleles and that is inherited as an incomplete dominant would give rise to three phenotypes. Single genes with more than two alleles—such as ABO bloodtype—would have more phenotypes, but still few compared to a trait produced by multifactorial inheritance.*

- 3** Consider the environmental factors in the game.
- Did all the factors make the same contribution to smoking susceptibility? Explain your answer using your results.
The factors vary in their contribution. For example, parental smoking behavior makes a larger possible contribution than other factors.
 - Could any of the factors be controlled by the individual? Explain.
Athletic activity and educational level can be chosen to some degree.
 - Which factors could not be controlled by the individual?
Parental smoking behavior cannot be controlled by the individual. Student answers will vary as to what factors they can and cannot control.
 - What is the difference between environmental factors that have positive values and those that have negative values?
*Environmental factors with positive values **promote** smoking. Environmental factors with negative values **protect against** smoking.*

- 4** Consider the genetic factors in the game.
- Did everyone who rolled the same number for parental smoking behavior receive the same alleles?
Since smoking behavior is a multifactorial trait, it is not likely that the same number rolled for parental smoking behavior represents the same alleles present in different individuals. For the purposes of this simulation, however, everyone rolling the same number on the die will be assigned the same number of high, neutral, and low risk smoking alleles. They may, however, represent different genes.
 - Why was the “environmental factor” of parental smoking behavior chosen to determine genetic factors?
It is the factor that would have the greatest dependence on genetic make-up.
 - How did the contribution of a single genetic factor compare to the total genetic contribution?
Any one genetic variant had only a small effect on the genetic contribution.

- 5** What does “chance” mean in the Smoking Risk Game?

Use this question as a discussion point rather than emphasizing whether the student answer is right or wrong. Explain that one way of looking at Chance in this game is to consider a population of people. For example, on a Chance scale of 100, a score of 80 would mean that for every 100 people with the same genetic makeup and environmental factors, approximately 80 of those people would be smokers.

- 6** Our knowledge of the genetic factors affecting addiction to smoking is incomplete. How could learning about these factors be beneficial? How could increased knowledge be harmful?

It could be beneficial to know if one was at risk for smoking so that the individual could be aware of this risk and adjust their behavior accordingly. They might refrain from experimenting with smoking and from placing themselves in environments that would promote smoking behavior. Also, if a person has certain genetic factors, some treatments for smoking addiction may be more effective than others. This would let the person choose the method of quitting most likely to help. This knowledge could be harmful if the individual accepted it as determining one’s fate.

- 7** In what ways does the game reflect how multifactorial traits work in real life, and in what ways is it inaccurate?

The game shows that a variety of environmental and genetic factors affects a multifactorial trait, and that a single genetic factor has little effect in determining phenotype. It is inaccurate because the specific contributions and number of genetic and environmental factors is unknown.

- 8** Based on the smoking behavior of your person's "parents," were you surprised by your person's chance of being a smoker? Why or why not?

Answers will vary depending on what the student rolled on the die for parental smoking behavior and what final Chance score they ended up with. Students whose person has two smokers for parents in the game will probably find it consistent if their person ends up having a high chance of being a smoker himself. Students who have two smokers for parents but end up not having a high chance for smoking may find that outcome surprising. They will see that other environmental factors as well as genetic factors may help them overcome the strong influence of parental smoking.

Key to Student Sheet F4.2, Reflection Questions

- 1** Are multifactorial traits inherited?

Student answers should indicate they recognize that

- *Multifactorial traits are influenced by genetic and environmental factors.*
- *Any single genetic factor has very little influence on the phenotype of a multifactorial trait.*
- *The same genetic factors in different individuals would result in different phenotypes depending on the environmental factors to which an individual is exposed.*

- 2** How do multifactorial traits affect our ability to develop genetic tests for predicting a condition?

Student answers might include the following ideas:

- *Because the genetic component of a multifactorial trait is often not well understood (because multiple genes are involved and not all of them have been identified), genetic testing would be limited in its ability to predict.*
- *Even if the genetic component is well defined, it may result in different phenotypes under different environmental conditions.*
- *We need to consider how information resulting from a genetic test would affect the individual.*

References

Twin Studies on Smoking

Broms, U., Silventoinen, K., Madden, P. A. F., Heath, A. C., and Kaprio, J. Genetic Architecture of Smoking Behavior: A Study of Finnish Adult Twins. *Twin Research and Human Genetics* 2006;9:64-72.

Carmelli, D., Swan, G. E., Robinette, D., and Fabsitz, R. Genetic influence on smoking--a study of male twins. *New England Journal of Medicine* 192;327:829-833.

Netherlands Organization For Scientific Research. Smoking Is In The Genes. *ScienceDaily* Dec 1, 2004. Available at: <http://www.sciencedaily.com/releases/2004/11/041123172547.htm> (Accessed Sept 3 2010)

Saint Louis University. It's In Their Genes: Study Of Twins Connects Smoking Addiction With Major Depression. *ScienceDaily* 2007, July 16, 2007. Available at: <http://www.sciencedaily.com/releases/2007/07/070716132424.htm> (Accessed Sept 3 2010)

Stallings, M. C., Hewitt, J. K., Beresford, T., Heath, A. C., and Eaves, L. J. A Twin Study of Drinking and Smoking Onset and Latencies from First Use to Regular Use. *Behavior Genetics*, 1999; 29:409-421.

Zickler, P. Evidence Builds That Genes Influence Smoking Behavior. *NIDA Notes* 2000; 15. Available at: http://archives.drugabuse.gov/NIDA_Notes/NNVol15N2/Evidence.html (Accessed Sept 3, 2010)

Environmental Factors that Affect Smoking Behavior

Refer to list of references for students given for the extension activity at the end of *Presenting the Activity*.

Genetic Contribution Cards

<p style="text-align: center;">Genetic Contribution</p> <p style="text-align: center;"><i>Use this card if you rolled a 1 or 2 on the die for Parental Smoking Behavior</i></p> <p>High Risk Alleles: 5</p> <p>Neutral Risk Alleles: 15</p> <p>Low Risk Alleles: 30</p>	<p style="text-align: center;">Genetic Contribution</p> <p style="text-align: center;"><i>Use this card if you rolled a 1 or 2 on the die for Parental Smoking Behavior</i></p> <p>High Risk Alleles: 5</p> <p>Neutral Risk Alleles: 15</p> <p>Low Risk Alleles: 30</p>
<p style="text-align: center;">Genetic Contribution</p> <p style="text-align: center;"><i>Use this card if you rolled a 3 on the die for Parental Smoking Behavior</i></p> <p>High Risk Alleles: 20</p> <p>Neutral Risk Alleles: 15</p> <p>Low Risk Alleles: 15</p>	<p style="text-align: center;">Genetic Contribution</p> <p style="text-align: center;"><i>Use this card if you rolled a 4 on the die for Parental Smoking Behavior</i></p> <p>High Risk Alleles: 30</p> <p>Neutral Risk Alleles: 15</p> <p>Low Risk Alleles: 5</p>
<p style="text-align: center;">Genetic Contribution</p> <p style="text-align: center;"><i>Use this card if you rolled a 5 or 6 on the die for Parental Smoking Behavior</i></p> <p>High Risk Alleles: 20</p> <p>Neutral Risk Alleles: 20</p> <p>Low Risk Alleles: 10</p>	<p style="text-align: center;">Genetic Contribution</p> <p style="text-align: center;"><i>Use this card if you rolled a 5 or 6 on the die for Parental Smoking Behavior</i></p> <p>High Risk Alleles: 20</p> <p>Neutral Risk Alleles: 20</p> <p>Low Risk Alleles: 10</p>

Criteria for causality

Strength of association. A strong association exists between the event and outcome.

Dose-response relationship. An increased dose or amount of the event is associated with a greater risk for having the outcome.

Temporal sequence. The potentially causative event must occur before the outcome.

Consistency with other studies. The result should be mostly consistent with what is already known in the field.

Biological plausibility. The result should make biological sense.

STUDENT SHEET F4.1:

If One Twin Smokes, Will the Other?

When Mrs. Jeffreys' husband lost his job at the shipyards, she didn't know what she would do. She was pregnant with twins, and they already had four children. Her part time job as a hotel maid would hardly be enough to support the family. Mr. Jeffreys tried for several months to find work but was unsuccessful. Finally, the down-on-their-luck couple made the difficult decision to give up the twins for adoption when they were born. After Mrs. Jeffreys gave birth to identical twins, Michael and Joseph, she decided she couldn't bear to give them both up, so the couple decided to keep one of the boys. Joseph joined the Jeffreys family, and a couple who lived several hundred miles down the coast adopted Michael.

When Michael was 30, he registered with an agency to help him locate his biological parents. He wondered what his parents were like, why they had given him up for adoption, and where he had come from. Within a year, Michael's biological parents were found. Michael also discovered he had five brothers and sisters, including an identical twin brother! Michael and his twin arranged to meet. Joe and Michael were amazed when they saw each other. They looked so much alike! They were about the same height and weight, and both had short hair. They even had the same laugh. Like his father, Joe had become a longshoreman. Michael had followed a different path, attending college as his adoptive parents had, and receiving a degree in marine science. Currently he worked at a marine research institute studying the effect of pollution on water quality. Joe and Michael discovered that both of them liked spicy food, were allergic to cats, loved to play poker, and couldn't stand black coffee. But Joe and Michael were different too. Michael enjoys bicycling, and Joe likes to go fishing on the bay.

Joe was a chain smoker. He had tried to quit several times but had always gone back to smoking. He wondered if Michael smoked too. Neither of Michael's adoptive parents had smoked, whereas Mr. Jeffreys was a chain smoker, and Mrs. Jeffreys had smoked until Joe was in middle school. All four of Joe's brothers and sisters also smoked. Do you think it likely that Michael smokes?

Analysis Questions

Record your answers to these questions in your notebook.

- 1 Why do you think Joe is a smoker? List the reasons why and support each with evidence from the scenario.
- 2 Do you think it is likely that Michael smokes? Why or why not? Use information from the scenario to support your answer.
- 3 If Michael had remained in the Jeffreys family, do you think he would have been a smoker?

STUDENT SHEET F4.2:

Smoking Risk Game

In this activity, you will determine how different factors could contribute to a person's chance of being a smoker as an adult. This game is only a simulation. **You cannot predict your own chance of being a smoker by playing this game.**

The environmental factors listed below are known to be associated with an individual's chance of being a smoker as an adult. You will determine the chance of being a smoker for a person having a particular set of environmental and genetic factors.

Directions

- 1 Roll one die five separate times to determine the influence of each environmental factor. Use the tables below to see how strongly each factor influences the chance.
- 2 For each factor, record the number rolled and the points scored on the Game Record Sheet.

Note: Environmental influences with positive scores indicate factors that promote smoking. Environmental influences with negative scores indicate factors that **protect against** smoking.

Environmental Factors

1. Parental Smoking Behavior

Number rolled	Environmental Influence	Points
1, 2	Neither parent smokes	-10
3	One parent smokes	+10
4	Both parents smoke	+20
5	Both parents smoke but one parent quits when child is 5,	+10
6	Both parents smoke, but one parent quits when child is 15	+20

2. Friends'/Coworkers' Smoking Behavior

Number rolled	Environmental Influence	Points
1, 2	Most do not smoke	-10
3, 4	Some smoke	+5
5, 6	Almost all smoke	+10

STUDENT SHEET F4.2: *continued...*

3. *Education of Individual*

Number rolled	Environmental Influence	Points
1	Bachelors degree or beyond	-5
2, 3	Some college	-3
4, 5	High school graduate	0
6	Not a high school graduate	+5

4. *Athletic Activity Level*

Number rolled	Environmental Influence	Points
1	Iron Man Competitor	-10
2	Runs 5 miles a day	-10
3	Works out at gym 3 times/week	-5
4, 5	Walks to and from work (1mile) once a week	-1
6	Couch potato	0

5. *Stress Level*

Number rolled	Environmental Influence	Points
1, 2	Financially secure, fun job	0
3, 4	Some financial worries, job can be stressful at times	+3
5, 6	Financial difficulties, stressful job	+5

Genetic Factors

- 1 Use the number you rolled for Parental Smoking Behavior to select a Genetic Contribution Card. Your teacher will tell you where these are located. These cards indicate the number of high, low, and neutral risk gene variants your person has inherited from his/her parents.
- 2 Calculate your person's points for Genetic Contribution as shown on the Game Record Sheet. Note that high, neutral, and low risk alleles are assigned different point values. Record the Genetic Contribution score.
- 3 Add the total Environmental Contribution and total Genetic Contribution together to obtain the total score. Use the Chance Conversion Scale to convert the total score to the chance (out of 100) that your person will be a smoker as an adult.
- 4 Use a Post-It note to plot Chance on the class bar graph.

STUDENT SHEET F4.2: *continued...*

Analysis Questions

Sketch the class graph in your notebook and then answer the following questions in your notebook.

- 1 What does the graph tell you?
- 2 What would the graph look like if smoking behavior was determined by a single gene with little or no environmental contribution (e.g. pea seed coat color, cystic fibrosis)?
- 3 Consider the environmental factors in the game.
 - e. Did all the factors make the same contribution to smoking susceptibility? Explain your answer using your results.
 - f. Could any of the factors be controlled by the individual? Explain.
 - g. Which factors could not be controlled by the individual?
 - h. What is the difference between environmental factors that have positive values and those that have negative values?
- 4 Consider the genetic factors in the game.
 - d. Did everyone who rolled the same number for parental smoking behavior receive the same alleles?
 - e. Why was the "environmental factor" of parental smoking behavior chosen to determine genetic factors?
 - f. How did the contribution of a single genetic factor compare to the total genetic contribution?
- 5 What does "chance" mean in the Smoking Risk Game?
- 6 Our knowledge of the genetic factors affecting addiction to smoking is incomplete. How could learning about these factors be beneficial? How could increased knowledge be harmful?
- 7 In what ways does the game reflect how multifactorial traits work in real life, and in what ways is it inaccurate?
- 8 Based on the smoking behavior of your person's "parents," were you surprised by your person's chance of being a smoker? Why or why not?

Optional Extensions

Extension 1

You will be assigned an environmental factor or gene to investigate. Find out what research has been done on this factor and what is known about its effect on smoking behavior.

Extension 2

What other factors do you think might affect smoking? Research one of these factors and write a brief description of your findings. Be sure to cite your sources.

STUDENT SHEET F4.2: *continued...*

Smoking Risk Game Record Sheet

Determine the risk of smoking behavior by adding together the total genetic and environmental contributions.

I. Environmental Factors

Record the number rolled and points in the table below. Add the points together to find the total environmental contribution:

<u>Environmental Factor</u>	<u>Number Rolled</u>	<u>Points</u>
Parental Smoking Behavior	_____	_____
Friends/Coworkers Smoking Behavior	_____	_____
Education of Individual	_____	_____
Athletic Activity level	_____	_____
Stress Level	_____	_____
Total Environmental Contribution		

II. Genetic Factors

Record the number of high, neutral, and low risk alleles from your Genetic Contribution Card. Calculate the points for each type of allele and record below. Add the points together to obtain the total genetic contribution

<u>Allele Type</u>	<u># Alleles</u>	<u>Points</u>
High Risk	_____ × 1 =	_____
Neutral Risk	_____ × 0 =	_____
Low Risk	_____ × -1 =	_____
Total Genetic Contribution		

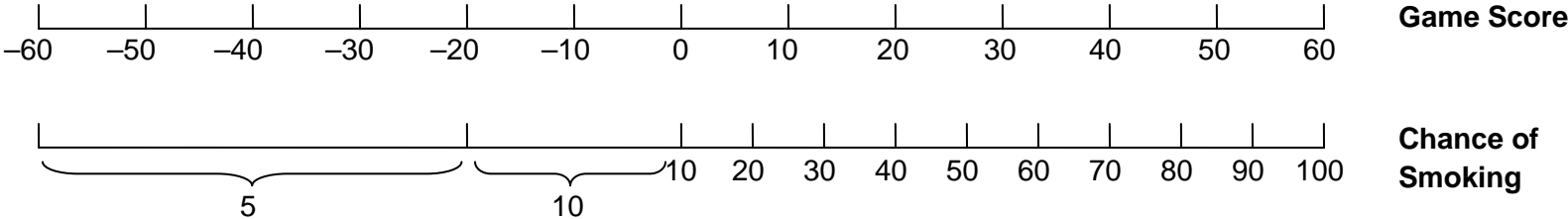
III. Calculate your Chance of Smoking:

Total Environmental+ Contribution	+	Total Genetic Contribution	=	Total Score

Using the Chance Conversion Scale, find the total score you obtained on the *Game Score* scale and read down to find the *Chance of Smoking* on the line below. (Estimate Chance to the nearest whole number.)

STUDENT SHEET F4.2: *continued...*

Chance Conversion Scale



STUDENT SHEET F4.2: *continued...*

Reflection Questions

Answer the following questions and place in your notebook.

- 1 Are multifactorial traits inherited?
- 2 How do multifactorial traits affect our ability to develop genetic tests for predicting a condition?

ACTIVITY E5

What is a Useful Genetic Test?

OVERVIEW

This activity is designed to help students think about 1) what constitutes a useful genetic test and 2) whether genetic tests that provide information about which smoking cessation treatment works best for a person should be developed and made available to the public.

Time

120 minutes.(e.g. two 50-minute periods and 20 minutes of a third period)

Materials

for each student

- Student Sheets F5.1, F5.2, F5.3, F5.4, F5.5, F5.6, F5.7, F5.8, and F5.9

for the class

- Transparency of Overhead Master F5.1

Learning Objectives

Students will:

- learn some of the reasons for doing genetic testing: newborn screening, prenatal testing, diagnostic testing, carrier screening, and predictive testing.
- learn about two major criteria that can be used to evaluate genetic tests, clinical utility and clinical validity, and how to apply them in evaluating tests.
- apply their knowledge by evaluating a commercially available genetic test that predicts which smoking cessation treatment works best for a person (NicoTest™).
- examine the ethical implications of genetic testing for a complex trait like smoking behavior, such as misuse of genetic information and discrimination.

Getting Ready

- 1 Please make sure to read the entire activity in advance.
- 2 Photocopy Student Sheets F5.1, F5.2, F5.3, F5.4, F5.5, F5.6, F5.7, F5.8, and F5.9, as well as the NicoTest™ web page (one of each per student).
- 3 Prepare a transparency of Overhead Master F5.1

Tips & Tricks

- The NicoTest™ website is no longer available online, so the web page has been provided as part of Student Sheet F5.1.
- In Activity E3, students learned about genes that might affect smoking behavior, including genes that code for receptors for dopamine or for the enzymes responsible for the breakdown of nicotine. The two genes used in NicoTest™, *DRD2* and *CYP2A6* code for a dopamine receptor and a liver enzyme that breaks down nicotine, respectively.

Presenting the Activity

The day before you begin the lesson, give students **Student Sheet F5.1** and a copy of the NicoTest™ web page. Assign this activity as homework. Ask students to evaluate the NicoTest™ as presented on the official NicoTest™ web page, and answer the questions on the handout.

Day 1 (50 minutes)

- 1** Introduce the lesson by reminding students that they have been learning how the body responds to smoking, and how genes may be involved in nicotine addiction. Now they will have an opportunity to look more closely at genetic testing. They will also evaluate several currently available genetic tests, including the smoking behavior genetic test they looked at for homework, NicoTest™, and analyze the tests' pros and cons.

Briefly discuss NicoTest™ with the students, using the questions as a guide. Ask students to report on their findings from the NicoTest web page. Do not attempt to critically evaluate NicoTest at this time. **However, do ask students what they think of NicoTest. Would they take it if they were a smoker who wanted to quit?** At this point, the only information students will have about NicoTest is from the product website, so they may not be able to answer this question. By asking this question, you can help students understand that information may be missing from the site that they would like to have in order to make an informed decision on whether to get tested. Be sure you communicate to students that it is OK to not have a firm answer right now and they will learn more about NicoTest later. **You may also ask what further information students would like to have.** Accept all answers uncritically and do not evaluate them. Answers to the NicoTest™ questions are provided in the teacher key.

- 2** Distribute **Student Sheet F5.2** to each student. Have students read it and break into small groups to answer the questions. Hold a class discussion on the material covered in the reading and ask students to share their responses to the questions with the class. Discussion ideas and answers are found in the teacher key.
- 3** Distribute **Student Sheet F5.3**. Discuss with your students that the chart is a tool to evaluate genetic tests. Based on the placement of a genetic test into one of 4 boxes in the chart, scientists, ethicists and doctors can determine how useful a genetic test might be, and whether or not it should be offered to patients. Use the information presented in the Teacher Background section to help you explain the chart to your students and field their questions.

Tips & Tricks

- Students may be confused by the terms, clinical validity and clinical utility. Make sure that they understand these terms, and ask students whether they can explain what they mean in their own words.
- Also make sure that students understand the meaning of penetrance and pleiotropy.

Presenting the Activity, Day 1 continued...

4 Practice using the *Genetic Conditions Chart* in **Student Sheet F5.4** with your students to assign a test for a genetic disorder to box 1, 2, 3, or 4. Put **Overhead F5.1** on your overhead/document projector. Use Hemophilia as an example or another genetic condition your class is familiar with. Explain (or remind) students that Hemophilia is a sex-linked recessive disorder that leads to excessive bleeding due to a failure in blood clotting. It can be fatal. The penetrance is high, and there is a very effective treatment called Factor VIII (a blood clotting protein). What box should the Hemophilia test be placed into? Guide students by first asking them about Clinical Validity. Is penetrance high or low? When they say penetrance is high, they have narrowed the answer to either Box 1 or 2. Then ask about clinical utility. Is there a treatment? The answer is yes. Therefore, the Hemophilia test goes into Box 1.

Definition: **Penetrance** is the frequency that a particular allele is expressed by the individuals who have it.

5 Distribute **Student Sheet F5.4** and have students do it that night for homework. Students should read through the four genetic conditions listed and determine into which box on the *Genetic Test Category Chart* they would place a genetic test for each. Students should also complete the questions at the end of the *Genetic Conditions Chart*.

Day 2 (50 minutes)

6 Briefly ask students which box on the *Genetic Test Category Chart* they placed each test into. Resolve any discrepancies and arrive at consensus, if possible.

The answers are:

- HD, Box 2;
- PKU, Box 1;
- HH, Box 3;
- AD, Box 4. AD may be somewhat ambiguous. Penetrance of AD due to the APOE4 mutation is 30%. Students might place it in Box 4 if they regard 30% to be low, or in Box 2 if they regard 30% to be high. We regard 30% to be low and so have assigned the test for AD to Box 4.

As you carry out this discussion with your students, write the name of the genetic condition in the appropriate box. Then discuss which ethical principle guides the potential use of the genetic information for each condition as follows:

1. testing for PKU (Box 1) is guided by justice—providing equal access to the test as part of newborn screening to ensure that the condition is detected early so treatment can begin as soon as possible;

Tips & Tricks

- Be sure to review the four ethical principles—autonomy, justice, non-maleficence, and beneficence—prior to assigning this activity.

Presenting the Activity, Day 2 continued...

2. *application of HD testing (Box 2) is guided by autonomy—the right of the individual to decide whether to be tested;*
3. *testing for HH (Box 3) is guided by beneficence and non-maleficence—weighing the benefits of testing against the harm of being labeled;*
4. *testing for AD (Box 4) is guided by non-maleficence—avoiding harm to an individual by providing information about an allele that has low penetrance and for which there is no cure.*

Collect the responses to the questions on the *Genetic Conditions Chart* in **Student Sheet F5.4**. If time permits, you can discuss the responses in class, but to move along through the activity, skip the discussion. Answers can be found in the teacher key.

7 Distribute **Student Sheets F5.5** and **F5.6** to the students. Tell students that they are now going to look at the sort of research that is done to determine whether or not there is a genetic basis for the variation people show in what smoking cessation treatment works best for them. This is the sort of research that led scientists to form a company and develop the NicoTest. (However, the Penn study does not provide data on either of the mutations assayed by NicoTest.) You can use the Purpose/Application/Background sections in **Student Sheet F5.6** to guide and support your introduction of this topic. Ask students to read the press release in **Student Sheet F5.5** and then ask if there are any questions. Verify student understanding and clarify any points of confusion. Alternatively, since the press release is less than a page, you could also read it out loud or call on students to read it out loud to the class.

8 Now tell students that they will be looking at some real data from the Penn Study and ask them to read **Student Sheet F5.6** and answer the questions. They should pay particular attention to the study data on the graph and the research conclusions. Go over the questions in class. Answers are provided in the teacher key. Important points to cover:

- Make sure students understand that the DRD2 allele in the Penn Study is different from the DRD2 allele that NicoTest tests for.
- This research shows that a genetic factor can contribute to the variation in people's response to smoking cessation treatments.
- Research can be interesting, reveal new information, and suggest possible applications, such as a genetic test. But that doesn't mean the research is necessarily ready to be turned into a product and offered for sale. Promising research leads to further research. After further research, testing, and consideration of benefits and harms to patients, research may be commercialized.

Tips & Tricks

- You may want to complete this activity in class, especially if the content or reading level seems too complex for your students to complete as a homework assignment.

Presenting the Activity, Day 2 *continued*...

9 Homework: Explain to students that for homework, they will examine an alternative view on NicoTest. Because the information a company provides on its products is designed to increase sales, it is always good practice for consumers to seek product information from an unbiased source. That is why *Consumer Reports* magazine is in business! Distribute **Student Sheets F5.7** and **F5.8** to students. Have students read the article in **F5.7** and answer questions 1-4 in **F5.8**.

Day 3 (20 minutes)

10 Collect the homework assigned the previous day, and discuss questions 1-4. Answers are provided in the teacher key.

11 Final Assessment – Reflection Question: Pass out **Student Sheet F5.9** to students. Assign the **Reflection Question** as a final assessment for students to do at home. Allow at least a couple of days. Student answers should be at least three paragraphs. Have students place their answer to the Reflection Question, as well as their other handouts, in their portfolios. If desired, you can also give students the option of answering the **bonus question** for extra credit.

Teacher Background on the Genetic Test Category Chart

Use this information to guide your discussion of the chart with students. The chart evaluates genetic tests based on two key features:

- a. **Clinical validity.** How well does the test predict whether the patient will get the disease? This is determined in part by the test's technical accuracy and in part by the penetrance of the disease.
- b. **Clinical utility.** Will the information provided by the test aid in medical decision making? Is an effective medical treatment available for the disease?

In some instances a genetic test may be required in medical care because the test accurately predicts the disease and an effective treatment is available, resulting in a clear and vital benefit to the patient. This situation corresponds to Box 1 in the chart and can be justified by the ethical principles of beneficence and non-maleficence. However, there may be a test that has high clinical validity but no treatment is available. In this situation, a test would be offered but patient autonomy would be the guiding ethical principle in whether or not the patient is tested. A test of this nature would be placed in Box 2. A genetic test would be placed in Box 3 if the test had low clinical validity but an effective treatment was available for the condition. Often a test that falls into this category would be administered only to provide additional confirmation of an already tentatively diagnosed condition. If a genetic test falls into Box 4, it would usually not be offered to patients.

Note that the chart does not take into account how accessible the treatment may be to the patient, an important ethical concern.

Teacher Keys

Key to Student Sheet F5.1. NicoTest™: Is it for you?

- 1 What kind of sample is collected to obtain the genetic material for the test? What specific genes are identified by the NicoTest™?

NicoTest analyzes DNA obtained from a blood sample. The two genes studied in NicoTest are:

- *DRD2 – gene that codes for a type of dopamine receptor in the brain*
- *CYP2A6 – gene that codes for the CYP2A6 enzyme which breaks down nicotine in the liver*

- 2 How is the genetic information from the NicoTest™ used to help a person quit smoking?

The genetic information from NicoTest is used to help people quit smoking in two ways. According to the NicoTest web site, an individual's genotype for the DRD2 gene will help determine whether Bupropion or Nicotine Replacement Therapy should be used to help quit smoking. CYP2A6 is typed to help determine what dose of Nicotine Replacement Therapy should be prescribed.

- 3 Are genetic testing and a medication recommendation the only things offered by this company to help smokers quit?

No, genetic testing and a medication recommendation are not the only things currently offered to help smokers quit. The website also offers ongoing behavioral support through an online support group, an instant messaging tool, and motivational e-mails.

Key to Student Sheet F5.2. Why Do Genetic Testing?**Check Your Knowledge**

Students can self check their vocabulary using the reading.

- 1 What are some of the potential benefits of genetic testing?

The results of genetic testing can increase patient awareness of potential health issues so they can take preventative action, begin medical treatment, or better prepare themselves for the life consequences of the result. Patients may also use genetic testing to help make reproductive decisions. The test gives doctors and other health care providers information to aid in diagnosing patients and may confirm a diagnosis that has already been made. This allows them to better tailor treatment for their patient.

- 2 What are some of the possible drawbacks of genetic testing?

Genetic testing is limited by its clinical validity (how well it predicts disease) and utility (whether there is any treatment for the disease). Some genetic tests are not particularly good at predicting disease. In other cases, there are no treatment options, so the genetic test only provides the patient with information on future problems, which might worry the patient. As with any medical procedure, there is some physical risk to the patient from the test itself, but this is minimal with genetic testing. A potential risk is that the patient will not understand the concept of penetrance, and will assume that a positive test for a particular gene indicates that they will indeed develop the disease, not

realizing that environmental factors as well as their own unique genetic makeup (the influence of their other genes) also play a role. Also, genetic information can be misused, for example by insurers or employers. A genetic test for a gene associated with phenotypes in addition to the disease in question (pleiotropy) could result in a patient learning his risk for other conditions, which may not be information the patient wants.

- 3** Now that you have learned more about genetic testing and read the NicoTest website, do you have enough information to decide whether NicoTest is a “good” test to be offering to the public?

No

- 4** If you don’t have enough information, what more would you like to know?

Students will come up with a variety of responses. They should want to know how effective this test is at predicting what the best cessation method is. They might want to see the actual data! They might ask, what is the penetrance of the genetic variations being tested for? How reliable is the test? They might want to know what will happen to patients’ genotyping results. Who will have access to them? Will g-Nostics keep the information after they have given the results to the patient? They might want to know if the results will provide information about any other traits (pleiotropy).

Key to Student Sheet F5.4. Genetic Conditions Chart – Evaluating Genetic Tests

- 1** Which box on the Genetic Category Chart should each genetic test be placed into?

HD, Box 2; PKU, Box 1; HH, Box 3; AD, Box 4. AD may be somewhat ambiguous. Penetrance of AD due to the APOE4 mutation is 30%. Students might place the AD test in Box 4 if they regard 30% to be low, or in Box 2 if they regard 30% to be high. We regard 30% to be low and so have assigned the test for AD to Box 4.

- 2** How is penetrance related to the usefulness of a genetic test?

A genetic test for a gene with high penetrance is useful because it is more likely to accurately predict whether a patient will develop the disease. Tests for genes with low penetrance give more ambiguous results and this kind of information needs to be presented to patients carefully to ensure they understand that just because they may possess a particular genotype, since the gene has low penetrance, they may never develop the disease.

- 3** How are the treatment options for a disease related to the usefulness of a genetic test?

A genetic test for a condition that can be medically treated is very useful because it can be used to identify people who could benefit from effective treatment (perhaps even lifesaving treatment) if they develop the disease. Positive results from a genetic test could also indicate the need for increased monitoring for disease development, which can also positively impact patient health. For example, when women test positive for disease-associated mutations in BRCA1, they can get mammograms more frequently and starting at a younger age, so that if cancer is detected, it can be treated right away, resulting in higher survival rates.

- 4 Why might the ethical principle of non-maleficence (minimize harm) be an acceptable justification for mandatory newborn testing for PKU?

Non-maleficence means to “do no harm.” Genetic testing for PKU is done with a heel prick, which causes minimal discomfort and almost no risk. It is a clinically valid test (both sensitive and specific), and the gene exhibits high penetrance. PKU causes brain damage within months of birth if untreated and the treatment is so simple (dietary modification), giving the test high clinical utility. By testing for PKU at birth, you harm no one and potentially prevent a devastating and easily preventable condition from developing.

- 5 For genetic tests that fall into Box 2 of the *Genetic Test Category Chart*, why do you think ethicists placed importance on the autonomy of the patient in deciding whether or not to be tested? (Remember that the ethical principle of autonomy holds that patients have the right to make self-determining choices.) Do you think testing in this situation is “useful”? Explain your reasoning.

If there is no way to treat the disease, then having a test predicting that a patient will develop the disease has limited usefulness. In some cases, patients may feel that they would rather not know since there is no treatment that will help them. Others may wish to be forewarned so they can prepare for the life consequences of their diagnosis. In either case, the information provided by the test won’t help the doctor treat the patient. Based on their individual values and concerns, a patient must make the decision himself about whether to be tested.

Key to Student Sheet F5.8. A Second Look at NicoTest™

Questions

- 1 Dr. Robert Walton is a scientific officer at g-Nostics, the company that sells NicoTest™. He is also on the faculty at Oxford University and has conducted research on the *DRD2* gene, one of the genes that is assayed in the NicoTest™. Dr. Walton was the author on a scientific paper that concluded that *DRD2* had little effect on a person’s smoking behavior. Is the dual role of Dr. Walton at g-Nostics and Oxford ethical? Why, or why not?

It could be considered a “conflict of interest” that Dr. Walton is serving in these dual roles. His position at the company and the company’s goal of being profitable might affect his ability to be scientifically neutral in evaluating the data obtained in his Oxford laboratory. There could be a temptation to not publish data that makes NicoTest look bad or to overemphasize promising but inconclusive data. And if he does publish research from his Oxford lab that appear to contradict claims made about NicoTest by g-Nostics, his credibility at the company could be undermined.

- 2 What are the main ethical concerns of GeneWatchUK in their criticism of NicoTest™? Which of these concerns do you think is the most important? Explain.

Expect students to choose different concerns, so answers will vary.

- 3 Do you think the outcome of the NicoTest™ could be harmful to your health? Explain.

Because the test is sold over the Internet and does not require direct contact with a medical professional, information provided by the test might be misinterpreted by the consumer and result in harm to an individual. For example, someone receiving a “negative” test result might assume that neither Nicotine Replacement Therapy or Wellbutrin would help him quit smoking, and so he would

not try either of these cessation methods. This might result in his continuing to smoke more years than he would have if he had sought treatment.

- 4 Place NicoTest™ on the Genetic Test Category Chart. Would it fall into Box 1, 2, 3 or 4? Explain.

The GeneWatch press release raises doubts about the accuracy of the test. How penetrant are the mutations that are tested for by NicoTest? The evidence is not conclusive that if a person has either mutation, he is more likely to respond to a particular treatment. There are many genes contributing to smoking behavior. The test is giving undue weight to just a couple of them, and not accounting for environmental factors either. In short, these genes would be considered to have low penetrance, and therefore the test would have low clinical validity, placing it in either Box 3 or 4. Whether Box 3 or 4 is the most appropriate depends on how effective treatment is. The highest “quit rates” for specific cessation treatments are never more than 40%, and even these rates decline with time (many smokers relapse after a few months). So, given a lack of a highly effective treatment, the most appropriate box would be Box 4. But students can probably also make a good case for choosing Box 3.

Key to Student Sheet F5.9. Final Reflection on Genetic Testing

Final Question.

You are a smoker trying to quit and are considering using a genetic test to help you choose the cessation treatment that would work best for you. Discuss 1) what features the genetic test would have to have in order for you to want to use it and 2) possible concerns that might make you think twice about using the test. Support your answer by referring to what you have learned from the NicoTest website, the Penn Study, and the GeneWatch UK press release. You may also want to refer to what you have learned about evaluating genetic tests using the Genetic Test Category Chart.

Answers will vary. Make sure both #1 and #2 are discussed and that adequate support from the readings the students have done is provided. Students should cite both scientific and ethical concerns. Referring to the Genetic Test Categories Chart to help them decide what would make a good test should get high marks.

Bonus question (optional)

GeneWatch UK says that any genetic test should be available only through medical professionals, and not sold directly to the general public. The California Department of Public Health has recently warned 13 genetic testing companies to stop marketing their products directly to California consumers because they are in violation of state licensing and testing laws. Do you agree that genetic tests should not be offered directly to consumers? Why or why not? (In the U.S., a similar objection was raised to allowing pharmaceutical companies to directly advertise their medications to consumers, which prior to the early 1980s, was not permitted.)

This is designed as an extra credit question. Students can google “direct to consumer prescription advertising” to identify a number of information sources to help support their answer with that precedent. One reference is given in the references section on the student reading, A Second Look at NicoTest.

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Genetic Conditions Chart

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Genetic Test Category Chart

		<u>Clinical Validity</u>	
		HIGH	LOW
<u>Clinical Validity</u>	HIGH	<p>Box 1 Effective treatment is available for this condition and the test accurately predicts disease (high penetrance)</p> <p>Conclusion: Required testing.</p>	<p>Box 2 Highly effective treatment is not available for this condition but the test accurately predicts disease (high penetrance)</p> <p>Conclusion: Allow patient autonomy in deciding to test.</p>
	LOW	<p>Box 3 Effective treatment is available for this condition, but the test does not accurately predict disease (low penetrance)</p> <p>Conclusion: Test may be useful to confirm a medical diagnosis.</p>	<p>Box 4 Highly effective treatment is not available for this condition and the test does not accurately predict disease (low penetrance)</p> <p>Conclusion: Test does not benefit patients and should not be offered.</p>

*Adapted from Burke W, Pinsky L, and Press N 2001. Categorizing Genetic Tests to Identify Their Ethical, Legal and Social Implications. *American Journal of Medical Genetics*, 2001 106:233-240.

STUDENT SHEET F5.1: NicoTest Web Page (printed July 2009)

<http://vcc.nicotest.com/>

NicoTest™

About the NicoTest

NicoTest™ is a Smoking Cessation Solution that combines pharmacogenetics and Online Cognitive Behavioural Therapy (CCBT) to deliver Personalised Treatment.

The NicoTest™ can be ordered from our secure website by clicking [here](#) or ask your pharmacists for the NicoTest™.

How Does it Work?

The NicoTest™ takes a small blood sample from a smoker and analyses it for 2 genes. One gene is DRD2 dopamine receptor and the other is CYP2A6. The first gene enables us to tell smokers whether they should use Zyban (Bupropion) or Nicotine Replacement Therapy (NRT). The second gene indicates dosing (whether the smoker should have a high, medium or low dose of medication). The NicoTest™ is simple and painless. The NicoTest™ Computerised Cognitive Behavioural Therapy (CCBT) is an online programme that helps smokers adapt their behaviour to their new smoke free lifestyle. This software has been used in North America successfully for 5 years and is endorsed by the American Cancer Society and the Canadian Cancer Society.

The NicoTest *Flight to Freedom* starts with a detailed series of questions to find out why you smoke. Your test results and your responses to the questions in your *Flight to Freedom* are used to work out the best way for you to stop smoking. The NicoTest™ provides you with a Personalised Treatment Report to help you to quit. You can also log in to our 24-hour support service on the internet that will guide and help you on your road to success.

What Happens After I Order the Test?

Simply return your sample in the pre-paid envelope and complete Milestone 1 to 3 in your *Flight to Freedom*. Once the sample analysis is complete your Personalised Treatment Report (PTR) will be emailed directly to you and uploaded to your Suitcase.

The PTR combines specific, appropriate treatment and a series of lifestyle pointers to maximise your chances of success. Your PTR will also include a personalised coping plan to manage weight gain and stress as you become a non-smoker.

Please note that your PTR will take about 14 days to process from the time you return your sample. In the meantime, we suggest you continue with the exercises on this site as we will also need all the information you provide in Milestones 1 to 3 to issue your Personalised Treatment Report.

Click [here](#) to buy the NicoTest or ask your pharmacists for the NicoTest™.

Name: _____ Date: _____ Period: _____

STUDENT SHEET F5.1:

NicoTest™: Is it for You?

Read the copy of the NicoTest™ web page (no longer available online) and browse through the information and claims that are made.

As you look at this web page, answer the following questions:

- 1 What kind of sample is collected to obtain the genetic material for the test? What specific genes are identified by the NicoTest™?
- 2 How is the genetic information from the NicoTest™ used to help a person quit smoking?
- 3 Are genetic testing and a medication recommendation the only things offered by this company to help smokers quit?

STUDENT SHEET F5.2:

Why Do Genetic Testing?

Types of Genetic Tests

Genetic tests reveal information about a person's genes. Some genetic tests examine the DNA directly for a particular genetic mutation. Others are indirect and look for the presence or absence of enzyme activity resulting from that gene.

When are Genetic Tests Used?

Genetic tests are used in a number of situations, for example, in:

- Newborn screening. Infants are screened for specific genetic conditions, such as phenylketonuria (PKU), in order to allow early medical intervention. Screening is done within hours or days of birth and is required by most states.
- Prenatal testing. When a pregnant woman is at high risk for having a baby with a genetic condition, the fetus can be tested using a technique such as amniocentesis.
- Diagnostic testing, such as the test for Duchenne's Muscular Dystrophy, is used to confirm or rule out a diagnosis in a patient showing symptoms that suggest the disease.
- Carrier screening, such as the test for Sickle Cell Disease, identifies people who carry only one copy of a particular mutation. People can use this information to help them make future reproductive decisions, such as whether or not to have children.
- Predictive testing is used to identify people with family histories of genetic disease, for example people carrying mutations in BRCA1, which increase the risk for breast cancer. Early identification can signal the need for more frequent disease screening in people who test positive, allows earlier medical treatment, and can lead to better results for the patient.

How useful a genetic test is depends both on its **clinical validity** and **clinical utility**.

Clinical Validity

Clinical validity refers to how well the test predicts if the person has or will develop the genetic condition. It depends on 1) the test's accuracy and technical performance--how well it correctly identifies whether a person has the mutation or not and 2) the genotype's **penetrance**. Penetrance is not a feature of the test, but is related to the expression of a person's genotype. It may depend on a person's genetic make-up (other genes) and on environmental factors. The penetrance of a genotype indicates how likely it is that the mutation will result in the genetic disease. For example, not all people with a BRCA1 mutation will develop breast cancer, so the penetrance of this genotype is less than 100%. In contrast, people with the Huntington's Disease mutation almost always develop the disease, so the penetrance of this mutation is virtually 100%.

Clinical Utility

Clinical utility refers to whether the test results can aid in medical decision making and improve patient health. It is related to the practical information the test provides. For example, infants testing positive for PKU can be fed an altered diet that will prevent severe mental retardation. So because there is an effective treatment for PKU, the test has high clinical utility. A positive genetic test for Huntington's

STUDENT SHEET F5.2 *continued...*

Disease, on the other hand, has low clinical utility, because there is no way to treat or prevent this fatal condition. Even so, a genetic test with low clinical utility can have other value, such as allowing people carrying the mutation to plan and prepare for their shortened lives, or to make reproductive decisions.

Ethical Concerns

Some genes influence more than one phenotypic trait. When changes in a gene have more than one effect in an organism, it is called **pleiotropy**. For example, some mutations in the DRD2 (Dopamine Receptor 2) gene have been associated with several conditions, including nicotine addiction, ADHD, predisposition to gambling, and heavy alcohol use. Some day in the future a person might be able to take a DRD2 genetic test for nicotine addiction and end up learning not only about his risk for nicotine addiction but also his potential for these other traits as well. This “extra knowledge” might be unwanted and more than the person bargained for. The information could be misused and cause harm to the person being tested. Because penetrance is often not 100%, a positive test does not necessarily mean the chance of developing any of the traits is high. Can insurance companies be trusted to understand this type of complicated, “gray area” information? Can patients themselves be educated enough to understand? Would it be better not to know genetic test results if they can be so uncertain and could cause needless worry? These are all questions worth asking as the benefits and drawbacks of genetic tests are evaluated.

An important ethical concern related to genetic tests is **discrimination**, which occurs when a person or group of people are treated unfairly because of their genetics. For example, a person might be denied health insurance or employment if he carried a particular mutation, even if he didn’t have the disease. Or if a larger than average proportion of a group of people carried a certain mutation, it could lead to discrimination against all who belong to the group, for example by branding all group members with harmful stereotypes. Education is vital to avoiding such damaging consequences, and laws against genetic discrimination are important too. In 2008, President Bush signed into law the Genetic Information Nondiscrimination Act, which protects Americans against discrimination based on genetics in employment and health insurance. It is still too soon to know the impact of this act.

Another ethical concern is that associations between certain mutations and conditions may promote **determinism**—a fatalistic attitude in patients about their future health: “I’ve got the gene, so I’ll get the disease. Why should I keep trying (to lower my blood pressure, to quit smoking, to lose weight)?” Due to low penetrance, carrying a certain gene may not guarantee any health outcome—bad or good. But if learning they carry a certain mutation causes some people to stop trying to improve their health, should the test be offered to the public? Would it result in more harm than good? Alternatively, people who found out they had a gene that predisposed them to nicotine addiction might try extra hard to never even experiment with cigarettes, so for these people, getting the test would be helpful. People will react differently to learning their genetic information. Education about complex genetic issues is certainly key to both preventing harm and fighting discrimination.

Name: _____ Date: _____ Period: _____

STUDENT SHEET F5.2 *continued...*

Reflect on the Reading

After reading **Why Do Genetic Testing?**, check your vocabulary knowledge below, answer the questions, and be prepared to discuss them in class. Support your answers with specific examples from the reading:

Check Your Knowledge

Match each phrase or word to its definition.

Penetrance	How accurate a genetic test is in predicting if a person will develop a genetic disease
Clinical utility	When a mutation affects more than one trait
Pleiotropy	How useful a genetic test is in helping determine patient care
Clinical validity	How likely it is that a mutation will result in the disease
Carrier screening	When a genetic test is used to identify people who have only one copy of a mutation

Questions

- 1 What are some of the potential benefits of genetic testing?
- 2 What are some of the possible drawbacks of genetic testing?
- 3 Now that you have learned more about genetic testing and read the NicoTest website, do you have enough information to decide whether NicoTest is a “good” test to be offering to the public?
- 4 If you don’t have enough information, what more would you like to know?

STUDENT SHEET F5.3:

Genetic Test Category Chart

The chart below was developed by ethicists* to evaluate genetic tests and help determine the situations in which these tests should be offered, if at all. The chart divides genetic tests into four categories (boxes) by evaluating each test according to two criteria:

- **Clinical Validity** indicates how well the presence or absence of the mutation predicts disease, based partly on the test's technical accuracy and partly on the penetrance of the disease.
- **Clinical Utility** indicates whether the test result will aid in medical decision making and whether there is an effective treatment for the condition.

The chart includes a description of the Clinical Validity and Utility of a test from each category, as well as a conclusion about whether the genetic test should be offered to patients.

You will use the chart to evaluate tests for four different genetic conditions.

		<u>Clinical Validity</u>	
		HIGH	LOW
<u>Clinical Validity</u>	HIGH	<p>Box 1 Effective treatment is available for this condition and the test accurately predicts disease (high penetrance)</p> <p>Conclusion: Required testing.</p>	<p>Box 2 Highly effective treatment is not available for this condition but the test accurately predicts disease (high penetrance)</p> <p>Conclusion: Allow patient autonomy** in deciding to test.</p>
	LOW	<p>Box 3 Effective treatment is available for this condition, but the test does not accurately predict disease (low penetrance)</p> <p>Conclusion: Test may be useful to confirm a medical diagnosis.</p>	<p>Box 4 Highly effective treatment is not available for this condition and the test does not accurately predict disease (low penetrance)</p> <p>Conclusion: Test does not benefit patients and should not be offered.</p>

*Adapted from Burke W, Pinsky L, and Press N. Categorizing Genetic Tests to Identify Their Ethical, Legal and Social Implications. American Journal of Medical Genetics, 2001; 106:233-240.

**The ethical principle of autonomy holds that patients have the right to make self-determining choices.

STUDENT SHEET F5.4: **Genetic Conditions Chart – page 1**

For each of the genetic conditions below, use the information provided as well as the *Genetic Test Category Chart* to evaluate whether or not a genetic test for each condition should be offered to patients. Be sure to fill in the column on the right.

Condition	Gene	Clinical validity (penetrance)	Clinical utility (treatment options)	Box on Genetic Test Category Chart (fill in)
Huntington's disease (HD) is an autosomal dominant, progressive, neurodegenerative disorder that causes uncontrolled movements, loss of intellectual faculties, and emotional disturbance. It begins to develop in adulthood and progresses until death 10-20 years later.	HD is caused by an expanded GAC repeat (more repeat copies) in the HD gene.	High penetrance. Close to 100% of people inheriting one copy of the HD mutation will develop the disease in their lifetimes. The age of onset varies, but is often after people have begun families. Whether a person carries the HD allele is determined by DNA analysis.	There is no treatment to prevent HD. Non-curative medical treatments can provide some relief from emotional, psychological, and muscular symptoms. It is important to remain physically fit. Since symptoms often don't develop until after people have reproduced, genetic test information can only help some with HD make reproductive decisions.	
Phenylketonuria (PKU) is an autosomal recessive disorder that disrupts the body's ability to break down the amino acid phenylalanine, resulting in severe mental retardation.	PKU is caused by mutations in the PAH gene, which codes for the enzyme phenyl-alanine hydroxylase. Absence of the enzyme results in PKU.	Penetrance is very high, near 100%. Diagnosis is by a simple test that detects the level of phenylalanine in the blood.	PKU is effectively treated with a lifetime diet low in phenylalanine that includes a tyrosine supplement.	

STUDENT SHEET F5.4: Genetic Conditions Chart – page 2

Condition	Gene	Clinical validity (penetrance)	Clinical utility (treatment options)	Box on Genetic Test Category Chart (fill in)
<p>Hereditary hemochromatosis (HH) is an autosomal recessive iron overload disorder that causes the body to absorb and store too much iron. The excess iron is stored in organs, especially the liver, heart, and pancreas. HH can lead to liver disease and cancer, diabetes, heart failure, arthritis, and endocrine disorders.</p>	<p>Two alleles of the iron absorption gene <i>HFE</i>, C282Y and H63D, can cause HH.</p>	<p>83% of people with HH are C282Y homozygotes. Having disease-associated alleles does not always lead to HH. Penetrance is ~1% in C282Y homozygotes. Penetrance is thought to be lower in women due to blood loss during menstruation. Diagnosis is by a blood test for iron, followed by a genetic test for <i>HFE</i> to confirm.</p>	<p>After diagnosis, one pint of blood is removed 1-2 times per week to lower the iron level, and then once every few months for life to maintain a normal iron level. Iron supplements should be avoided. If cirrhosis of the liver has developed, alcohol should be avoided and the liver monitored regularly for cancer by ultrasound.</p>	
<p>Alzheimer's disease (AD) is a progressive, degenerative form of dementia that impairs memory, thinking, and behavior and can affect language, decision-making, judgment, attention, and personality. In some people, it develops and progresses quickly, in others, slowly.</p>	<p>Several genes are associated with increased risk of developing AD. The most well established is the <i>APOE4</i> allele of apolipoprotein E.</p>	<p><i>APOE4</i> is associated with ~50% of AD cases. Having <i>APOE4</i> is not always associated with getting AD. Penetrance is 30% in <i>APOE4</i> homozygotes. The average age of AD onset is 68 years with 2 E4 alleles, 75 with 1 E4 allele, and 84 years with no E4. Because the age of AD onset varies, some <i>APOE4</i> homozygotes will not live long enough to develop AD.</p>	<p>There is no treatment that prevents AD. Some treatments can slow progression and help manage patient confusion, agitation, and behavior problems.</p>	

Name: _____ Date: _____ Period: _____

STUDENT SHEET F5.4 *continued...*

Evaluating Genetic Tests: Student Questions.

Answer these on a separate piece of paper.

- 1 Which box on the Genetic Category Chart should each genetic test be placed into?

- 2 How is penetrance related to the usefulness of a genetic test?

- 3 How are the treatment options for a disease related to the usefulness of a genetic test?

- 4 Why might the ethical principle of non-maleficence (minimize harm) be an acceptable justification for mandatory newborn testing for PKU?

- 5 For genetic tests that fall into Box 2 of the *Genetic Test Category Chart*, why do you think ethicists placed importance on the autonomy of the patient in deciding whether or not to be tested? (Remember that the ethical principle of autonomy holds that patients have the right to make self-determining choices.) Do you think testing in this situation is “useful”? Explain your reasoning.

STUDENT SHEET F5.5:

Univ. of Pennsylvania School of Medicine Press Release

This press release describes the Lehrman study (2006) on DRD2 variation and smoking cessation treatment. (http://www.uphs.upenn.edu/news/News_Releases/aug05/smkgene_print.htm)

Penn Study Shows Genes May Affect Response to Different Quit-Smoking Medications

August 29, 2005

(Philadelphia, PA) - A study by researchers at the Transdisciplinary Tobacco Use Research Center (TTURC) of the University of Pennsylvania School of Medicine indicates that a smoker's genetic make-up may affect whether they quit or not while using either bupropion (Zyban®) or nicotine replacement therapies (NRTs) such as the nicotine patch or nasal spray. The results appear in the August issue of *Neuropsychopharmacology*.

"This study provides new evidence that genetic differences in the brain-reward pathways of smokers may reveal whether they would benefit more from Zyban® or nicotine replacement therapy as an aid to quitting smoking," said lead author Professor Caryn Lerman, PhD, Director of the TTURC and Associate Director for Cancer Control Population Sciences at Penn's Abramson Cancer Center.

Lerman led a research team that completed two randomized clinical trials each with a six-month follow-up period: a double blind placebo-controlled trial of bupropion and an open-label trial of transdermal nicotine patch versus nicotine nasal spray. Both trials examined the roles of functional genetic variation in the dopamine D2 Receptor (DRD2) gene called DRD2 -141C. At this location in the DRD2 gene, people carry one of two different variants, a Del C variant or an Ins C variant (Del is for deletion and Ins is for Insertion). The research team found that smokers with two copies of the DRD2 -141 Ins C variant were significantly more likely to be abstinent at the six-month follow-up if they used Zyban®, as compared to smokers carrying the Del C variant. By contrast, smokers carrying the Del C variant had significantly higher quit rates if they used NRTs as compared to those with the Ins C variant.

This research may have important implications for the delivery of quit-smoking medications that are targeted to individual smokers' needs. "Although these results require confirmation in a larger study prior to translation to practice," said Lerman, "they do suggest that genetic information may be useful in selecting the type of nicotine dependence treatment that will be most beneficial for a particular smoker."

This research was funded by the National Cancer Institute and the National Institute on Drug Abuse and was conducted by the University of Pennsylvania Transdisciplinary Tobacco Use Research Center.

STUDENT SHEET F5.6:

Does a Person's Genes Affect Which Smoking Cessation Treatment Works Best for Them?

Read the University of Pennsylvania press release in Student Sheet F5.5.

Purpose of Research

This type of research in the Penn study attempts to determine whether there is a genetic basis for the variability of success in quitting smoking in response to different cessation treatments. Do people with certain genetic variations respond better to one treatment than to another?

Potential application of research

Doctors have shown interest in a genetic test that would help them tailor a patient's smoking cessation treatment.

Background Knowledge

In Lesson 3 you learned about smoking cessation treatments such as Nicotine Replacement Therapy (NRT) and Zyban (bupropion). In the brain, bupropion inhibits the reuptake of dopamine into nerve cells. Remember, dopamine is the neurotransmitter released in response to nicotine. It is the key chemical messenger involved in the brain's reward pathway and is the reason people find smoking pleasurable. When dopamine reuptake is blocked, more dopamine molecules remain active for longer, resulting in continued activation of the reward pathway. More dopamine = more pleasure!

It is plausible that variation in the genes in the dopamine pathway, such as the genes for dopamine receptors, may affect nicotine addiction and treatment response. The single base insertion allele of the dopamine receptor 2 used in this study, "*DRD2* -141C Insertion/Deletion," is transcribed more efficiently than the deletion allele, which could lead to higher dopamine levels in the brain. **Note that this is a different *DRD2* allele than is tested by NicoTest, and results with this allele do not apply to NicoTest.**

Study Data

Examine the graph on the following page. It contains data from two studies from the University of Pennsylvania and has been simplified for this lesson. Study participants, all smokers, were given either bupropion, nicotine replacement therapy (NRT), or placebo for 10 weeks as they attempted to quit smoking. They were followed for 6 months to determine who had successfully quit smoking. Participants were genotyped for the *DRD2* -141C Insertion/Deletion allele. The graph shows quit data at the 10 week mark in the study.

Research Conclusions

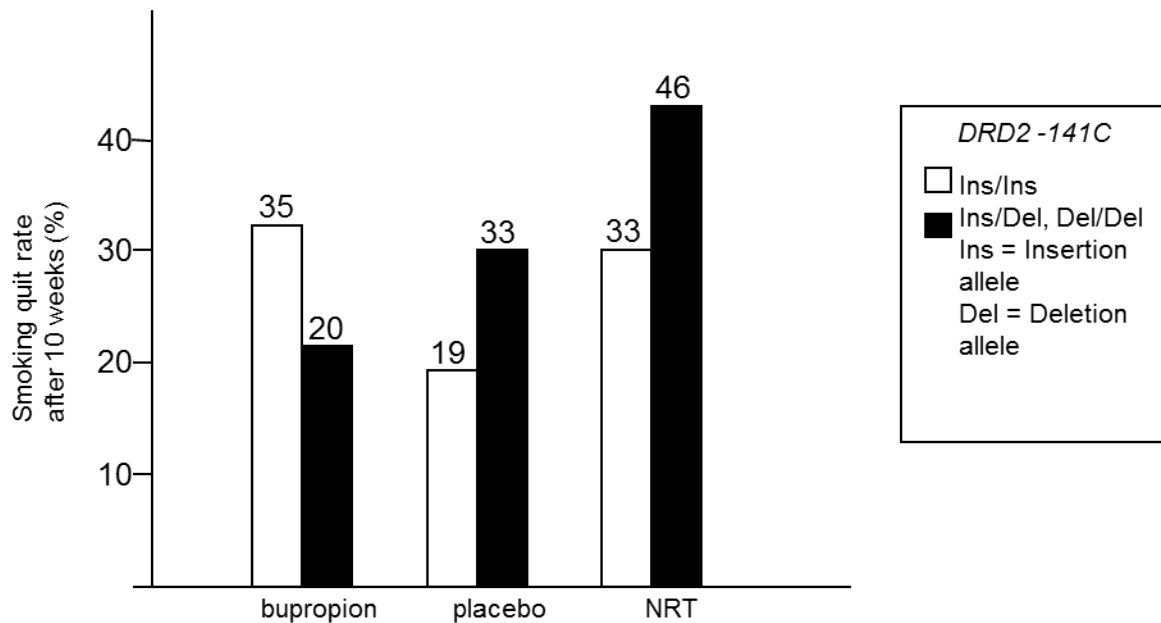
DRD2 -141C Insertion allele ("Ins"). When study participants were given bupropion, smokers who had two copies of the Ins allele had a higher rate of quitting success after 6 months than did smokers with 1-2 copies of the Deletion allele ("Del"). **Therefore, bupropion treatment may be more effective for people with the *DRD2* -141C Insertion allele than with the Del allele.**

How could our knowledge of the dopamine pathway explain this result? One idea is that people with the Insertion allele might have more dopamine or a circumstance mimicking that effect (e.g. dopamine receptor that binds dopamine more tightly) and thus experience greater pleasure when smoking. This

STUDENT SHEET F5.6 *continued...*

could make quitting harder than if they had the Deletion allele and felt less pleasure. Therefore, increasing dopamine levels by another means, such as through bupropion treatment, might preferentially help people containing the Insertion allele.

DRD2 -141C Deletion allele ("Del"). When smokers were given NRT, those who had either one or two copies of the Del allele had a higher rate of quitting smoking after 10 weeks than those with two copies of the Ins allele. However, after 6 months, this result did not hold up. Therefore, NRT might possibly be more effective in people with the *DRD2*-141C Deletion allele, especially in early stages of cessation.



Name: _____ Date: _____ Period: _____

STUDENT SHEET F5.6 *continued...***Questions**

Discuss and answer the following questions within your group. You may use information from what you have read about the University of Pennsylvania study and may also consider what you have learned from *Why Do Genetic Testing?* and the Genetic Test Category Chart.

- 1 Look at the study data bar graph. Which genotype, *DRD2* -141C Ins/Ins or Ins/Del + Del/Del, was able to quit smoking more easily when given:
 - Bupropion?
 - Placebo?
 - Nicotine Replacement Therapy?

- 2 What genotype, *Ins/Ins* or *Ins/Del + Del/Del*, naturally has a harder time quitting smoking (with no treatment)?

- 3 Does the Penn study data support the idea that genetic factors contribute to the variation in people's response to different cessation treatments?

- 4 Suppose that there is a genetic test for the *DRD2* -141C Ins/Del allele and that you are a smoker and want to quit smoking. You take the test and learn you are homozygous for *DRD2* -141C Ins (your genotype is Ins/Ins). How would this affect your plan to stop smoking, if at all? Would you talk to your doctor about using Bupropion? Nicotine replacement therapy? Neither? Explain.

- 5 Based on your knowledge of this study, do you think there is enough information for researchers to go ahead and develop a genetic test for *DRD2* -141C that would determine what smoking cessation treatment a person should use? Why or why not? If you don't think there is enough information to answer this question, what more would you need to know?

STUDENT SHEET F5.7:

GeneWatch UK Press Release

From GeneWatch UK website
([http://www.genewatch.org/article.shtml?als\[cid\]=492860&als\[itemid\]=504445](http://www.genewatch.org/article.shtml?als[cid]=492860&als[itemid]=504445))

GeneWatch PR: A sales pitch not science - Oxford University attacked for marketing of misleading 'nicotine addiction' gene test

For immediate release: Tues 4 Jan 2005

(GeneWatch UK today called for Oxford University to withdraw its funding and support for a genetic test claimed to be related to nicotine addiction. The new test, NicoTest, was launched on 2nd December by g-Nostics Ltd, a 'spin out' company from Oxford University (1). Oxford University is one of g-Nostics' shareholders and g-Nostics says its claims are based on research by the university's scientists (2).

In a new briefing, reported by the Observer newspaper (3), GeneWatch reveals:

- The claimed link between the gene and nicotine addiction does not meet the usual standards of scientific evidence (it is not statistically significant).
- There is a conflict of interest between g-Nostic's scientific officer's role in promoting a commercial product and at the same time providing and interpreting the evidence given to its customers whilst emphasising his link to Oxford University (4).
- The website promoting the test gives seriously misleading figures for both the usefulness of treatment and the value of the test in deciding who should get which treatment.
- The NicoTest website ignores scientific evidence that the test is unlikely to be useful for men.
- The website fails to give customers other information that might make them think twice before they take the test.

GeneWatch warns that using the NicoTest could mislead smokers and potentially harm health: it recommends that people do not take the test.

"People thinking about buying this genetic test should know that they are reading a misleading sales pitch not scientific evidence", said Dr Helen Wallace, Deputy Director of GeneWatch UK. "Oxford University is tarnishing its name by failing to keep its research and its commercial spin-offs separate. Are they snake-oil merchants or a university?"

In addition to advising people not to take the test, GeneWatch has written to g-Nostics Ltd, Oxford University and the Human Genetics Commission, seeking the withdrawal of the NicoTest and has made a complaint to the Trading Standards office (5). GeneWatch believes that an independent regulator should be set up to assess all genetic tests before they are marketed. Genetic tests should also not be sold directly to the public, but only via medical professionals who can ensure that they are properly interpreted.

STUDENT SHEET F5.7 *continued...*

"Unless the Government acts swiftly to regulate genetic tests, there will be more disreputable claims, which risk misleading people and may harm their health," said Dr Wallace. "Without regulation, the Human Genome Project is in danger of becoming a massive marketing scam. The people assessing health claims for genetic tests should not be the same people that are profiting from selling them."

Some genetic tests are useful for certain individuals and are already available in the NHS, but others are based on weak or contradictory evidence. Proper regulation would mean the claimed link between the gene and the disease, behaviour or drug response would be independently assessed - as would its usefulness in deciding who should get which health advice or treatment (6).

Under the Government's ten year science and innovation framework, universities are increasingly encouraged to make links with businesses and commercialise discoveries, as part of the 'knowledge-based economy' (7). But most studies linking genes to common diseases or behaviour (such as addiction) later turn out to be wrong. Conflicts of interest can arise if further scientific research does not back the original marketing plan or patent claim and the confidence of the public in the independence of university scientists will be eroded.

"Who is selling knowledge and who is selling spin?" said Dr Wallace. "With science up for sale it becomes impossible to tell what is evidence and what is marketing."

Notes to editors:

1. The website for NicoTest is: www.nicotest.com .
The website for the company is: www.g-nostics.com .
The test launch was widely reported, for example:
<http://news.bbc.co.uk/1/hi/health/4061137.stm>
2. The links between the company and Oxford University are reported on: <http://www.isis-innovation.com/about/news/gnostics.html> .
The university is also listed as a shareholder on the company's website: <http://www.g-nostics.com/index.php/investors> .
3. GeneWatch's briefing 'Three reasons not to buy the NicoTest genetic test' is available on: http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Nicotest_brief_final.pdf
The Observer article is available on:
http://observer.guardian.co.uk/uk_news/story/0,6903,1382068,00.html
4. Dr Robert Walton is Chief Scientific Officer, Lead Inventor and co-founder of g-Nostics: <http://www.g-nostics.com/?Dr%20Robert%20Walton> . He is a co-author of many of the scientific papers relating to the test, based on research conducted when he was head of the General Practice Research Group at the Department of Clinical Pharmacology, University of Oxford. These papers have been quoted selectively on the company's website, omitting evidence that does not back the company's claims. (Author's note: This link is no longer active).
5. Letters available on request.
6. More information on other companies selling genetic tests is available in GeneWatch's briefing 'Genetic tests and health: the case for regulation', on:
<http://www.genewatch.org/HumanGen/Publications/Briefings.htm#Brief28>
7. HM Treasury, DTI and DfES (2004). Science & innovation investment framework 2004-2014.

STUDENT SHEET F5.8:

A Second Look at NicoTest™

Read the GeneWatch UK press release from **Student Sheet F5.7**.

Background Knowledge

- This press release is written by GeneWatch UK. According to their website, GeneWatch UK is a not-for-profit organization that analyzes new genetic technologies. They are interested in the impacts of these technologies on public interest, environmental protection, and animal welfare. They believe that the public should have a voice in determining whether or not new genetic technologies are used.
- The GeneWatch UK press release is dated January 4, 2005 and was released as a response to the first published NicoTest™ web site.
- The press release is based on a 9 page advisory document written by GeneWatch UK called, *Three Reasons Not to Buy the NicoTest™ Genetic Test*. More information on the organization's objections to the test is available in this advisory document (reference below).
- In this press release, GeneWatch states its objections to NicoTest™ and calls for Oxford University to cease their funding and support of NicoTest™, which is sold by the company g-Nostics.

References

GeneWatch UK. GeneWatch PR: A sales pitch not science – Oxford University attacked for marketing of misleading 'nicotine addiction' gene test. GeneWatch UK press release, Jan 4, 2005. Available at [http://www.genewatch.org/article.shtml?als\[cid\]=492860&als\[itemid\]=504445](http://www.genewatch.org/article.shtml?als[cid]=492860&als[itemid]=504445) (Accessed Sept 7, 2010).

GeneWatch UK. Three Reasons Not to Buy the NicoTest™ Genetic Test. 2004. Available at http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Nicotest_brief_final.pdf (Accessed Sept 7, 2010).

Huang, A. J. The Rise of Direct-to-Consumer Advertising of Prescription Drugs in the United States. *Journal of the American Medical Association* 2000; 284:2240. Reprint available at <http://jama.ama-assn.org/cgi/reprint/284/17/2239.pdf>.

Name: _____ Date: _____ Period: _____

STUDENT SHEET F5.8 *continued...*

Questions

Discuss and answer the following questions within your group. Be sure to use information from the article as well as the Genetic Test Category Chart and the NicoTest™ website.

- 1 Dr. Robert Walton is a scientific officer at g-Nostics, the company that sells NicoTest™. He is also on the faculty at Oxford University and has conducted research on the *DRD2* gene, one of the genes that is assayed in the NicoTest™. Dr. Walton was the author on a scientific paper that concluded that *DRD2* had little effect on a person's smoking behavior. Is the dual role of Dr. Walton at g-Nostics and Oxford ethical? Why, or why not?
- 2 What are the main ethical concerns of GeneWatchUK in their criticism of NicoTest™? Which of these concerns do you think is the most important? Explain.
- 3 Do you think the outcome of the NicoTest™ could be harmful to your health? Explain.
- 4 Place NicoTest™ on the Genetic Test Category Chart. Would it fall into Box 1, 2, 3 or 4? Explain.

STUDENT SHEET F5.9:

Final Reflection on Genetic Testing

Final Question.

Please answer the following question on a separate piece of paper. Your answer should be at least 3 paragraphs.

You are a smoker trying to quit and are considering using a genetic test to help you choose the cessation treatment that would work best for you. Discuss 1) what features the genetic test would have to have in order for you to want to use it and 2) possible concerns that might make you think twice about using the test. Support your answer by referring to what you have learned from the NicoTest website, the Penn Study, and the GeneWatch UK press release. You may also want to refer to what you have learned about evaluating genetic tests using the Genetic Test Category Chart.

Bonus question (optional)

GeneWatch UK says that any genetic test should be available only through medical professionals, and not sold directly to the general public. The California Department of Public Health has recently warned 13 genetic testing companies to stop marketing their products directly to California consumers because they are in violation of state licensing and testing laws. Do you agree that genetic tests should not be offered directly to consumers? Why or why not? (In the U.S., a similar objection was raised to allowing pharmaceutical companies to directly advertise their medications to consumers, which prior to the early 1980s, was not permitted.)