Background: Cigarette smoke contains numerous harmful chemicals, including nicotine, an addictive chemical that in excessive amounts can be lethal (0.5-1.0 mg/kg person). Smoking causes a greatly increased risk of:

- Lung Cancer: smoke affects the lungs’ natural cleaning and repair system, impeding removal of germs, dirt and cancer causing chemicals from smoke;
- Chronic obstructive pulmonary disease (COPD): smoke damages lung tissue, resulting in inflammation (bronchitis), repair with stiffer scar tissue (fibrosis), and destruction of tissue (emphysema);
- Coronary heart disease: smoke contains carbon monoxide (which displaces O₂ binding on haemoglobin), nicotine (which increases heart rate but constricts arteries, and is also addictive), and atherosclerosis (buildup of cholesterol and fatty material on blood vessels).

Recently, tobacco companies have introduced electronic cigarettes (or e-cigs), an electronic inhaler meant to substitute for tobacco smoking. They use a heating element that vaporizes a liquid solution, and are often designed to mimic traditional cigarettes in their use and appearance. E-cigs don’t generate tobacco smoke (and its associated tar), so their use is often believed to be safer than smoking tobacco. They should theoretically have fewer toxic effects than traditional cigarettes, and the electronic systems often deliver less nicotine than smoking.

According to the WHO, “the solution is typically composed of nicotine, propylene glycol and other chemicals. Manufacturers report that cartridges contain 6–24 mg of nicotine, but sometimes can contain more than 100 mg.” The chemicals used in electronic cigarettes have not been fully disclosed; however, propylene glycol is a known irritant when inhaled. Testing suggests the presence other toxic chemicals and there are no adequate data on e-cigs’ emissions. Overall, the benefits and risks of electronic cigarette use are uncertain, but they are likely safer than smoking tobacco.

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1 “Questions and answers on electronic cigarettes or electronic nicotine delivery systems (ENDS)”. World Health Organization. www.who.int/tobacco/communications/statements/electronic_cigarettes/
2 www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/
4 en.wikipedia.org/wiki/Electronic_cigarette
4 O’Connor RJ (2012), Tobacco control 21: 181–90
Sampling and statistical methods

1. (5 marks) Consider a study of the risks of smoking, where the results are presented as follows:
   
   ... results show that the smoking group (compared to the control group) had higher rates of XYZ \( (p < 0.05) \).

   a. What was the null hypothesis, \( H_0 \)?
   
   b. On the basis of this study, can we say “smoking causes XYZ”? If not, what can we say?
   
   c. How is it possible to say, in general, that “smoking causes cancer”?

Consider a study to evaluate the health benefits of switching to E-cigarettes from regular cigarettes. Volunteers (who already smoke) are recruited, and asked, “Are you interested in switching to e-cigs?” The first 100 to answer “yes” are assigned to the experimental group (E). The first 100 to answer “no” are assigned to the control group (C). Other participants are rejected from the study.

2. (5 marks) Consider the sampling strategy described above:

   a. What type of sampling does this represent?

   b. Does this sampling approach introduce any sources of bias? Describe one source of bias in the sampling strategy.

   c. How does the source of bias above affect the interpretation of the results?

Over the next year, participants are tested each month for lung and cardiovascular health, and are surveyed to ask what they are doing and how they feel.

   Lung function is measured by calculating the airways resistance, \( R_{AW} \), and average results (\( \pm \) standard deviation) of \( 0.1 \pm 0.05 \text{kPa/(L/s)} \) are expected in the control group.

3. (5 marks) Consider the study size \( (N = 100 \text{ per group}) \) above. The hypothesis is that the experimental group will see a reduction in \( R_{AW} \); a reduction 20% in the experimental group is expected by the end of the first year of the study.

   a. Estimate the power of the study.

   b. What does term “power” mean?

You may use the following table of 1- and 2-tailed critical t-test values corresponding to various values of \( \alpha \) (using DF=199):

\[
\begin{array}{cccccccccc}
\alpha & 0.2000 & 0.1000 & 0.0500 & 0.0200 & 0.0100 & 0.0050 & 0.0020 & 0.0010 & 0.0005 \\
1-tail & 0.8434 & 1.2858 & 1.6525 & 2.0673 & 2.3452 & 2.6008 & 2.9121 & 3.1317 & 3.3401 \\
\end{array}
\]

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Research Ethics and Biomedical Engineering Practice

E-cigarettes are controversial. According to The Economist,

One worry is that young people will be lured into a dependence on nicotine they would otherwise have avoided... Another concern is that smokers who might have quit their expensive and inconvenient habit will carry on, switching to e-cigs in places where smoking is banned... A third fear is that these strangely trendy products will reglamorise smoking.6

Currently “E-cigarettes are sold as leisure products and as such are covered by safety and quality standards”; however, many countries consider e-cigarettes to be a medical device, like other smoking cessation products. In Canada, they are currently banned.7

4. (5 marks) Consider the ethics of allowing e-cigarettes over the counter (i.e. just like cigarettes are currently), instead of banning them.
   a. Who are the parties affected? List at least three groups and the advantages and disadvantages for each.
   b. What is the best decision? Choose an ethical approach (e.g. utilitarian, Kantian) and, using the approach, argue whether or not e-cigarettes should be available over the counter.

5. (5 marks) Assume Health Canada chose to regulate e-cigarettes as a medical device.
   a. List at least two considerations that would be made to choose a medical device class.
   b. What device class would e-cigarettes be?
   c. For a medical device, discuss the requirements for reporting any device malfunctions.

6. (5 marks) Consider a scenario in which several large cigarette companies want to show that e-cigarettes have lower risks. They fund a large, randomized controlled trial (i.e. the highest standard of evidence for a clinical decisions).

   A random selection of volunteers is gathered. Participants are told the study will last several years, and given a good compensation for their time ($100/week). In order to avoid discouraging non-smokers from participating, no detailed information on the study is given in the information to participants.

   Participants are randomly assigned to smoke cigarettes, e-cigarettes (treatment groups) or none (control). The treatment groups are required to smoke 5, 10 or 20 cigarettes a day. In order to ensure compliance, volunteers must install a tracking app on their phone which will detect the time and location where each cigarette is smoked. Tests of lung, heart, and cognitive are performed on participants each month.

   • Discuss (briefly) three ethical concerns with this study.

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7Financial Post, Nov 16th 2013, Online: business.financialpost.com/2013/11/16/how-e-cigarettes-have-become-a-very-wild-west-industry-in-canada/
Cells and electrophysiology

7. (5 marks) Smoking tobacco causes cancer. As indicated, smoke contains carcinogenic chemicals. These chemicals stay in contact with the lungs for longer, because smoke also damages the cleaning and repair systems in the lungs. Cancer is the uncontrolled replication of cells after genetic information is damaged.

   a. **How is genetic information stored in cells?**
   b. **Draw a block diagram of the key steps by which genetic information is turned into proteins.**
   c. Will the presence of chemicals in the airways create an osmotic pressure on lung tissue? **Describe the effect and the direction of flow of liquids.**

8. (5 marks) Atherosclerosis is a build up of plaque in which arterial walls thicken and the lumen (internal diameter) narrows. The name derives from a “lump of gruel” (from the greek: ἀθηρα). Atherosclerosis of the arteries which provide blood to the heart is especially serious. If sufficiently severe, a portion of heart muscle may die (in a heart attack or infarct).

   a. **Draw the normal (resting) lead I ECG signal.** Indicate the key electrical events in the heart and their position in relation to the signal.
   b. Sometimes an infarct leads to ventricular fibrillation (V-fib). **What is V-fib?** Discuss the how the conduction pattern of heart muscle differs during V-fib from a normal ECG. Use a diagram as required.
Oxygen transport and biomechanics

9. (5 marks) Cigarette smoke contains carbon monoxide (CO), which is toxic in high doses.
   
   a. How are $O_2$ and $CO_2$ normally transported in the blood?
   
   b. How does CO interfere with the transport in the previous question?
   
   c. Consider a subject with a blood CO level such that $S_aO_2 = 95\%$. Discuss two acute consequences for the subject. You may discuss the subject at rest or while trying to exercise.

10. (5 marks) COPD is an obstructive lung disease, in which subjects suffer shortness of breath, cough, and sputum (fluid) production. The most common cause is tobacco smoking. Airways narrow due to chronic bronchitis (inflammation of airways, and excessive production of fluids) and emphysema (destruction of lung tissue, resulting in reduction of the tethering effect between tissues).

   a. How does chronic bronchitis narrow airways?
   
   b. How does emphysema narrow airways?
   
   c. A subject has Lung compliance of $C_L = 1.0\ L/kPa$ and (due to COPD) and airways resistance of $R_{AW} = 0.60\ kPa/(L/s)$. From FRC, he breathes a tidal volume $500\ mL$ in $2\ s$. Estimate the maximum pressure from lung muscles required for this task.

11. (5 marks) If the aortic valve leaflets stiffen, they may become unable to adequately open, and would thus be called “stenotic”.

   a. Assume the pressure drop across a normal aortic valve is $3\ mmHg$ and that over a stenotic valve is $20\ mmHg$. In all cases, the heart works to maintain systolic pressure of $130\ mmHg$ and diastolic pressure of $85\ mmHg$\textsuperscript{8}. Sketch left ventricular and aortic pressure vs. time for each case (normal and stenotic).

   b. To measure the mechanical properties of the valve, a catheter is inserted into the heart. It holds the end of the valve leaflet and gently pulls to calculate stress and strain. Sketch the shape of the stress-strain curve. Label the different regions of mechanical behaviour. How does the curve differ for normal and stenotic valves?

   c. The relatively simple test in the previous question will not give complete information about the mechanical properties of the aortic leaflet. Discuss two limitations or aspects which should be considered for such testing.