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ΑΓΩΓΗΣ ΚΑΙ ΑΘΛΗΤΙΣΜΟΥ

ACUTE EFFECTS OF CONVENTIONAL AND ELECTRONIC CIGARETTE SMOKING AND SECOND-HAND SMOKE ON LUNG FUNCTION

της

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Περίληψη

Το ηλεκτρονικό τσιγάρο (ΗΤ), μια συσκευή που μοιάζει πολύ εξωτερικά με τα συμβατικά τσιγάρα (ΣΤ), λειτουργεί με μια επαναφορτιζόμενη μπαταρία κι έναν ατμοποιητή ο οποίος είναι υπεύθυνος για τη δημιουργία εκνεφώματος νικοτίνης και άλλων χημικών, το οποίο εισπνέει ο καπνιστής. Η ολοένα αυξανόμενη χρήση τους οδήγησε στην έκφραση σοβαρών προβληματισμών από τον Παγκόσμιο Οργανισμό Υγείας και άλλους φορείς όσον αφορά την έλλειψη ερευνών σχετικά με την αποτελεσματικότητα και την ασφάλειά τους. Σκοπός της μελέτης αυτής είναι να εξετάσει τις βραχυπρόθεσμες επιπτώσεις του ενεργητικού και παθητικού καπνίσματος ΣΤ και ΗΤ στον ανθρώπινο οργανισμό όσον αφορά τη λειτουργικότητα και φλεγμονή των πνευμόνων. Προσφέρθηκαν να συμμετάσχουν 15 καπνιστές (≥15 τσιγάρα/ημέρα; 7 γυναίκες) και 15 μη καπνιστές (7 γυναίκες) εθελοντές. Οι καπνιστές υποβλήθηκαν σε μια κατάσταση ελέγχου, μία κατάσταση ενεργητικού καπνίσματος ΣΤ και μία κατάσταση ενεργητικού καπνίσματος ΗΤ ενώ οι μη καπνιστές υποβλήθηκαν σε μία κατάσταση ελέγχου, μία κατάσταση παθητικού καπνίσματος ΣΤ και μία κατάσταση παθητικού καπνίσματος ΗΤ. Εξετάστηκαν η πνευμονική λειτουργικότητα, η κοτινίνη ορού καθώς και το εκπνεόμενο μονοξείδιο του άνθρακα (CO) και μονοξείδιο του αζώτου (FeNO). Αποτελέσματα: Το ενεργητικό και το παθητικό κάπνισμα ΣΤ προκάλεσε επιδείνωση της πνευμονικής λειτουργικότητας διάρκειας <1 ώρας. Τόσο το ενεργητικό όσο και το παθητικό κάπνισμα ΗΤ δεν επηρέασε σημαντικά την πνευμονική λειτουργικότητα. Η κοτινίνη ορού αυξήθηκε σημαντικά σε όλες τις καταστάσεις (εκτός από τις καταστάσεις ελέγχου) ενώ το εκπνεόμενο CO αυξήθηκε μόνο μετά τη χρήση ΣΤ. Το FeNO δε μεταβλήθηκε σημαντικά σε καμία από τις καταστάσεις. Συμπεραίνεται ότι ούτε το ενεργητικό αλλά και ούτε το παθητικό

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κάπνισμα ηλεκτρονικού τσιγάρου έχει σημαντική επίδραση στη φυσιολογική πνευμονική λειτουργικότητα.

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Abstract

The electronic cigarette (e-cigarette), a battery-powered device that simulates tobacco cigarettes by vaporizing nicotine and other chemicals into an inhalable vapor, is becoming increasingly popular yet the World Health Organization and other institutions have expressed serious concerns about the lack of research on its safety and efficacy. Our objective was to conduct the first comprehensive and standardized assessment of the acute and short term impact of active and passive e-cigarette smoking on the function and inflammation of the lungs, as compared to active and passive tobacco cigarette smoking. In a randomized crossover trial, 15 smokers (≥15 cigarettes/day; 7 females) and 15 never-smokers (7 females) volunteered. Smokers underwent a control condition, an active tobacco cigarette smoking condition, and an active e-cigarette smoking condition. Never-smokers underwent a control condition, a passive tobacco cigarette smoking condition and a passive e-cigarette smoking condition. Lung function, serum cotinine, exhaled carbon monoxide (CO) and the fraction of exhaled nitric oxide (FeNO) were assessed. Results showed that active and passive tobacco cigarette smoking resulted in deteriorated lung function lasting <1 hour. Active and passive e-cigarette smoking did not significantly affect lung function. Serum cotinine increased significantly after all conditions (excluding control conditions), while exhaled CO increased only following active and passive tobacco cigarette smoking. FeNO was not statistically significantly altered in any condition. It is concluded that, for the e-cigarettes tested, neither a brief session of active smoking nor a 1-hour passive e-cigarette smoking interfere significantly with normal lung function.

KEYWORDS: e-cigarette, tobacco cigarette, respiratory system, lung inflammation, health.

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List of abbreviations

$ACTIVE_{E\text{-}CIG}$	active e-cigarette smoking condition
$ACTIVE_{CON}$	active smoking control condition
$ACTIVE_{TOB}$	active tobacco cigarette smoking condition
BALF	bronchoalveolar lavage fluid
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
$eCIG_{NIC}$	e-cigarette liquid nicotine content (in mg) per ml
e-cigarette	electronic cigarette
ENDS	electronic nicotine delivery systems
$FEF_{25\text{-}75}$	forced expiratory flow between 25% and 75% of FVC
FeNO	exhaled nitric oxide fraction
FEV_1	forced expiratory volume in 1 second
FEV_1 /FVC	forced expiratory volume in 1 second to forced vital capacity ratio
FVC	forced vital capacity
iNOS	inducible NO synthase
IOS	impulse osscilometry system
LCMS	liquid chromatography mass spectrometry
$MEF_{75\%}$	maximum expiratory flow at 75% of expired vital capacity
NO	nitric oxide
NRT	nicotine replacement therapy
$PASSIVE_{E\text{-}CIG}$	passive e-cigarette cigarette smoking condition
$PASSIVE_{CON}$	passive smoking control condition
$PASSIVE_{TOB}$	passive tobacco cigarette smoking condition
PEF	peak expiratory flow
SHS	second-hand smoking
TOB_{NIC}	tobacco cigarette nicotine content (in mg)
TSNA	tobacco specific N-nitrosamines

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Introduction

History of tobacco and smoking

History of tobacco and smoking goes back as 18,000 years ago, when mankind first encountered tobacco plant species in America. Humans who first populated the continent discovered *nicotiana tabacum* and *nicotiana rustica*, the two tobacco species most consumed today, as they grew natively there. It is much later though that cultivation of tobacco took place: estimations range from 5,000-3,000 BC and locate the first cultivation site in the Peruvian/Ecuadorean Andes (Gately, 2001; Gilman & Xun, 2004).

The plant had been smoked as a ritual activity well before it was cultivated by the Mayans, the Aztecs, the Caribs and lots of other tribes in the western hemisphere (Gilman & Xun, 2004). The earliest tobacco use seems to have started by the Mayan civilisation, which flourished about 2000 BC - 900 BC, when people began to chew and smoke the leaves of the tobacco plant for pleasure and ritual, as well as using the leaves for healing the wounds due to its mild analgesic and antiseptic properties (Gately, 2001). The Mayans though, contrary to the natives of North America who used pipes as the most common way of smoking, smoked primitive cigars and cigarettes (Gilman & Xun, 2004).

By the time Christopher Columbus reached America in 1492, tobacco plants were abundant all over the continent and there was widespread use of tobacco smoking. During an exploratory mission to America's inland two members of his crew, Rodrigo de Jerez and the interpreter Louis de Torres, encountered inhabitants of Cuba smoking tobacco leaves and tried it out, becoming the first European smokers in history. It is reported that both of them became habitual smokers during the three months' Columbus voyage to the "Indes" (Gately, 2001).

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In Columbus' second voyage to America, this time as a conqueror with 17 ships and 1200 men, Europeans had become familiar with smoking and watching the Indian slaves smoke made them denounce the habit (Gately, 2001). Gonzalo Fernandez de Oviedo, military governor of Hispaniola discards smoking as something evil, especially harmful which makes the natives "lazy and useless" (Gately, 2001; Gilman & Xun, 2004). Bartolome de Las Casas, a priest that edited the lost manuscript of Columbus' travels, makes a commentary on smoking identifying that it intoxicates, "makes the flesh dull" and decreases appetite. When he tried to convince smokers that tobacco was evil, they told him it was beyond their control to stop it. Addiction was noticed but not understood, it was simply perceived as sin (Gately, 2001).

In Europe the public learned how to smoke and the consequences of smoking were not yet known; the encounter with tobacco and the smoking habit was something new, a new costly experience affordable only by the upper class. However, from a luxury it became available to the majority of the people rather quickly (Gilman & Xun, 2004). This was assisted by the fact that tobacco was recognized as a means of promoting health. In 1571 Nicolas Monardes, a famous physician of Seville, presented tobacco as "the holy herb" that could cure illness both physical and psychic, help someone relax and even cure syphilis, a disease imported from the New World. Soon, smoking incorporated in culture and art (Gilman & Xun, 2004). In England tobacco was considered especially effective against bubonic plague, which resulted in greater spread of the habit even in children (Gately, 2001).

Outside Europe, across the Ottoman Empire smoking proliferated with great speed. In Central Asia and India the most favourite way of smoking was mixing tobacco with other herbs and sandal-wood through a water-pipe, the hookah. Portuguese and French traders introduced pipe smoking to the African continent. Then,

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smoking expanded to Japan in April 1600 by an Englishman and just a decade later even children had acquired the habit. Via Japan and South China Sea smoking was brought by traders to China and it instantly became a beloved habit for the Chinese, who related it to all tea rituals and made it a daily necessity. Smoking rapidly evolved into a global practice, an endemic (Gilman & Xun, 2004).

This new habit, adopted by all classes of society in everyday life, now aroused a number of problems. At a time it was considered that smoking caused workers to neglect their duties. There was also the fear of fire outbreaks from a careless smoker, since most of the houses and furniture was wooden. Most significant though were the medical concerns on the harmful consequences that aroused in the early 17th century both in Europe and in the East (Gilman & Xun, 2004).

In few European countries like Switzerland and the German state of Saxony tobacco was not welcome and smoking was prohibited. Smokers were even sentenced to death in Luneburg, a penalty that was valid till 1691 (Gately, 2001). Similar efforts were made in countries outside Europe by both rulers and clergy. The Ottoman sultan Murad IV (1623-1640) was probably the first governor to prohibit smoking. Anti-smoking laws and bans were also reinforced in China from the Chongzhen emperor and the following dynasty, in England by James I and in Russia by the Patriarch of Moscow, who forbade the sale of tobacco and punished smokers by whipping their nostrils so badly that no skin remained. Still, none of those prohibitions managed to refrain people from smoking (Gilman & Xun, 2004).

It did not take long for rulers to realise that they were unable of suppressing the smoking habit; therefore they attempted to control it through state monopoly. This policy brought them wealth, established their domination and satisfied the populace (Gilman & Xun, 2004).

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The English language term “smoking” appears in the late 18th century, replacing descriptions such as “drinking smoke” (Lloyd & Mitchinson, 2007). Tobacco eventually was smoked not only in cigars for the privileged and in pipes for the masses but also in cigarettes (Gilman & Xun, 2004). In the United States tobacco use reached a plateau until the American Civil War in 1860s, when the industrialisation of cigarette production took place from the craftsman James Bonsack (Burns, 2006).

Anti-smoking groups in Nazi Germany began to take action and published articles against the consumption of tobacco in the journal Der Tabakgegner (The Tobacco Opponent) in 1912 and 1932. Unfortunately, these groups quickly lost popular support. By the end of the Second World War, American cigarette manufacturers quickly re-entered the German black market. Illegal smuggling of tobacco took place and the anti-smoking campaign met an inglorious end. In 1948-9 a total of 93,000 tons of tobacco was sent to Germany by the United States as part of the Marshall Plan (Proktor, 2000).

More and more scientific evidence was brought to light in the 1980s, obliging tobacco companies to claim contributory negligence as the consequences of smoking on human health were unknown or missing evidence. No significant action was taken by health authorities until 1998, when the four largest United States tobacco companies and the Attorneys General of 46 states signed the Tobacco Master Settlement Agreement ("Tobacco Master Settlement Agreement," 1998). This agreement forbade tobacco advertisement targeting in young people below 18 years of age and imposed penalties for health compensation; eventually more tobacco companies took part and it ended the largest civil settlement in United States history, even though finally it was not applied in several magazines, thus failing to protect young people from these advertisements (King & Siegel, 2001).

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Since then, a lot of anti-smoking laws, policies and campaigns tried to safeguard human's right to breathe fresh air, encouraging smokers to quit, prohibiting smoking to common places and aiming at smoke-free homes. In Europe and the United States rates of smoking display a significant decline, in the developing world however tobacco consumption continues to rise (WHO, 2011).

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From “holy herb” to today’s scourge

Tobacco plant was initially used for medical and ritual purposes but eventually it ended up smoked for recreational purposes. The habit of smoking has spread worldwide and has become a favourite activity for lots of people, in different kind of places and times of the day. At present, tobacco consumption is increasing globally, though it is decreasing in some high-income and upper middle-income countries (WHO, May 2012.). According to a report published on 2008 from the World Health Organisation, Greece was 6th in consuming tobacco worldwide, having 48% age-standardised adult smoking prevalence (WHO, 2008b).

WHO identifies smoking as a “leading cause of death, illness and impoverishment” (WHO, May 2012.). Despite the global initiatives and the implementation of measures against the tobacco epidemic, the tobacco scourge kills one person every six seconds. Approximately half of the smokers will eventually die of a tobacco-related disease. In total, smoking kills nearly 6 million people each year, of whom more than 5 million are users and ex users and more than 600.000 are non smokers exposed to second-hand smoke (WHO, May 2012.).

Breathing other people's cigarette smoke is known as passive, involuntary or second-hand smoking (SHS). It can also be called ‘environmental tobacco smoke’ ("ASH Research Report: SecondHand Smoke ", April 2011). SHS is a mixture of the ‘mainstream’ smoke which is exhaled by the smoker and ‘sidestream’ smoke produced by the burning cigarette, which accounts for most of SHS (World Health Organisation, 2006).

Passive smoking kills approximately 600,000 people per year; furthermore there is substantial evidence that no safe level of exposure to SHS exists. Tobacco smoke

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contains more than 4000 chemicals; 250 of them are proved to be deleterious for human health and at least 50 of them are identified as carcinogenic (WHO, May 2012.).

Both active and passive smoking have acute and long-term effects on health by causing damage in nearly all systems of the human organism and thereby resulting in high morbidity and increased risk for premature death (table 1) (World Health Organisation, 2004, 2006).

Table1. Diseases and other adverse health effects for which smoking is identified as a cause [12-13]

Active smoking consequences	
Cancer	Bladder cancer, Cervical cancer, Esophageal cancer, Kidney cancer, Laryngeal cancer, Leukemia, Lung cancer, Oral cancer, Pancreatic cancer, Stomach cancer
Cardiovascular diseases	Abdominal aortic aneurysm, Atherosclerosis, Cerebrovascular disease, Coronary heart disease
Respiratory diseases	Chronic obstructive pulmonary disease, Pneumonia, Respiratory effects in utero, Respiratory effects in childhood and adolescence, Respiratory effects in adulthood, Other respiratory effects
Reproductive effects	Fetal death and stillbirths, Fertility, Low birth weight, Pregnancy complications
Other effects	Cataract, Diminished health status/morbidity, Hip fractures, Low bone density, Peptic ulcer disease
Passive smoking consequences	
Cardiovascular disease	Coronary heart disease, Stroke, Atherosclerosis
Respiratory diseases (adult)	Acute respiratory symptoms, Chronic respiratory symptoms, COPD, Asthma onset and worsening, Pulmonary function decline, Bronchitis and pneumonia, Acute respiratory infections
Respiratory diseases (children)	Lower respiratory tract infections, Middle ear effusions, Chronic cough, asthma, lung growth and pulmonary function affection
Cancer	Lung cancer, Breast Cancer, Nasal Sinus Cavity Carcinoma
Reproductive and Developmental Effects	Sudden Infant Death Syndrome, Preterm Delivery, Low Birth Weight, Childhood Cancer(Leukemias, Lymphomas, Brain tumors)
Other	Odor annoyance, Eye irritation, Nasal irritation

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Literature Review: Smoking and lung function

Active smoking and lung function

Active smoking triggers a number of biologic processes like oxidant stress, inflammation and a protease/antiprotease imbalance that cause irritation and injury both in airways and alveoli. If this injury persists it ultimately results to the development of chronic obstructive pulmonary disease (COPD) (U.S. Department of Health and Human Services, 2010).

COPD refers to a group of diseases that cause airflow blockage and breathing-related problems and includes emphysema, chronic bronchitis, and in some cases asthma (Rennard, 1998). COPD is a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing (Lopez, et al., 2006). Across the world, cigarette smoking is the most commonly encountered risk factor for COPD (GOLD, 2011).

Chronic tobacco use also accounts for a number of respiratory health problems: all major respiratory symptoms like cough, phlegm, and dyspnea, acute respiratory illnesses, increased non-specific bronchial hyperesponsiveness and asthma-related symptoms (i.e. wheezing) (U.S. Department of Health and Human Services, 2010; Urrutia, et al., 2005; World Health Organisation, 2004). Furthermore, there is sufficient evidence that active smoking causes a significant deterioration in lung function which starts earlier in age and is accelerating with the passing of years (Urrutia, et al., 2005; World Health Organisation, 2004; Yang & Yang, 2002), as well as a slowed growth of lung function in adolescents (D. R. Gold, et al., 1996; World Health Organisation, 2004). These risks increased with increasing number of cigarettes smoked per day (Urrutia, et al., 2005; World Health Organisation, 2004).

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In accordance to these findings, smokers with normal lung function have significantly lower values for forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) ratio (FEV_1/FVC) and forced expiratory flow between 25% and 75% of FVC (FEF_{25-75}) than did non smokers, suggesting the presence of subclinical airflow limitation possibly due to increased resistance to airflow, even though this impairment was not of sufficient magnitude to be regarded as clinical evidence of airway obstruction (Yang & Yang, 2002). A deterioration of FEV_1 and FEV_1/FVC were also directly associated with the number of cigarettes smoked per day (Urrutia, et al., 2005).

Furthermore, smoking reduces the production of endogenous nitric oxide (NO)(Kharitonov, Robbins, Yates, Keatings, & Barnes, 1995) by cells lining the respiratory tract possibly via down-regulation of both endothelial NO synthase (eNOS) and inducible NO synthase (iNOS) (Hoyt, et al., 2003). Synthesis and functions of nitric oxide are depicted in figure 1. Since endogenous NO is important in defending the respiratory tract against infection, in counteracting bronchoconstriction and vasoconstriction and in inhibiting platelet aggregation, this effect may contribute to the increased risks of chronic respiratory and cardiovascular disease in cigarette smokers. Significantly lower concentrations of the exhaled nitric oxide fraction (FeNO) are found in smokers in a dose-dependent way, reducing as cigarette consumption augments (Kharitonov, et al., 1995; Sundy, et al., 2007).

Chronic lung disease is normally a long-term process. However, even brief exposures to air pollution stimulate mechanisms that contribute to its development (Flouris, 2009; Flouris, et al., 2009). Indeed, production growth factors and type 1 procollagen in the small airways is rapidly increased within the first few minutes of smoke inhalation (Churg, Tai, Coulthard, Wang, & Wright, 2006). Within five minutes

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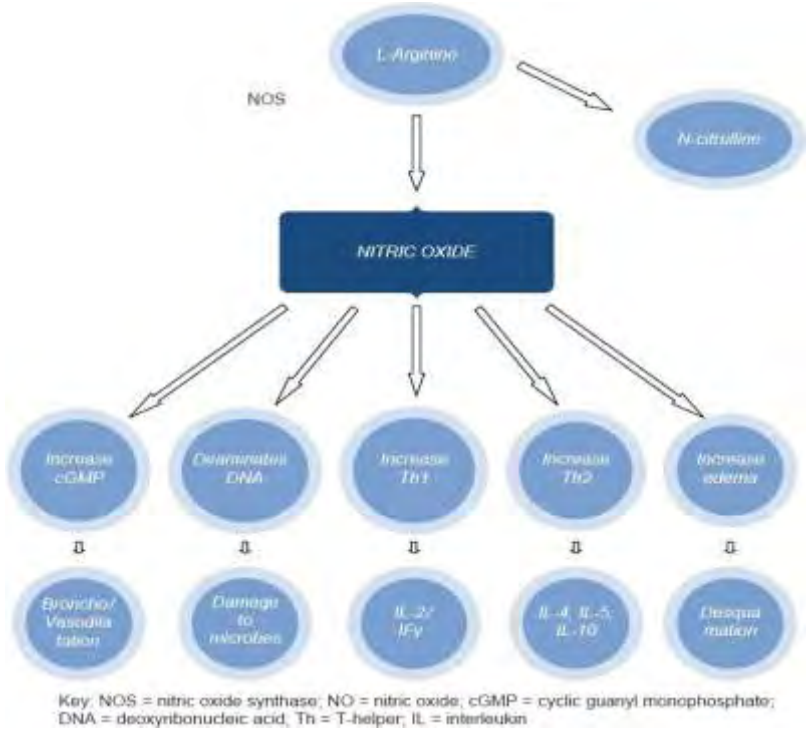

Figure 1. Synthesis and functions of nitric oxide (adopted from Abba et al., 2009)

leucocytes start bonding to endothelial cells (Lehr, et al., 1991), while lung inflammation is increased within the first 15 minutes (Yates, Breen, & Thomas, 2001).

By 20 minutes, platelet activation is increased (Davis, Shelton, Watanabe, & Arnold, 1989), while within one hour nearly all systems are affected (Flouris, et al., 2009; Flouris, Metsios, Jamurtas, & Koutedakis, 2008; Flouris, Vardavas, Metsios, Tsatsakis, & Koutedakis, 2010; Metsios, et al., 2007).

Limited data from human studies on the acute effects of smoking on lung function show that smoke exposure leads to tissue damage by several mechanisms. Smoking acts chemotactic to neutrophils and macrophages, attracting and activating these cells shortly after the first puffs of a cigarette. Increased chemotactic activity of the monocytes present at the bronchoalveolar lavage fluid (BALF) was also observed. In addition, active smoking increases the air space epithelial permeability within one hour of cigarette smoking causing serious impairment of the epithelial barrier which in

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turn could lead to destruction of the lung parenchyma (van der Vaart, et al., 2005; van der Vaart, Postma, Timens, & ten Hacken, 2004).

Another mechanism is the inhibition of fibroblasts, which are important in repair processes in the lung. Repetition of acute smoke exposure could thus result to irreversible damage. Furthermore, smoking suppresses the number of eosinophils either due to the anti-inflammatory properties of CO or due to a possible change in the Th1-Th2 type cytokine balance (van der Vaart, et al., 2005; van der Vaart, et al., 2004).

FeNO is also significantly reduced acutely, even by smoking a single cigarette, although this seems to be a transient effect (Kharitonov, et al., 1995). The greater short-term (hours to days) exposure to inhaled tobacco smoke was associated with greater decreases in FeNO levels (Sundy, et al., 2007).

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Passive smoking and lung function

SHS consists of ‘sidestream’ and ‘mainstream’ smoke, which both contain thousands of fine particles and chemicals. The number of smokers, the rhythm of their smoking and the total volume of air in which smoke is diffused are the main factors influencing the exact composition of SHS, which is fairly different whenever one or more of these factors change ("ASH Research Report: SecondHand Smoke ", April 2011; World Health Organisation, 2006).

The most studied carcinogenic compounds of SHS include polycyclic aromatic hydrocarbons, nitrosamine compounds, heterocyclic aromatic amines, and other miscellaneous organic compounds. Tobacco specific N-nitrosamines (TSNA) are powerful carcinogens that affect various tissues such as the oesophagus, the nasal cavity, and the lung (A. D. Flouris, C. I. Vardavas, et al., 2010).

Chronic repeated exposure to SHS causes acknowledged long-term health effects summarised above (Table 1). However, passive smoking has also significant immediate health effects: it can exacerbate respiratory problems, trigger asthma attacks, reduce coronary blood flow, irritate eyes and cause headaches, coughs, sort throats, dizziness and nausea ("ASH Research Report: SecondHand Smoke ", April 2011). Acute effects of SHS on the respiratory system are illustrated in Figure 2. As far as lung function is concerned, SHS increases lung inflammation and declines lung function (Eisner, et al., 2007; Flouris, et al., 2009; World Health Organisation, 2006); even after as little as 1 hour’s moderate exposure (Flouris, et al., 2009).

In specific, Flouris et al. (Flouris, et al., 2009) showed that one-hour exposure to SHS at bar/restaurant levels generates significant decrements on lung function, FEV_1, FEV_1/FVC, maximum expiratory flow at 75% of expired vital capacity ($MEF_{75\%}$), $MEF_{50\%}$, and $MEF_{25\%}$. These results closely resembled the airway obstruction apparent

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Figure 2. Acute effects of passive smoking to the respiratory system (*adopted with permission from Flouris et al.,2010)*

in smokers. The mechanisms proposed are airway irritation, oxidative stress, inflammation and direct induction of growth factors resulting in airway remodelling (Flouris & Koutedakis, 2011; A. D. Flouris, C. I. Vardavas, et al., 2010). Clinical implications of brief SHS exposure on the respiratory system like nasal congestion, irritation and increased rhinitis seem to develop due to nasal mucociliary clearance, C-fiber activation and epithelial permeability to environmental allergens (Flouris & Koutedakis, 2011; A. D. Flouris, C. I. Vardavas, et al., 2010).

Furthermore, within the first 15 min of moderate SHS exposure there is a decline in FeNO levels, which may be caused by the decreased production of NOS through the mechanism of negative feedback due to high levels of nitrogen oxides present in tobacco smoke. Other possible mechanisms include an increased breakdown or modification of nitric oxide by SHS oxidants or a SHS-induced accelerated uptake of

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nitric oxide (A. D. Flouris, C. I. Vardavas, et al., 2010). These deleterious effects of SHS are exacerbated when physical activity follows the SHS exposure, particularly in less fit individuals (Flouris & Koutedakis, 2011; Flouris, et al., 2012; A. D. Flouris, G. S. Metsios, A. Z. Jamurtas, & Y. Koutedakis, 2010).

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The introduction of the electronic cigarette

As the number of smokers worldwide is reaching record highs and anti-smoking policies are propagating (Flouris & Oikonomou, 2010; A. D. Flouris, C. I. Vardavas, et al., 2010), the industry of alternative smoking products is in the froth of excitement about the potential of increasing market shares and revenues. One of the most recently-introduced products in the germane market is the electronic cigarette (e-cigarette), also known as electronic nicotine delivery systems (ENDS), a battery-powered device that simulates tobacco cigarettes by vaporizing nicotine and other chemicals into an inhalable vapour. They consist of a rechargeable battery, a vaporization chamber and the liquid nicotine cartridge (figure 3).

Manufacturers claim that the liquid cartridge mainly contains nicotine and propylene glycol, a low toxicity compound found in many products of everyday life. Although believed to be safe, propylene glycol exposure is related to irritation of the respiratory system and asthma (Choi, Schmidbauer, Spengler, & Bornehag, 2010; Wieslander, Norback, & Lindgren, 2001).

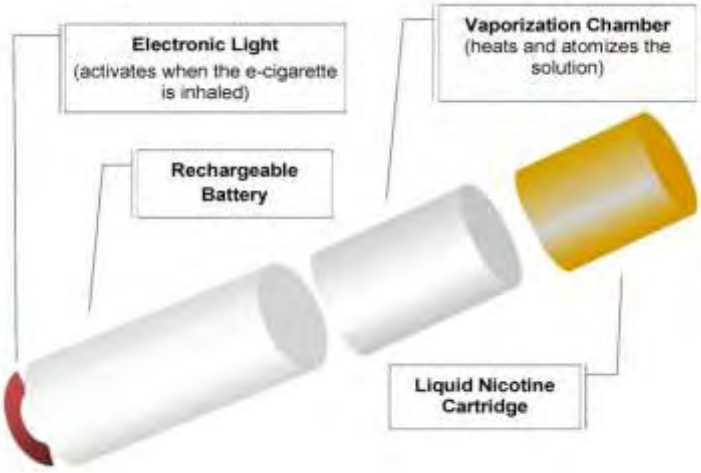

Figure 3. The electronic cigarette device *(adopted by Center for Public Health and Tobacco Policy - http://www.tobaccopolicycenter.org)*

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Three analyses of the liquid content are available so far. FDA analysis showed that nicotine release was not uniformly released in each puff and detected nicotine in cartridges labelled as containing zero nicotine. Moreover, TSNA and tobacco specific impurities were found at low levels as well as diethylene glycol – a highly toxic compound (Westenberger, 2009). Another analysis of an e-cigarette from a private enterprise tracked polycyclic aromatic hydrocarbons in the liquid in addition to the carcinogenic nitrosamines detected (Laugesen, 2008). The third report comes from the Greek institute "Demokritos" and besides the presence of propylene glycol does not detect any of the above compounds (Leondiadis, 2009).

The scarce available data suggests that sales of e-cigarettes are increasing (Pauly, Li, & Barry, 2007), while Google searches for "electronic cigarettes" have increased by 5000% over the past 2 years (Yamin, Bitton, & Bates, 2010). This technology became popular despite serious concerns expressed by the World Health Organization, the US Food and Drug Administration (FDA), and a number of Health Ministries worldwide (FDA, 2009; World Health Organisation, 2010) about the lack of research on its safety and efficacy (Etter, Bullen, Flouris, Laugesen, & Eissenberg, 2011; Flouris & Oikonomou, 2010).

Electronic cigarettes were initially proposed as a cessation aid by manufacturers but as there were no data available WHO asked companies not to promote them as therapeutic aids (WHO, 2008a; WHO study group on tobacco product regulation, 2009). Recently, Caponnetto et al. showed that three Caucasian smokers with a documented history of recurring relapses were able to quit and to remain abstinent for at least six months after taking up a cigarette. Authors claim that besides delivering nicotine to the lung, e-cigarette use preserves some of the gestures linked with the

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smoking habitude (for example the hand-to-mouth action of smoking), helping in this way on smoking cessation (Caponnetto, Polosa, Russo, Leotta, & Campagna, 2011).

However, according to a technical report published by WHO (WHO study group on tobacco product regulation, 2009), ENDS pose significant public health issues and raise questions for tobacco control policy and regulation. Manufacturers have not fully disclosed the chemicals used in ENDS; there are few data on their emissions or actual human exposure; their health effects have not been studied; and their marketing and use could undermine public smoking bans, which are important tobacco control interventions. The products could also undermine smoking cessation efforts by proposing unproven devices for smoking cessation in the place of products of proven efficacy. ENDS might also sabotage the prevention of tobacco use because of their appearance and marketing as safe alternatives to tobacco products for nontobacco users, including children.

Indeed, e-cigarette advertisements and related promotion activities are spreading to adolescents, mainly through the Internet (WHO study group on tobacco product regulation, 2009). A study of 4,341 middle and high school students in Korea showed that 10.2% had ever seen or heard of e-cigarettes, while 0.5% of them had used an e-cigarette. Male gender, perception of peer influence, satisfaction in school life and cigarette smoking experience were the factors determined to be statistically significant predictors of e-cigarette experience (Cho, Shin, & Moon, 2011).

Limited data available on ENDS use yield further concerns; it has been shown that they contain carcinogenic compounds (although in lower concentrations compared to tobacco cigarettes and similar to those existing in nicotine medications) (FDA, 2009; Laugesen, 2008); nicotine was present in all cartridges (including samples identified as containing no nicotine) (Hadwiger, et al., 2010; Westenberger, 2009); and similarly

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labelled cartridges emitted markedly different amounts of nicotine in each puff (Trtchounian, Williams, & Talbot, 2010; Westenberger, 2009).

Compared with conventional cigarettes, e-cigarettes require stronger vacuums (suction) to smoke and the effects of this on human health could be adverse. The amount of aerosol produced by e-cigarettes decreases as smoking continues, which eventually necessitates increasing puff strength to produce aerosol. Furthermore, the decreased efficiency of aerosol production during e-cigarette smoking makes dosing non-uniform over time and calls into question their usefulness as nicotine delivery devices (Trtchounian, et al., 2010).

In a recent study where 6 different e-cigarette brands were tested authors conclude that design flaws, lack of adequate labelling and concerns about quality control and health issues indicate that regulators should consider removing ENDS from the market until their safety can be adequately evaluated (Trtchounian & Talbot, 2011).

In the first clinical laboratory model for evaluating the acute effects of e-cigarettes in 32 ENDS-naive smokers, no significant changes were observed in plasma nicotine, heart rate and exhaled CO after use of 2 brands of e-cigarettes, contrary to the pronounced increase noticed 5-15 minutes after traditional cigarette use. Interestingly, e-cigarettes suppressed nicotine/tobacco abstinence symptoms for as long as 96 hours after use, although not as effectively as traditional cigarettes and had positive ratings of product acceptability (Vansickel, Cobb, Weaver, & Eissenberg, 2010).

In another clinical study, 40 ENDS-naive smokers were randomised to use e-cigarettes containing 16 mg nicotine or 0 mg capsules, Nicorette nicotine inhalator or their usual cigarette. The 16 mg e-cigarette alleviated desire to smoke after overnight abstinence was well tolerated and had a pharmacokinetic profile more like the Nicorette inhalator than a tobacco cigarette (Bullen, et al., 2010).

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In contrast to the previous laboratory reports that claim that ENDS does not increase plasma nicotine significantly (Vansickel, et al., 2010) or increase plasma nicotine in levels lower than nicotine inhalers or tobacco cigarettes (Bullen, et al., 2010), Etter et al. found substantial amounts of cotinine in the saliva of ENDS users, similar to conventional cigarette smokers levels and higher than found in NRT users (Etter & Bullen, 2011). According to the authors, this may be explained by important variations of puffing topography, experience in ENDS use or may apply only for the e-cigarettes brands used.

Regarding pulmonary effects of ENDS use only one study is published so far (Vardavas, et al., 2011). Researchers found that using an e-cigarette ad libitum for 5 minutes, even though it does not seem to affect lung function, it leads to a statistically significant decrease in exhaled FeNO. Moreover, an increase in flow resistance by approximately 18% as well as an increase in impedance and overall peripheral airway resistance was noted. These effects are similar to those seen with tobacco smoking and in experimental studies appear prior to changes in FEV_1 and PEF; thus authors imply that e-cigarette use has a significant health effect on lung function and inflammation which may not be of major clinical value yet but needs further studies to be assessed (Vardavas, et al., 2011).

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Aim of this study

Long-term effects of conventional cigarette smoking on lung function are well studied; this does not apply though for the acute effects for which there are scarce data. However, acute effects are equally important to be elucidated both in active and passive smoking; In active smoking it is clear that there is no safe level or tobacco consumption (World Health Organisation, 2004) and as far as passive smoking recent data show that even brief exposure to SHS provokes significant decline in lung function (Flouris, 2009; Flouris & Koutedakis, 2011; Flouris, et al., 2009; A. D. Flouris, C. I. Vardavas, et al., 2010). There is no published study examining the acute effects of active smoking on lung function and there are only a few studies on passive smoking (Flouris, 2009; Flouris & Koutedakis, 2011; Flouris, et al., 2009; A. D. Flouris, C. I. Vardavas, et al., 2010).

After the introduction of the electronic cigarette in the market, it was accepted with enthusiasm rather than skepticism. However, limited data exist on its efficacy and safety of use (Flouris & Oikonomou, 2010), no study has been published so far on its consequences from passive smoking and only one study examined its effects on lung function (Vardavas, et al., 2011).

In this study we investigated the acute and short term impact of active smoking on lung function and inflammation. Moreover, we assessed for the first time both active and passive e-cigarette smoking regarding its acute impact on lung function, as well as compared its effects with these of the conventional cigarette.

We hypothesized that active smoking has immediate effects on lung function, based on the knowledge that lung inflammation is stimulated only minutes after smoke inhalation (Yates, et al., 2001) and investigated the existence and magnitude of this impact. Regarding the electronic cigarette, we attempted to detect possible harmful

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changes on human pulmonary function both from its use and from the inhalation of its vapor and examine if these are of clinical significance.

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Methodology

Materials and Methods

Participants

Two groups of adult volunteers participated: 15 smokers (≥15 cigarettes/day; 7 females; 36.83±9.85 years; 25.61±4.05 BMI; 22.46±18.43 pack years) and 15 never-smokers (7 females; 28.87±10.45 years; 23.59±2.99 BMI). All volunteers provided written consent (the form of the written consent is attached on the supplement). Exclusion criteria included pregnancy, signs of acute illness, abnormal spirometry (conducted at baseline during each condition) and/or other evidence of pulmonary disease or other chronic conditions, and use of medication known to influence lung function. Smokers reporting previous use of e-cigarettes were also excluded for ethical reasons (i.e., possible relapse into tobacco cigarette smoking) (Eissenberg, 2010; Vansickel, et al., 2010). All women participants were premenopausal with regular menstruation and were tested during the late luteal phase of their menstrual cycle.

Experimental Design

The study was conducted according to the principles expressed in the Declaration of Helsinki and was approved by the University of Thessaly Ethics Review Board (document attached on supplement). Each group attended three conditions administered in a random order and separated by a minimum of five days (figure 4). The group of smokers underwent a control condition ($ACTIVE_{CON}$), an active tobacco cigarette smoking condition ($ACTIVE_{TOB}$), and an active e-cigarette smoking condition ($ACTIVE_{E\text{-}CIG}$), each lasting 30 minutes. In $ACTIVE_{CON}$, smokers were asked to

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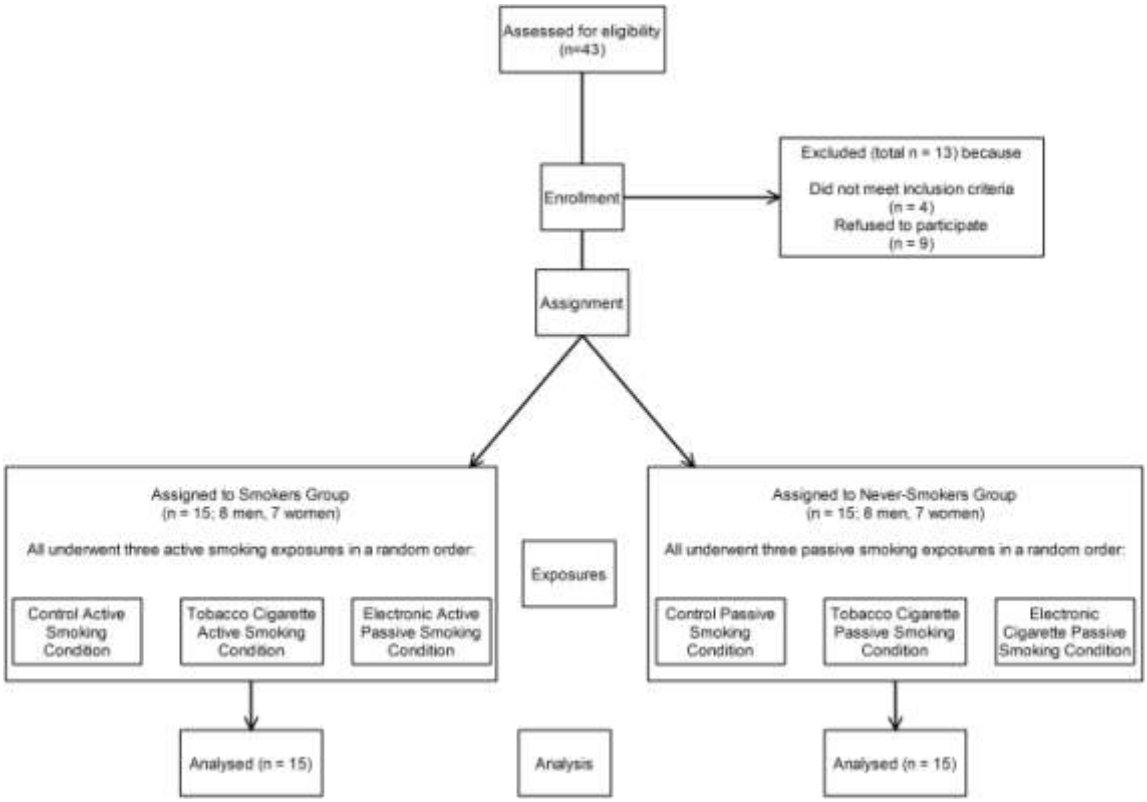

Figure 4. Flowchart of the participant recruitment and assessment process

pseudo-smoke an unlit-cigarette from a brand of their choice. In $ACTIVE_{TOB}$, smokers were asked to smoke two tobacco cigarettes from a brand of their choice. In $ACTIVE_{E\text{-}CIG}$, smokers were asked to puff an e-cigarette in order to absorb enough nicotine to match two of their favorite tobacco cigarettes.

The group of never smokers underwent a control condition ($PASSIVE_{CON}$), a passive tobacco cigarette smoking condition ($PASSIVE_{TOB}$), and a passive e-cigarette cigarette smoking condition ($PASSIVE_{E\text{-}CIG}$), each lasting one hour. In $PASSIVE_{CON}$, participants were exposed to normal room air. In $PASSIVE_{TOB}$ and $PASSIVE_{E\text{-}CIG}$, participants were exposed to air polluted with tobacco cigarette smoke and e-cigarette vapor, respectively, adjusted to simulate bar/restaurant levels (Flouris, et al., 2009).

Prior to each condition, participant's exhaled CO was measured. As previously reported (Bullen, et al., 2010), the assigned condition was allocated if CO was ≤15 ppm

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in smokers and ≤1 ppm in never smokers. If CO was >15 ppm in smokers, >1 ppm in never-smokers, or the participant reported active smoking or excessive passive smoking in the previous 10 hours, the condition was rescheduled. For never-smokers, previous measurements were performed before, immediately after, and one hour after active and passive smoking (figure 3). We evaluated forced FVC, FEV_1, FEV_1/FVC, peak expiratory flow (PEF), and forced expiratory flow in the middle 50% of FVC (FEF_{25-75}). The fraction of exhaled nitric oxide (FeNO) was monitored as a marker of airway inflammation. Exhaled CO and serum cotinine were assessed as indicators of active and passive e-cigarette and tobacco cigarette smoking.

Active Smoking Protocol

In the $ACTIVE_{CON}$ condition, smokers were asked to pseudo-smoke an unlit-cigarette from a brand of their choice for 30 minutes. In the $ACTIVE_{TOB}$ condition, smokers were asked to smoke two tobacco cigarettes from a brand of their choice within 30 minutes. Finally, in the $ACTIVE_{E\text{-}CIG}$ condition, smokers were asked to take a number of puffs from an e-cigarette device (Giant, Nobacco G.P., Greece) within 30 minutes. A new cartridge (within its expiration date) and a fully charged battery were used for each session. The e-cigarette liquid used (Nobacco USA Mix, Nobacco G.P., Greece) had a “tobacco taste” and contained 11mg/ml of nicotine, which is an average concentration since the range of nicotine content in e-cigarette liquids usually ranges between 0 to 36 mg/ml. Previous research has shown that a given number of puffs on an e-cigarette result in significantly less nicotine absorption compared to that generated by the same number of puffs from a tobacco cigarette (Eissenberg, 2010; Vansickel, et al., 2010). Thus, results from studies maintained an equal number of puffs across products may reflect a lower nicotine dose instead of reduced particulates, tars and CO.

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Therefore, it was deemed appropriate to calculate the number of puffs for each participant in the $ACTIVE_{E\text{-}CIG}$ condition based on (i) the nicotine content of their tobacco cigarette, (ii) the tobacco cigarette to e-cigarette nicotine absorption ratio, (iii) the nicotine concentration in the e-cigarette liquid, as well as (iv) the number of puffs required to consume 1 ml of liquid in an e-cigarette. The information required in order to derive (ii), (iii), and (iv) was obtained through a pilot study using an independent sample of 178 e-cigarette smokers that were previous tobacco cigarette smokers.

Given that the vast majority e-cigarettes are sold online (Etter, et al., 2011), the internet is the most appropriate means to reach users. We therefore posted two survey forms, in English and Greek, on the survey website www.surveymonkey.com over a 3-month period between September 14 2011 and December 13 2011. Links to the survey were posted on international (e-cigarette-forum.com, minicigarette.net, vaporboards.com, electroniccigaretteforum.net, new-smoke.com, vaportalk.com, vaporgossip.com) and Greek (e-kapnisma.gr) websites that provide information about e-cigarettes and/or sell them. Eligible participants were people who declared that they were previous tobacco cigarette users and were currently using e-cigarettes and who could also provide the brand names of both the tobacco cigarette and the e-cigarette that they had used most often. Participants were asked to respond to five survey questions: “1. On average, how many tobacco cigarettes did you use to smoke per day?” (response from 1 to >120 with increments of 1); “2. What brand of tobacco cigarettes did you use to smoke?”; “3. What is the quantity (in mg) of nicotine in the liquid you use for your e-cigarettes?” (Response from 1 to >36 with increments of 1); “4. On average, how many ml of e-cigarette liquid do you use per day?” (Response from 0.5 to >10 with increments of 0.5); “5. On average, how many times do you puff your e-cigarette in order to smoke 1ml of liquid?” (Response from 1 to >200 with increments of 1).

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A total of 178 e-cigarette users completed the survey. Of those, 141 completed the English survey, while 37 completed the Greek survey. Responses from both surveys were analyzed simultaneously. Results from questions 1 through 4 revealed that nicotine consumption via e-cigarettes was 1.5 times higher than nicotine consumption via tobacco cigarettes. Assuming that the users aimed for the same effect, this means that the average tobacco cigarette/e-cigarette nicotine absorption ratio is 1.5. Results from the 5th question demonstrated that the median number of puffs required to consume 1 ml of e-cigarette liquid was 50. Thus, e-cigarette puffs can be corrected to match a tobacco cigarette in terms of nicotine absorption after taking into account the nicotine content of the e-cigarette liquid. Based on the above, the e-cigarette puffs equivalent to that of 1 tobacco cigarette, while controlling for nicotine absorption, was calculated as:

$$\textbf{e-cigarette puffs} = (\mathbf{TOB_{NIC}} \cdot \mathbf{1.5} \cdot \mathbf{50}) / \mathbf{eCIG_{NIC}}$$

where TOB_{NIC} is the tobacco cigarette nicotine content (in mg), 1.5 is the average tobacco cigarette/e-cigarette nicotine absorption ratio, 50 is the average number of puffs required to consume 1 ml of liquid, and $eCIG_{NIC}$ is the e-cigarette liquid nicotine content (in mg) per ml. Since the above equation was used to calculate the total number of puffs during the $ACTIVE_{E\text{-}CIG}$ condition, the result was multiplied by 2 since that was the number of tobacco cigarettes smoked in the $ACTIVE_{TOB}$ condition. Based on the obtained information, the e-cigarette puffs in the $ACTIVE_{E\text{-}CIG}$ condition were calculated as: [[tobacco cigarette nicotine content (in mg) · 1.5 · 50] / e-cigarette liquid nicotine content (in mg) per ml] · 2. The total number of puffs during the $ACTIVE_{E\text{-}CIG}$ condition ranged from 3 [for a subject who smoked “extra light” cigarettes (0.2 mg of nicotine per cigarette)] to 14 (for two subjects who smoked cigarettes containing 1 mg

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of nicotine per cigarette). The median puff number was 11, and the mean±sd puff number was 10.4±2.7.

Passive Smoking Protocol

In the $PASSIVE_{CON}$ condition, never-smokers were exposed to normal room air for one hour inside a $60m^3$ environmentally controlled chamber (air temperature: 21°C; air velocity: 0.05 m/s; humidity: 45%). In the $PASSIVE_{TOB}$ condition, participants were exposed to air polluted with tobacco cigarette smoke at a stable CO concentration to simulate bar/restaurant levels (23±1ppm; CO90 CO-CO_2 analyzer, Martindale Electric Ltd., Watford, UK), for one hour inside the same chamber, as previously described (A. Flouris, G. Metsios, A. Jamurtas, & Y. Koutedakis, 2010; Flouris, et al., 2009; Flouris, et al., 2008; Metsios, et al., 2007). The desired CO concentration of the gas mixture was achieved by combustion of cigarettes from various popular brands (i.e., equal number of Camel, Davidoff Classic, Gauloises Filter, Original Red Lucky Strike, Marlboro Reds, Prince Classic and Silk Cut Purple King Size tobacco cigarettes). Mainstream smoke was generated from cigarettes by using an air pump (DYN, Volos, Greece) set at an air flow rate of 4 l/min. Cigarettes were half smoked using the air pump and then were left lit for 2 min to generate sidestream smoke, and then the rest of the cigarettes were smoked. An average of 29.2±0.9 cigarettes was smoked in order to achieve the required level of CO in the exposure chamber. In the $PASSIVE_{E\text{-}CIG}$ condition, participants were exposed to air polluted with e-cigarette vapor for one hour in the same chamber. In this case, a simulated a bar/restaurant e-cigarette smoking environment was achieved by smoking e-cigarettes via the same air pump set at an air flow rate of 4 l/min for the same time as in the $PASSIVE_{TOB}$ condition.

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In previous experiments (A. Flouris, et al., 2010; Flouris, et al., 2009; Flouris, et al., 2008; Metsios, et al., 2007) our research group simulated a passive smoking environment by placing lit cigarettes in ashtrays and using nearby fans to circulate the air in the room (i.e., 100% sidestream smoke). In the current study, the increased oxygen and burn temperature produced by applying air current within the cigarettes via the air pump may have resulted in more efficient combustion and "cleaner" smoke. Therefore, we conducted a pilot study to assess lung function prior to and following the current protocol and the one adopted in our previous studies. Seven never-smokers participated in the two conditions that were conducted at the same time on two separate days using identical pre-calibrated equipment. Within each individual data collection time point (i.e., baseline, immediately post and 1-hour post exposure), Mann–Whitney U tests were used to detect changes between the previously used ($PASSIVE_{TOB1}$) and the current ($PASSIVE_{TOB2}$) protocol. The results, presented in Table 2, demonstrated that lung function tended to be slightly less affected by the current protocol (e.g., FEV_1 and PEF were slightly lower while CO was slightly higher immediately following passive smoking in the $PASSIVE_{TOB1}$), yet no statistically significant difference was observed between the two protocols ($P>0.05$).

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Table 2. Lung function results (mean±sd) across time during the two tobacco cigarette passive smoking protocols.

Protocol	Time	FeNO	CO	FVC	FEV_1	FEV_1/FVC	PEF	FEF_{25-75}
$PASSIVE_{TOB1}$	Baseline	14.4±7.6	1.0±0.0	5.3±1.1	4.4±0.8	0.8±0.1	9.3±2.2	4.4±1.0
	Post	13.1±7.8	2.9±0.7	5.2±1.0	4.2±0.7	0.8±0.1	8.9±1.8	4.3±1.0
	1h Post	11.6±8.3	3.7±0.8	5.2±1.1	4.3±0.8	0.8±0.1	9.0±2.0	4.4±1.1
$PASSIVE_{TOB2}$	Baseline	15.3±8.9	1.0±0.0	5.3±1.1	4.4±0.8	0.8±0.1	9.3±1.9	4.4±1.0
	Post	11.4±8.2	2.7±1.4	5.2±1.0	4.3±0.9	0.8±0.1	9.1±2.0	4.3±1.2
	1h Post	10.7±9.0	4.0±1.3	5.2±1.1	4.3±0.8	0.8±0.1	9.2±2.2	4.3±1.2

Note: FeNO = exhaled nitric oxide; CO = exhaled carbon dioxide; FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; PEF = peak expiratory flow; FEF_{25-75} = forced expiratory flow in the middle 50% of FVC; $PASSIVE_{TOB1}$ = previously-used tobacco cigarette passive smoking protocol; $PASSIVE_{TOB2}$ = current tobacco cigarette passive smoking protocol.

Lung Function

Spirometry was performed by the same technician according to the American Thoracic Society recommendations (American Thoracic Society, 1995) using a portable spirometer (Spirobank II; MIR, Rome, Italy) to ensure reliability. Values measured included forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC ratio, peak expiratory flow (PEF), and forced expiratory flow in the middle 50% of FVC (FEF_{25-75}). Moreover, exhaled CO was assessed using a portable breath CO monitor (Breath CO Monitor; Clement Clarke International, Essex, UK) and exhaled nitric oxide (FeNO) was measured using a portable NO analyzer (NObreath, Bedfont, Rochester, UK) at 50 ml/s exhalation flow.

Cotinine Biochemical Analysis

Serum cotinine was measured via liquid chromatography mass spectrometry (LCMS) analysis using techniques similar to those described earlier by our group (A. Flouris, et al., 2010; Flouris, et al., 2009; Flouris, et al., 2008; Metsios, et al., 2007).

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Veins of the antecubital fossa were accessed for the collection of 5ml of whole blood. Blood was centrifuged and serum samples were frozen without delay to -20°C until analyzed. Two milliliters (2 ml) of each sample was placed in test tubes. Ketamine (10 μl from a 10 ppm solution) was inserted into each sample as an internal standard. Further, 1.5 ml ammonium formate (5mM, pH=3.1) was added to each sample that was followed by a solid phase extraction step. Column (Varian, bond Elut–C18, 100mg, 1 ml) activation was executed by adding 1 ml methanol and 1 ml ammonium formate. Thereafter, the sample solution was passed through the column and washed with 1 ml of water. Elution was performed by 1 ml of methanol containing 5% ammonium hydroxide (v/v). The collected solution was acidified by 100 μl HCl (1% in methanol) and evaporated under gentle nitrogen steam at 25°C (Miller, Norris, Rollins, Tiffany, & Wilkins, 2010). A reconstitution in 100 μl of methanol was followed and the solution was promoted to LCMS analysis.

A LCMS system (Shimadzu LCMS-2010 EV, Shimadzu Co., Kyoto, Japan) equipped with an electrospray ionization interface, an autosampler, solvent degasser, binary pump, and a heated/cooled column compartment was used for cotinine extraction from serum samples. The column was a Discovery C18 Column (25cm x 4.6mm, 5μm; SupelCo, Bellefonte, USA). Both mass spectrometer and HPLC inlet were controlled by Shimadzu LCMS solution software (LCMS Solution version 3) that was also used for data acquisition and processing. The instrument was tuned and calibrated using autotune procedures recommended by the manufacturer. CDL and heat block temperatures were 250°C and 200°C, respectively. The detector voltage was 1.5 kV and the nebulizing gas flow 1.5 L/min.

Twenty μl (20 μl) from each extracted sample were placed in to the chromatograph column at a temperature of 45°C. A gradient of 10mM ammonium

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acetate, pH = 5.2, (solvent A) and an acetonitrile (solvent B) were selected for routine use: starting at 10% of solvent B, 90% B (15 min linear ramp), 10% B (5 min). The total mobile phase flow rate was 0.6 mL/min. The detection was done in SIM (selected ion monitoring) positive mode using ion fragments with m/z 163, 204 for nicotine, m/z 177, 218 for cotinine and m/z 238, 279 for ketamine. The fragments that were used for quantification were m/z 163, m/z 177 and 238 for nicotine, cotinine and ketamine, respectively.

Sample Size Estimation

Given the two distinct subpopulations (i.e., smokers and never-smokers) investigated in this study, sample size was determined separately and the highest number of subjects required was used. For active smoking in smokers, the minimum required sample size was determined using a recent e-cigarette study (Eissenberg, 2010) where plasma nicotine was measured prior to and immediately following tobacco cigarette (2.0 vs. 16.8 $ng \cdot ml^{-1}$) and e-cigarette (2.0 vs. 2.5 $ng \cdot ml^{-1}$) active smoking. Given the lack of previous passive e-cigarette smoking studies, the minimum required sample size for passive smoking in never-smokers was determined using a tobacco cigarette passive smoking study (Metsios, et al., 2007) where serum cotinine was measured prior to and immediately following a similar 1-hour tobacco cigarette passive smoking exposure (8 vs. 23.17 $ng \cdot ml^{-1}$) and a control exposure (8.27 vs. 9.17 $ng \cdot ml^{-1}$).

Sample size calculations were conducted using G*Power 3.0 (Faul, Erdfelder, Lang, & Buchner, 2007). The “Repeated measures: Within factors, ANOVA-approach” incorporated in the “F tests” family with “a priori” as the type of power analysis was used to calculate the power of the within effect. The “Number of groups” and “Number of measurements” fields are set to 1 and 9, respectively. Error probability and “Corr

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among rep measures" were set to 0.05 and 0.5, respectively, and – since sphericity obviously holds in this study – nonsphericity correction was set to 1. The minimum required sample size was determined by calculating the variance of the within effect. Using the aforementioned published data (Eissenberg, 2010; Metsios, et al., 2007), the "Variance explained by special effect" was equal to 14.6 and 16.1 for the active and passive smoking, respectively, while the "Variance within groups" was set to $9^2 = 81$ in both cases. The resulting minimum required sample size, given a predetermined Type I error rate of 0.05, was 8 participants for both occasions. The protocols of power analyses and the corresponding central and noncentral distributions are provided in figure 4. In order to confidently detect a reasonable departure from the null hypothesis, the total sample size studied in each sub-population was nearly doubled to 15 subjects.

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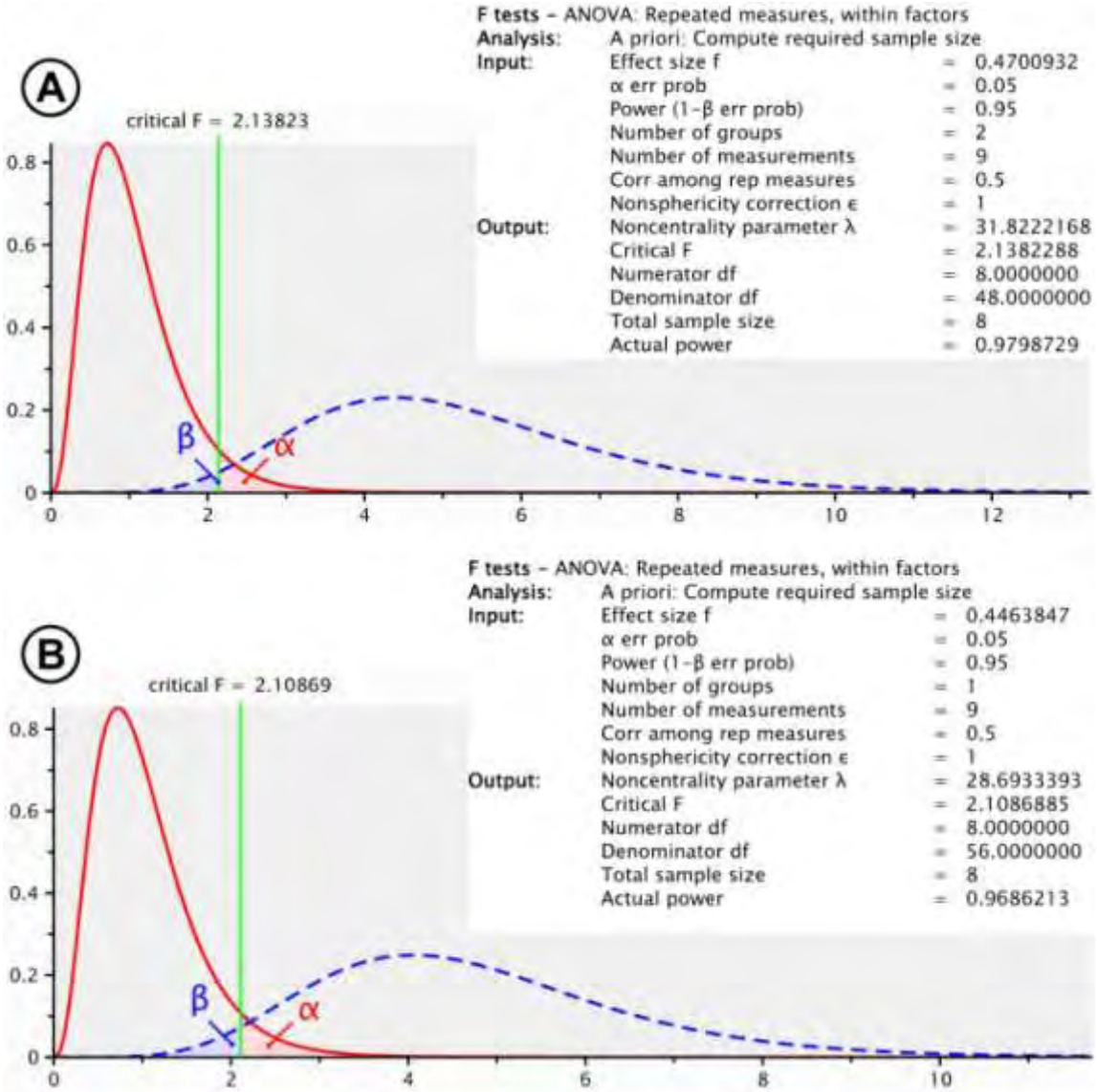

Figure 5. Protocols of power analyses and the corresponding central and noncentral distributions

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Statistical Analysis

A priori power calculations demonstrated that a sample size of 15 participants per group (i.e., smokers and never-smokers) provided >95% power. In order to focus the analyses entirely on the effect of active and passive smoking while removing any diurnal variation, values from the two control conditions (i.e., $ACTIVE_{CON}$ and $PASSIVE_{CON}$) were subtracted from the values of the tobacco cigarette conditions (i.e., $ACTIVE_{TOB}$ and $PASSIVE_{TOB}$) and the electronic cigarette conditions (i.e., $ACTIVE_{E\text{-}CIG}$ and $PASSIVE_{E\text{-}CIG}$). Friedman tests followed by post hoc Wilcoxon signed-rank tests were used to assess changes over time (i.e., prior to, immediately after, and one hour after active or passive smoking) during $ACTIVE_{TOB}$, $ACTIVE_{E\text{-}CIG}$, $PASSIVE_{TOB}$, and $PASSIVE_{E\text{-}CIG}$ on all examined variables (i.e., FVC, FEV_1, FEV_1/FVC ratio, PEF, $FEF_{25\text{-}75}$, CO, FeNO, and cotinine). Within each individual data collection time point, Mann–Whitney U tests were used to detect changes between $ACTIVE_{TOB}$ and $ACTIVE_{E\text{-}CIG}$, as well as between $PASSIVE_{TOB}$ and $PASSIVE_{E\text{-}CIG}$. The accepted level of significance was $P \leq 0.05$. Where applicable, the level of significance was adjusted for multiple comparisons using the Bonferroni correction (i.e., 0.05 / n; where n is the number of comparisons). As such, levels of significance for the Friedman tests and the Wilcoxon signed-rank tests were set at $P \leq 0.002$, $P \leq 0.017$, respectively.

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Results

Results for both active and passive smoking are illustrated in figures 6 and 7 respectively, while the absolute values appear in tables 3 and 4. Lung function was compromised immediately after active and passive tobacco cigarette smoking, while after one hour the majority of lung function parameters had returned to normal levels. No such changes were observed immediately or 1-hour after active or passive e-cigarette smoking. Specifically, Friedman tests revealed that FEV_1/FVC ($\chi^2 = 12.67$; $P = 0.002$), CO ($\chi^2 = 26.27$; $P < 0.001$), and cotinine ($\chi^2 = 14.93$; $P = 0.001$) changed significantly across time during $ACTIVE_{TOB}$. Post hoc Wilcoxon signed-rank tests demonstrated that FEV_1/FVC ($z = -2.48$, $P = 0.013$) was significantly reduced, while CO ($z = -3.42$, $P = 0.001$) and cotinine ($z = -3.24$, $P = 0.001$) were significantly increased immediately following smoking during the $ACTIVE_{TOB}$. One hour following smoking in the $ACTIVE_{TOB}$, CO ($z = -3.41$, $P = 0.001$) and cotinine ($z = -2.90$, $P = 0.004$) remained significantly higher than normal. In the $ACTIVE_{E\text{-}CIG}$ condition, results from Friedman tests showed that the only variable that significantly fluctuated across time was serum cotinine ($\chi^2 = 18.53$; $P < 0.001$). Post hoc tests revealed an increase in cotinine both immediately after ($z = -3.29$, $P = 0.001$) and one hour after ($z = -3.32$, $P = 0.001$) smoking in the $ACTIVE_{E\text{-}CIG}$ condition (figure 6).

Friedman tests revealed that CO ($\chi^2 = 17.18$; $P < 0.001$) changed significantly across time during $PASSIVE_{TOB}$. Serum cotinine also showed considerable change across time which, however, did not reach our conservative significance level ($\chi^2 = 10.13$; $P = 0.006$). Post hoc Wilcoxon signed-rank tests demonstrated that the FEV_1/FVC ($z = -2.38$, $P = 0.017$) was reduced whereas CO ($z = -3.31$, $P = 0.001$) and cotinine ($z = -2.96$, $P = 0.003$) were increased immediately following smoking in the $PASSIVE_{TOB}$ condition. The increased levels of CO ($z = -2.99$, $P = 0.003$) and cotinine

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(z = -2.62, P = 0.009) were observed even one hour after passive smoking in $PASSIVE_{TOB}$. Friedman tests for $PASSIVE_{E\text{-}CIG}$ showed no fluctuations across time. Post hoc tests demonstrated no statistically significant changes immediately following smoking in the $PASSIVE_{E\text{-}CIG}$ condition. In the same condition, cotinine demonstrated an upward trend immediately following smoking, similar to that observed during $PASSIVE_{TOB}$, and was significantly increased one hour after the exposure (z = -2.70, P = 0.007) (figure 7).

Given the reduction of FEV_1/FVC, it is important to note that FEV_1 also declined during both $ACTIVE_{TOB}$ and $PASSIVE_{TOB}$. However, this effect did not reach statistical significance probably due to relatively increased variability.

When comparing tobacco cigarette and e-cigarette smoking, Mann–Whitney U comparisons showed that the only variable found to be significantly different was CO which was increased both immediately following (active smoking: z = -4.39, P < 0.001; passive smoking: z = -4.37, P < 0.001) as well as one hour after (active smoking: z = -3.21, P = 0.001; passive smoking: z = -3.56, P = 0.001) tobacco cigarette smoking (figures 6 and 7).

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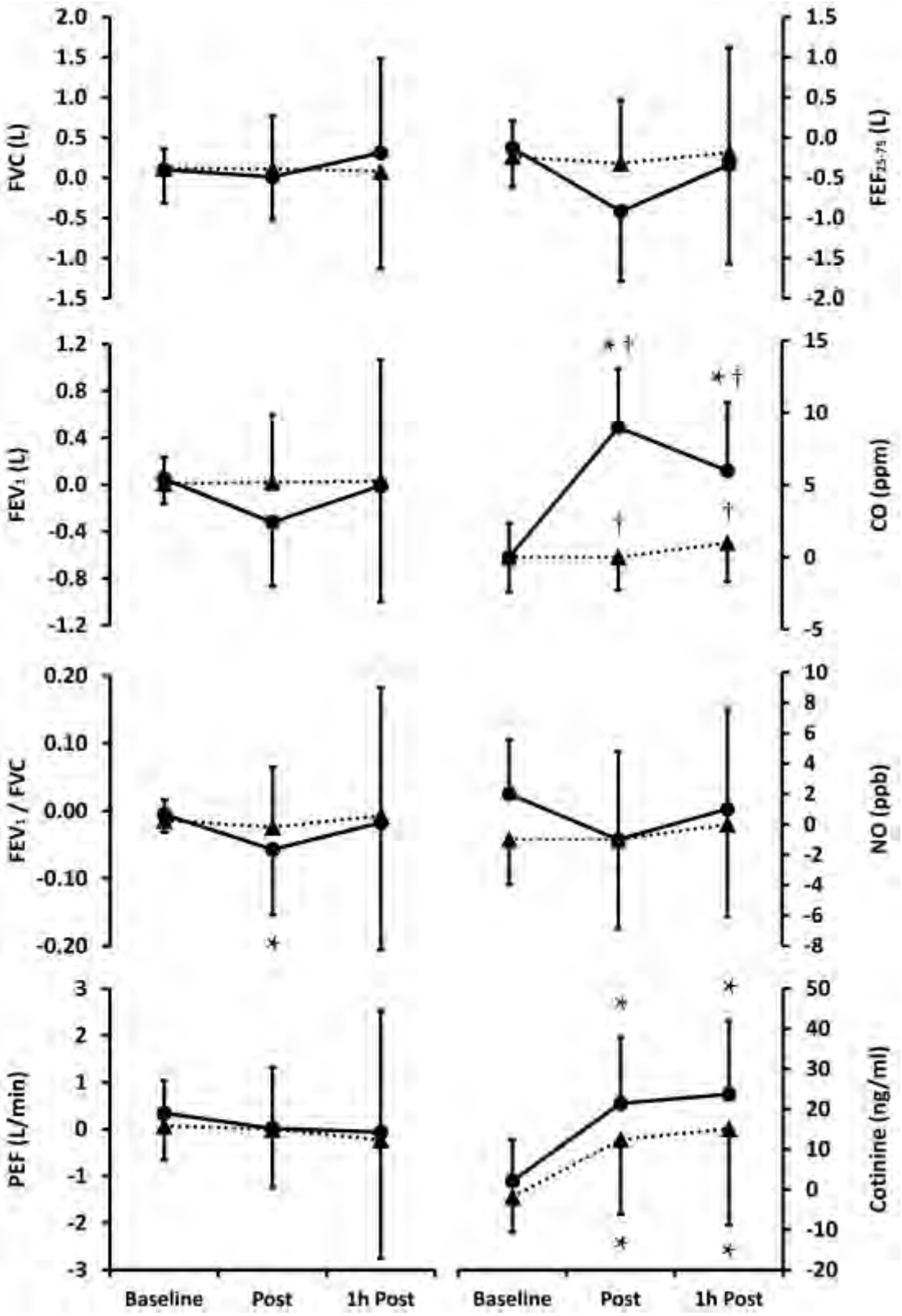

Figure 6. Change from the control condition in all the examined parameters prior to, immediately following, as well as 1 hour following active smoking. Results are presented as median±mean absolute deviation. Solid lines represent tobacco cigarette smoking, while dotted lines represent e-cigarette smoking. Asterisks indicate statistically significant change from baseline values, while crosses indicate statistically significant difference between e-cigarettes and tobacco cigarettes.

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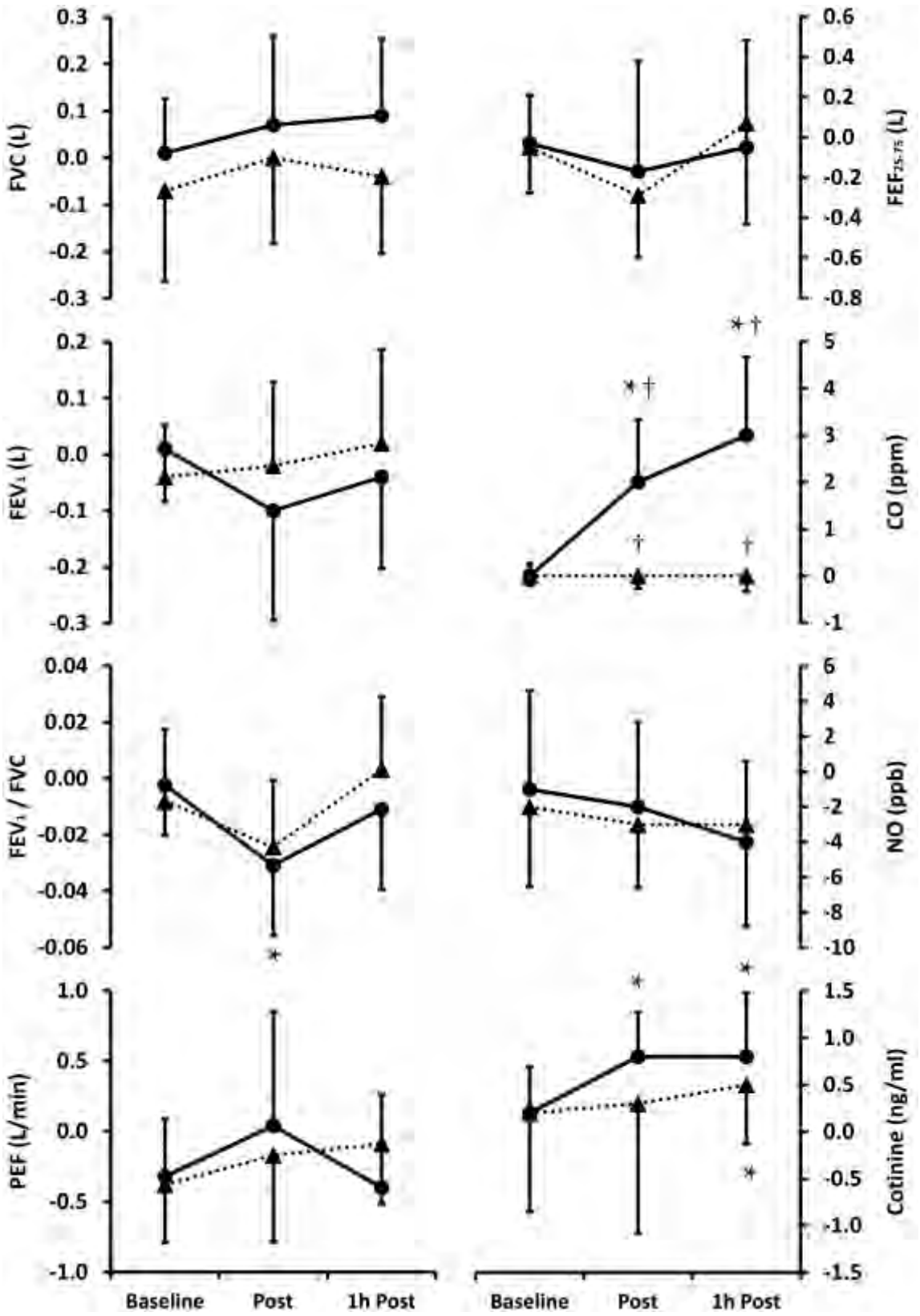

Figure 7. Change from the control condition in all the examined parameters prior to, immediately following, as well as 1 hour following passive smoking. Graph properties are identical to those of figure 6.

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Table 3. Absolute values (median±mean absolute deviation) for all parameters prior to, immediately following, as well as 1 hour following active smoking in smokers.

	Time	FeNO (ppb)	CO (ppm)	FVC (L)	FEV_1 (L)	FEV_1/FVC	PEF (L/min)	FEF_{25-75} (L)	Cotinine (ng/ml)
CON	Baseline	4.5±4.8	7.0±2.5	4.5±0.9	3.5±0.7	0.85±0.05	6.8±2.1	4.2±0.8	41.0±31.0
	Post	3.0±4.1	7.0±3.1	4.3±1.1	3.6±0.8	0.84±0.10	7.2±2.2	4.2±1.2	41.3±28.7
	1h Post	4.5±4.9	5.0±3.0	4.3±1.6	3.6±1.3	0.85±0.21	6.6±2.6	4.1±1.7	40.6±27.6
TOB	Baseline	5.0±5.5	7.0±2.7	4.5±1.0	3.7±0.7	0.83±0.05	7.3±2.4	3.9±0.8	43.7±31.5
	Post	4.0±4.9	16.0±4.5	4.1±1.1	3.3±0.6	0.78±0.06	6.6±1.9	3.4±0.8	61.3±36.6
	1h Post	3.0±4.6	14.0±4.6	4.6±1.1	3.5±0.7	0.81±0.06	6.4±2.3	4.1±0.8	60.6±34.3
E-CIG	Baseline	4.0±4.5	9.0±2.0	4.4±1.1	3.6±0.8	0.82±0.05	7.1±2.1	3.7±0.9	27.5±25.8
	Post	4.0±3.1	7.0±1.7	4.4±1.0	3.6±0.7	0.81±0.06	7.2±2.0	4.0±0.8	42.3±33.5
	1h Post	4.0±4.2	6.0±1.9	4.4±1.0	3.5±0.7	0.82±0.05	6.5±2.3	3.9±0.7	52.4±36.1

Note: FeNO = exhaled nitric oxide; CO = exhaled carbon dioxide; FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; PEF = peak expiratory flow; FEF_{25-75} = forced expiratory flow in the middle 50% of FVC; CON = control condition; TOB = tobacco cigarette active smoking condition; E-CIG = e-cigarette active smoking condition.

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Table 4. Absolute values (median±mean absolute deviation) for all parameters prior to, immediately following, as well as 1 hour following passive smoking in never-smokers.

	Time	FeNO (ppb)	CO (ppm)	FVC (L)	FEV_1 (L)	FEV_1/FVC	PEF (L/min)	FEF_{25-75} (L)	Cotinine (ng/ml)
CON	Baseline	14.0±7.4	1.0±0.1	4.8±1.0	4.1±0.8	0.88±0.06	9.7±1.8	4.6±1.1	1.5±0.7
	Post	14.0±6.7	1.0±0.1	4.6±1.0	4.1±0.8	0.89±0.06	9.4±1.5	4.5±1.2	1.7±0.7
	1h Post	14.0±7.3	1.0±0.2	5.0±1.0	4.1±0.8	0.88±0.06	9.5±1.8	4.8±1.0	1.9±0.6
TOB	Baseline	15.0±6.3	1.0±0.2	4.8±1.0	4.2±0.8	0.89±0.06	9.2±1.8	4.6±1.2	1.9±0.5
	Post	10.0±7.7	4.0±1.4	4.6±1.0	4.0±0.9	0.86±0.05	9.1±1.8	4.1±1.3	2.6±0.6
	1h Post	10.0±7.7	4.0±1.5	5.5±1.0	4.0±0.9	0.86±0.05	9.1±2.0	4.2±1.3	2.4±0.9
E-CIG	Baseline	10.0±7.1	1.0±0.1	5.1±1.0	4.1±0.8	0.89±0.05	8.9±1.7	4.6±1.2	1.8±0.9
	Post	11.0±8.1	1.0±0.1	4.4±1.0	3.9±0.8	0.86±0.05	9.2±2.0	4.8±1.2	2.3±1.2
	1h Post	10.0±8.1	1.0±0.3	4.5±1.0	4.0±0.8	0.88±0.05	8.5±2.0	4.7±1.1	2.2±0.7

Note: FeNO = exhaled nitric oxide; CO = exhaled carbon dioxide; FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; PEF = peak expiratory flow; FEF_{25-75} = forced expiratory flow in the middle 50% of FVC; CON = control condition; TOB = tobacco cigarette active smoking condition; E-CIG = e-cigarette active smoking condition.

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Discussion

In this study we present the first comprehensive assessment regarding the impact of acute and short term active and passive e-cigarette smoking on the function and inflammation of the lungs, as compared to active and passive tobacco cigarette smoking. The results suggest that acute active and passive e-cigarette smoking generate a mild lung airflow obstruction and a small increase in lung inflammation that last <1 hour and appear to be of minimum clinical significance. On the other hand, acute active and passive tobacco cigarette smoking increase lung inflammation and undermine lung function, as serially shown in previous studies (Eisner, et al., 2007; A. Flouris, et al., 2010; Flouris, et al., 2009; Flouris, et al., 2008; Metsios, et al., 2007; Yates, et al., 2001).

Chronic lung disease is normally a long-term process. However, even brief exposures to air pollution stimulate mechanisms that contribute to its development (Flouris, 2009; Flouris, et al., 2009). Acute smoking causes localised lung inflammation, platelet aggregation, reduction of the number of eosinophils, suppression of repair mechanisms and impairment of the epithelial barrier (van der Vaart, et al., 2004). All these mechanisms are heavily linked with the development and/or exacerbation of chronic lung disease. While it is essential to study the effects of long-term e-cigarette use, investigating the acute phase of e-cigarette vapor inhalation is crucial and represents an essential step in the research agenda (Etter, et al., 2011).

It is true that technology is not always a benign force and some of the reasons in support of skepticism concerning progress are valid (Flouris & Oikonomou, 2010). In the case of smoking, however, the progress from tobacco cigarettes to e-cigarettes could, potentially, have beneficial effects for public health. That is if the design, implementation, and commercialization of this technology adhere to appropriate

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regulations in order to protect consumer's health. Till now, neither of these requirements has been achieved in a way that ENDS use could be safe and risk-free.

In our study, the effects of e-cigarettes on lung function and inflammation were not vastly different from those generated by tobacco cigarettes. Nevertheless, e-cigarettes produced a much smaller detrimental impact on the respiratory system; at least in the acute phase that was assessed in the present study. Therefore, there is hope that with further advancement of this technology in the future, the effects on health may be reduced even more.

It is important to note that the present results apply to the specific e-cigarette device and liquid tested and may not describe appropriately the acute usage of other devices and/or liquids. Volunteers were ENDS-naive users and it is possible that the health effects are different in experienced users. Moreover, puffing topography may play a role; in our study the observed changes in lung function and inflammation were not produced by extreme and/or prolonged tobacco cigarette or e-cigarette inhalation. The protocols used for active and passive smoking have been standardized by our group (A. Flouris, et al., 2010; Flouris, et al., 2009; Flouris, et al., 2008; Metsios, et al., 2007) and/or others (Bullen, et al., 2010; Vansickel, et al., 2010). Furthermore, the observed cotinine levels suggest a moderate and brief inhalation. Yet, our lung function results are limited by the impossibility of blinding our participants to active and passive smoking. However, suggestibility does not appear to underlie acute physiological responses to smoke inhalation (Urch, et al., 1988).

E-cigarette use is acceptable in indoor spaces in many countries due to lack of regulations and/or manufacturers' assertions that the vapor released does not contain any chemicals. It is the first time that passive e-cigarette smoking is tested and even though it did not influence lung function or markers of inflammation like FeNO,

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plasma cotinine was raised significantly on participants 1 hour after exposure to e-cigarette vapor, implying that nicotine may be present.

As far as active e-cigarette smoking is concerned, finding show little impact on lung function compared to tobacco smoking; however, spirometry may fail to detect the initial and possibly mild effects from the short-term inhalation of e-cigarette vapor on the respiratory system while repetitive use may provoke significant changes. In another study where lung function was normal, e-cigarette use was related to an increase on flow resistance detected by impulse osscilometry (IOS); thus it is likely that these oncoming pathophysiological changes may not be represented in spirometric findings yet (Vardavas, et al., 2011).

With these in mind, it is concluded that acute active and passive e-cigarette smoking generate a mild lung obstruction and a small increase in lung inflammation that last <1 hour and appear to be of minimum clinical significance. In contrast, acute active and passive tobacco cigarette smoking produce marked lung inflammation and undermine lung function. Future research should target the health effects of long-term e-cigarette usage, while extensive research via independent organizations must be incorporated within the design and implementation of this technology in order to protect consumer health.

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18/05/2024 18:48:53 EEST - 18.119.172.243

Bibliography

American Thoracic Society. (1995). Standardization of Spirometry, 1994 Update. *Am J Respir Crit Care Med, 152*(3), 1107-1136.

ASH Research Report: SecondHand Smoke (April 2011). Retrieved Accessed: 19 May 2012, from http://www.ash.org.uk/files/documents/ASH_597.pdf

Bullen, C., McRobbie, H., Thornley, S., Glover, M., Lin, R., & Laugesen, M. (2010). Effect of an electronic nicotine delivery device (e cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: randomised cross-over trial. *Tob Control, 19*(2), 98-103.

Burns, E. (Ed.). (2006). *The Smoke of the Gods: A Social History of Tobacco*: Temple University Press.

Caponnetto, P., Polosa, R., Russo, C., Leotta, C., & Campagna, D. (2011). Successful smoking cessation with electronic cigarettes in smokers with a documented history of recurring relapses: a case series. *J Med Case Reports, 5*(1), 585.

Cho, J. H., Shin, E., & Moon, S. S. (2011). Electronic-cigarette smoking experience among adolescents. *J Adolesc Health, 49*(5), 542-546.

Choi, H., Schmidbauer, N., Spengler, J., & Bornehag, C. G. (2010). Sources of propylene glycol and glycol ethers in air at home. *Int J Environ Res Public Health, 7*(12), 4213-4237.

Churg, A., Tai, H., Coulthard, T., Wang, R., & Wright, J. L. (2006). Cigarette smoke drives small airway remodeling by induction of growth factors in the airway wall. *Am J Respir Crit Care Med, 174*(12), 1327-1334.

Davis, J. W., Shelton, L., Watanabe, I. S., & Arnold, J. (1989). Passive smoking affects endothelium and platelets. *Arch Intern Med, 149*(2), 386-389.

Eisner, M. D., Wang, Y., Haight, T. J., Balmes, J., Hammond, S. K., & Tager, I. B. (2007). Secondhand smoke exposure, pulmonary function, and cardiovascular mortality. *Ann Epidemiol, 17*(5), 364-373.

Eissenberg, T. (2010). Electronic nicotine delivery devices: ineffective nicotine delivery and craving suppression after acute administration. *Tob Control, 19*(1), 87-88.

Etter, J. F., & Bullen, C. (2011). Saliva cotinine levels in users of electronic cigarettes. *Eur Respir J, 38*(5), 1219-1220.

Etter, J. F., Bullen, C., Flouris, A. D., Laugesen, M., & Eissenberg, T. (2011). Electronic nicotine delivery systems: a research agenda. *Tob Control, 20*(3), 243-248.

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. [Research Support, Non-U.S. Gov't]. *Behav Res Methods, 39*(2), 175-191.

FDA. (2009). FDA and Public Health Experts Warn About Electronic Cigarettes. from http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm173222.htm

Flouris, A., Metsios, G., Jamurtas, A., & Koutedakis, Y. (2010). Cardiorespiratory and immune response to physical activity following exposure to a typical smoking environment. *Heart 96*, 860-864.

Flouris, A. D. (2009). Acute health effects of passive smoking. *Inflamm Allergy Drug Targets, 8*(5), 319-320.

Flouris, A. D., & Koutedakis, Y. (2011). Immediate and short-term consequences of secondhand smoke exposure on the respiratory system. *Curr Opin Pulm Med, 17*(2), 110-115.

Flouris, A. D., Metsios, G. S., Carrill, A. E., Jamurtas, A. Z., Stivaktakis, P. D., Tzatzarakis, M. N., et al. (2012). Respiratory and immune response to maximal physical exertion following exposure to secondhand smoke in healthy adults. *PLoS One, 7*(2), e31880.

Flouris, A. D., Metsios, G. S., Carrillo, A. E., Jamurtas, A. Z., Gourgoulianis, K., Kiropoulos, T., et al. (2009). Acute and short-term effects of secondhand smoke on lung function and cytokine production. *Am J Respir Crit Care Med, 179*(11), 1029-1033.

Institutional Repository - Library & Information Centre - University of Thessaly
18/05/2024 18:48:53 EEST - 18.119.172.243

Flouris, A. D., Metsios, G. S., Jamurtas, A. Z., & Koutedakis, Y. (2008). Sexual dimorphism in the acute effects of secondhand smoke on thyroid hormone secretion, inflammatory markers and vascular function. *Am J Physiol Endocrinol Metab, 294*(2), E456-462.

Flouris, A. D., Metsios, G. S., Jamurtas, A. Z., & Koutedakis, Y. (2010). Cardiorespiratory and immune response to physical activity following exposure to a typical smoking environment. *Heart, 96*(11), 860-864.

Flouris, A. D., & Oikonomou, D. N. (2010). Electronic cigarettes: miracle or menace? *BMJ, 340*, c311.

Flouris, A. D., Vardavas, C. I., Metsios, G. S., Tsatsakis, A. M., & Koutedakis, Y. (2010). Biological evidence for the acute health effects of secondhand smoke exposure. *Am J Physiol Lung Cell Mol Physiol, 298*(1), L3-L12.

Gately, I. (Ed.). (2001). *Tobacco: A Cultural History of How an Exotic Plant Seduced Civilization*. London, England: Simon & Schuster UK Ltd.

Gilman, L. S., & Xun, Z. (Eds.). (2004). *Smoke: A Global History of Smoking*. London, England: Reaktion Books.

GOLD. (2011). *Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease*: Global Initiative for Chronic Obstructive Lung Disease.

Gold, D. R., Wang, X., Wypij, D., Speizer, F. E., Ware, J. H., & Dockery, D. W. (1996). Effects of cigarette smoking on lung function in adolescent boys and girls. *N Engl J Med, 335*(13), 931-937.

Hadwiger, M. E., Trehy, M. L., Ye, W., Moore, T., Allgire, J., & Westenberger, B. (2010). Identification of amino-tadalafil and rimonabant in electronic cigarette products using high pressure liquid chromatography with diode array and tandem mass spectrometric detection. *J Chromatogr A, 1217*(48), 7547-7555.

Hoyt, J. C., Robbins, R. A., Habib, M., Springall, D. R., Buttery, L. D., Polak, J. M., et al. (2003). Cigarette smoke decreases inducible nitric oxide synthase in lung epithelial cells. *Exp Lung Res, 29*(1), 17-28.

Kharitonov, S. A., Robbins, R. A., Yates, D., Keatings, V., & Barnes, P. J. (1995). Acute and chronic effects of cigarette smoking on exhaled nitric oxide. *Am J Respir Crit Care Med, 152*(2), 609-612.

King, C., 3rd, & Siegel, M. (2001). The Master Settlement Agreement with the tobacco industry and cigarette advertising in magazines. *N Engl J Med, 345*(7), 504-511.

Laugesen, M. (2008). *Safety report on Ruyan e-cigarette, cartridge and inhaled aerosol.* Christchurch, New Zealand: Health New Zealand Ltd.

Lehr, H. A., Hubner, C., Finckh, B., Angermuller, S., Nolte, D., Beisiegel, U., et al. (1991). Role of leukotrienes in leukocyte adhesion following systemic administration of oxidatively modified human low density lipoprotein in hamsters. *J Clin Invest, 88*(1), 9-14.

Leondiadis, L. (2009). *Results of chemical analyses in NOBACCO electronic cigarette refills.* . Athens, Greece: Mass Spectrometry and Dioxin Analysis Laboratory, National Centre for Scientific Research (“Demokritos”).

Lloyd, J., & Mitchinson, J. (Eds.). (2007). *The Book of General Ignorance*: Harmony Books.

Lopez, A. D., Shibuya, K., Rao, C., Mathers, C. D., Hansell, A. L., Held, L. S., et al. (2006). Chronic obstructive pulmonary disease: current burden and future projections. *Eur Respir J, 27*(2), 397-412.

Metsios, G. S., Flouris, A. D., Jamurtas, A. Z., Carrillo, A. E., Kouretas, D., Germenis, A. E., et al. (2007). A brief exposure to moderate passive smoke increases metabolism and thyroid hormone secretion. *J Clin Endocrinol Metab, 92*(1), 208-211.

Miller, E. I., Norris, H. R., Rollins, D. E., Tiffany, S. T., & Wilkins, D. G. (2010). A novel validated procedure for the determination of nicotine, eight nicotine metabolites and two minor tobacco alkaloids in human plasma or urine by solid-phase extraction coupled with liquid chromatography-electrospray ionization-tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci, 878*(9-10), 725-737.

Pauly, J., Li, Q., & Barry, M. B. (2007). Tobacco-free electronic cigarettes and cigars deliver nicotine and generate concern. *Tob Control, 16*(5), 357.

Institutional Repository - Library & Information Centre - University of Thessaly
18/05/2024 18:48:53 EEST - 18.119.172.243

Proktor, R. (Ed.). (2000). *The Nazi war on cancer*. Princeton, New Jersey: Princeton University Press.

Rennard, S. I. (1998). COPD: overview of definitions, epidemiology, and factors influencing its development. *Chest, 113*(4 Suppl), 235S-241S.

Sundy, J. S., Hauswirth, D. W., Mervin-Blake, S., Fernandez, C. A., Patch, K. B., Alexander, K. M., et al. (2007). Smoking is associated with an age-related decline in exhaled nitric oxide. *Eur Respir J, 30*(6), 1074-1081.

Tobacco Master Settlement Agreement. (1998, Accessed: 17 May 2012). from http://ag.ca.gov/tobacco/pdf/1msa.pdf

Trtchounian, A., & Talbot, P. (2011). Electronic nicotine delivery systems: is there a need for regulation? *Tob Control, 20*(1), 47-52.

Trtchounian, A., Williams, M., & Talbot, P. (2010). Conventional and electronic cigarettes (e-cigarettes) have different smoking characteristics. *Nicotine Tob Res, 12*(9), 905-912.

U.S. Department of Health and Human Services. (2010). *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General*. Atlanta: GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

Urch, R. B., Silverman, F., Corey, P., Shephard, R. J., Cole, P., & Goldsmith, L. J. (1988). Does suggestibility modify acute reactions to passive cigarette smoke exposure? *Environ Res, 47*(1), 34-47.

Urrutia, I., Capelastegui, A., Quintana, J. M., Muniozguren, N., Basagana, X., & Sunyer, J. (2005). Smoking habit, respiratory symptoms and lung function in young adults. *Eur J Public Health, 15*(2), 160-165.

van der Vaart, H., Postma, D. S., Timens, W., Hylkema, M. N., Willemse, B. W., Boezen, H. M., et al. (2005). Acute effects of cigarette smoking on inflammation in healthy intermittent smokers. *Respir Res, 6*, 22.

van der Vaart, H., Postma, D. S., Timens, W., & ten Hacken, N. H. (2004). Acute effects of cigarette smoke on inflammation and oxidative stress: a review. *Thorax, 59*(8), 713-721.

Vansickel, A. R., Cobb, C. O., Weaver, M. F., & Eissenberg, T. E. (2010). A clinical laboratory model for evaluating the acute effects of electronic "cigarettes": nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiol Biomarkers Prev, 19*(8), 1945-1953.

Vardavas, C. I., Anagnostopoulos, N., Kougias, M., Evangelopoulou, V., Connolly, G. N., & Behrakis, P. K. (2011). Acute pulmonary effects of using an e-cigarette: impact on respiratory flow resistance, impedance and exhaled nitric oxide. *Chest*.

Westenberger, B. J. (2009). *Evaluation of e-cigarettes.* : US Food and Drug Administration, Center for Drug Evaluation and Research.

WHO. (2008a). Marketers of electronic cigarettes should halt unproved therapy claims. Retrieved 25 May 2012, from http://www.who.int/mediacentre/news/releases/2008/pr34/en/

WHO. (2008b). *WHO Report on the global tobacco epidemic*: World Health Organisation.

WHO. (2011). *Report on the global tobacco epidemic: warning about the dangers of tobacco.*: World Health Organisation.

WHO. (May 2012., Accessed 17 May 2012: http://www.who.int/mediacentre/factsheets/fs339/en/index.html). Fact Sheet No339.

WHO study group on tobacco product regulation. (2009). *Report on the scientific basis of tobacco product regulation: third report of a WHO study group.*
: World Health Organization.

Wieslander, G., Norback, D., & Lindgren, T. (2001). Experimental exposure to propylene glycol mist in aviation emergency training: acute ocular and respiratory effects. *Occup Environ Med, 58*(10), 649-655.

World Health Organisation. (2004). *The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers*

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for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

World Health Organisation. (2006). *The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General Exit Notification.* . Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

World Health Organisation. (2010). *WHO Regulatory Consultation on the Safety of Electronic Nicotine Delivery Devices (ENDS)*. Geneva: World Health Organisation.

Yamin, C. K., Bitton, A., & Bates, D. W. (2010). E-cigarettes: a rapidly growing Internet phenomenon. *Ann Intern Med, 153*(9), 607-609.

Yang, S. C., & Yang, S. P. (2002). Bronchial responsiveness and lung function related to cigarette smoking and smoking cessation. *Chang Gung Med J, 25*(10), 645-655.

Yates, D. H., Breen, H., & Thomas, P. S. (2001). Passive smoke inhalation decreases exhaled nitric oxide in normal subjects. *Am J Respir Crit Care Med, 164*(6), 1043-1046.

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Supplement

Appendix A: Ethical Review Board Approval

ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ
ΤΜΗΜΑ ΕΠΙΣΤΗΜΗΣ ΦΥΣΙΚΗΣ ΑΓΩΓΗΣ ΚΑΙ ΑΘΛΗΤΙΣΜΟΥ

Εσωτερική Επιτροπή Δεοντολογίας

Τρίκαλα: 26/5/2011
Αριθμ. Πρωτ.: 322

Αίτηση Εξέτασης της πρότασης για διεξαγωγή Έρευνας με τίτλο:
Βραχυπρόθεσμες επιπτώσεις ενεργητικού και παθητικού καπνίσματος συμβατικού και ηλεκτρονικού τσιγάρου στην πνευμονική λειτουργικότητα και τη λειτουργία του καρδιαγγειακού συστήματος

Επιστημονικός υπεύθυνος – επιβλέπων: Δρ. Κουτεντάκης Ιωάννης

Επιστημονικός σύμβουλος: Δρ. Ανδρέας Φλουρής

Κύρια ερευνήτρια - φοιτήτρια: Χόρτη Μαρία

Ίδρυμα & Τμήμα: Τμήμα Επιστήμης Φυσικής Αγωγής και Αθλητισμού, του Πανεπιστημίου Θεσσαλίας

Η προτεινόμενη έρευνα θα είναι:

Ερευνητικό πρόγραμμα ☐ **Μεταπτυχιακή διατριβή X** Διπλωματική εργασία ☐ Ανεξάρτητη έρευνα ☐

Τηλ. επικοινωνίας: 2441023380 και 6936897470
Email επικοινωνίας: mariachorti@gmail.com

Η Εσωτερική Επιτροπή Δεοντολογίας του Τ.Ε.Φ.Α.Α., Πανεπιστημίου Θεσσαλίας μετά την υπ. Αριθμ. 2-9/13-4-2011 συνεδρίασή της εγκρίνει τη διεξαγωγή της προτεινόμενης έρευνας.

Η πρόεδρος της
Εσωτερικής Επιτροπής
Δεοντολογίας - ΤΕΦΑΑ

Χριστίνα Καρατζαφέρη
Επίκουρη Καθηγήτρια

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Appendix B: Written consent form

Έντυπο συναίνεσης δοκιμαζόμενου σε ερευνητική εργασία

1. Σκοπός της ερευνητικής εργασίας

Σκοπός αυτής της εργασίας είναι να μελετηθούν οι βραχυπρόθεσμες επιπτώσεις του καπνίσματος, ενεργητικού και παθητικού, συμβατικού και ηλεκτρονικού τσιγάρου, στον ανθρώπινο οργανισμό. Ειδικότερα, θα μελετηθούν τυχόν αλλαγές στην λειτουργία των πνευμόνων, στο καρδιαγγειακό, το ανοσολογικό και το ενδοκρινικό σύστημα. Το ηλεκτρονικό τσιγάρο είναι μια συσκευή προσομοίωσης του συμβατικού, που πρόσφατα έχει προωθηθεί στην αγορά ως εναλλακτική μορφή ή ως μέσο διακοπής του καπνίσματος. Είναι κατασκευασμένο ώστε να μιμείται τη διαδικασία του καπνίσματος, προσφέροντας όμως στο χρήστη τους έναν εναλλακτικό, πιο «υγιεινό» τρόπο καπνίσματος. Σύμφωνα με τους κατασκευαστές τους το ηλεκτρονικό τσιγάρο απαλλάσσει τον χρήστη του από τον καπνό, την πίσσα και χιλιάδες άλλες τοξικές ουσίες που περιέχουν τα συμβατικά τσιγάρα αλλά και τους ανθρώπους στον περιβάλλοντα χώρο από το παθητικό κάπνισμα.

2. Διαδικασία μετρήσεων

Θα χρειαστεί να έρθεις στο εργαστήριο τρεις φορές, με μεσοδιάστημα 7 ημερών. Θα πρέπει να προσέλθεις εγκαίρως, ώστε το πείραμα να ξεκινήσει στις 09:00 ακριβώς (τουλάχιστον 15 λεπτά πριν). Θα πρέπει να αποφύγεις την έντονη σωματική δραστηριότητα για 3 ημέρες πριν και να είσαι νηστικός (το τελευταίο γεύμα να έχει ολοκληρωθεί στις 11:00μμ το προηγούμενο βράδυ). Θα πρέπει να μην έχεις καπνίσει ούτε να έχεις εκτεθεί σε παθητικό κάπνισμα για 12 ώρες πριν την έναρξη της έρευνας, δηλαδή από τις 9:00μμ το προηγούμενο βράδυ. Κατά την διάρκεια του πειράματος απαγορεύεται η πρόσληψη τροφής, επιτρέπεται η πρόσληψη νερού.

Καπνιστές: Το πείραμα θα έχει διάρκεια 1,5 ώρας. Πριν το πείραμα θα πρέπει να δώσεις κάποια στοιχεία για την καπνιστική σου συνήθεια (από τι ηλικία ξεκίνησες να καπνίζεις, πόσα τσιγάρα καπνίζεις την ημέρα και για πόσα χρόνια). Την πρώτη ημέρα θα καπνίσεις 2 τσιγάρα της επιλογής σου, μέσα σε διάστημα μισής ώρας. Τη δεύτερη φορά θα καπνίσεις ηλεκτρονικό τσιγάρο. Την τρίτη φορά θα «καπνίσεις» ένα μη αναμμένο τσιγάρο της επιλογής σου. Θα πραγματοποιηθούν μετρήσεις αμέσως πριν το πείραμα, αμέσως μετά τη λήξη του πειράματος και 1 ώρα μετά τη δεύτερη μέτρηση.

Μη καπνιστές: Το πείραμα θα έχει διάρκεια 2 ωρών. Την πρώτη φορά θα υποβληθείς για 1 ώρα σε μέτριο παθητικό κάπνισμα συμβατικού τσιγάρου μέσα σε έναν ειδικά διαμορφωμένο χώρο που θα εξομοιώνει τις συνήθεις συνθήκες που επικρατούν σε ένα εστιατόριο/μπαρ. Τη δεύτερη φορά θα υποβληθείς σε παθητικό κάπνισμα ηλεκτρονικού τσιγάρου για 1 ώρα. Την τρίτη φορά θα περάσεις 1 ώρα σε ένα δωμάτιο με καθαρό αέρα. Θα πραγματοποιηθούν μετρήσεις αμέσως πριν το πείραμα, αμέσως μετά τη λήξη του πειράματος, και 1 ώρα μετά τη δεύτερη μέτρηση.

Οι μετρήσεις θα είναι:

- Κλινικές.

Θα κληθείς να φυσήξεις όσο πιο δυνατά μπορείς στο σπιρόμετρο για 3 συνεχόμενες φορές ώστε να γίνουν μετρήσεις της πνευμονικής σου λειτουργίας. Επίσης, θα φυσήξεις από μία φορά σε φορητούς μετρητές εκπνεόμενου μονοξειδίου του άνθρακα και μονοξειδίου του αζώτου.

- Εργαστηριακές. Για το σκοπό αυτό, θα πραγματοποιείται αιμοληψία κατά την οποία θα λαμβάνονται 15ml αίματος κάθε φορά.

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3. Κίνδυνοι και ενοχλήσεις
Κατά την διάρκεια του πειράματος αν είσαι μη καπνιστής υπάρχει κίνδυνος να έχεις κάποια δυσφορία από τον καπνό, η οποία δεν θα είναι μεγαλύτερη από αυτήν όταν παρευρίσκεσαι σε ένα συνηθισμένο εστιατόριο/μπαρ που καπνίζουν. Οποιαδήποτε στιγμή αισθανθείς κάποιο σύμπτωμα που σε προβληματίζει σε παρακαλούμε να το αναφέρεις και θα ληφθεί μέριμνα για την προστασία της υγείας και της προσωπικότητάς σου. Ακόμα υπάρχει ένας πολύ μικρός κίνδυνος δημιουργίας μώλωπα στην περιοχή του αγκώνα όπου και βρίσκεται η φλέβα από την οποία θα πραγματοποιηθεί η αιμοληψία. Θα γίνει κάθε προσπάθεια να ελαχιστοποιηθούν αυτοί οι κίνδυνοι. Υπάρχει πρόβλεψη πρώτων βοηθειών και εκπαιδευμένο προσωπικό για κάθε ενδεχόμενο.

4. Προσδοκώμενες ωφέλειες
Τα ευρήματα από την εργασία θα σου δώσουν την δυνατότητα:

- Να εκτιμήσεις τις βραχυπρόθεσμες επιπτώσεις του καπνίσματος (ενεργητικού και παθητικού) συμβατικού και ηλεκτρονικού τσιγάρου στον οργανισμό σου.
- Να διαπιστώσεις τις βλαβερές συνέπειες αλλά και τα πιθανά οφέλη για την υγεία σου που πιθανόν να προκύψουν από την σύγκριση των αποτελεσμάτων.
- Να οδηγηθείς ακόμη και σε διακοπή του καπνίσματος.

5. Δημοσίευση δεδομένων – αποτελεσμάτων
Η συμμετοχή σου στην έρευνα συνεπάγεται ότι συμφωνείς με τη δημοσίευση των δεδομένων και των αποτελεσμάτων της, με την προϋπόθεση ότι οι πληροφορίες θα είναι ανώνυμες και δε θα αποκαλυφθούν τα ονόματα των συμμετεχόντων. Τα δεδομένα που θα συγκεντρωθούν θα κωδικοποιηθούν με αριθμό, ώστε το όνομα σου δε θα φαίνεται πουθενά.

6. Πληροφορίες
Μη διστάσεις να κάνεις ερωτήσεις γύρω από το σκοπό, τον τρόπο πραγματοποίησης της εργασίας ή τον υπολογισμό της λειτουργικής σου ικανότητας. Αν έχεις κάποιες αμφιβολίες ή ερωτήσεις, ζήτησέ μας να σου δώσουμε πρόσθετες εξηγήσεις.

7.Ελευθερία συναίνεσης
Η άδειά σου να συμμετάσχεις στην εργασία είναι εθελοντική. Είσαι ελεύθερος να μην συναινέσεις ή να διακόψεις τη συμμετοχή σου όποτε επιθυμείς.

Διάβασα το έντυπο αυτό και κατανοώ τις διαδικασίες που θα εκτελέσω. Συναινώ να συμμετέχω στην εργασία.

Ημερομηνία: __/__/__

Ονοματεπώνυμο και υπογραφή συμμετέχοντος

Υπογραφή ερευνητή

Ονοματεπώνυμο και υπογραφή παρατηρητή

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Appendix C: Υπεύθυνη δήλωση πνευματικών δικαιωμάτων

Υπεύθυνη Δήλωση

Η κάτωθι υπογεγραμμένη Χόρτη Μαρία – ΑΕΜ 10/09, μεταπτυχιακή φοιτήτρια του Προγράμματος Μεταπτυχιακών Σπουδών «Άσκηση και Υγεία» του Τμήματος Επιστήμης Φυσικής Αγωγής και Αθλητισμού του Πανεπιστημίου Θεσσαλίας

δηλώνω υπεύθυνα ότι αποδέχομαι τους παρακάτω όρους που αφορούν

(α) στα πνευματικά δικαιώματα της Μεταπτυχιακής Διπλωματικής Εργασίας (ΜΔΕ) μου με τίτλο «**Βραχυπρόθεσμες επιπτώσεις ενεργητικού και παθητικού καπνίσματος συμβατικού και ηλεκτρονικού τσιγάρου στην πνευμονική λειτουργικότητα» (Acute Effects of Conventional and Electronic Cigarette Smoking and Second-hand Smoke on Lung Function)**

(β) στη διαχείριση των ερευνητικών δεδομένων που θα συλλέξω στην πορεία εκπόνησής της:

1. Τα πνευματικά δικαιώματα του τόμου της μεταπτυχιακής διατριβής που θα προκύψει θα ανήκουν σε μένα. Θα ακολουθήσω τις οδηγίες συγγραφής, εκτύπωσης και κατάθεσης αντιτύπων της διατριβής στα ανάλογα αποθετήρια (σε έντυπη ή/και σε ηλεκτρονική μορφή).

2. Η διαχείριση των δεδομένων της διατριβής ανήκει από κοινού σε εμένα και στον πρώτο επιβλέποντα καθηγητή.

3. Οποιαδήποτε επιστημονική δημοσίευση ή ανακοίνωση (αναρτημένη ή προφορική), ή αναφορά που προέρχεται από το υλικό/δεδομένα της εργασίας αυτής θα γίνεται με συγγραφείς εμένα τον ίδιο, τον κύριο επιβλέποντα ή και άλλους ερευνητές (όπως πχ μέλους –ών της τριμελούς συμβουλευτικής επιτροπής), ανάλογα με τη συμβολή τους στην έρευνα ή στη συγγραφή των ερευνητικών εργασιών.

4. Η σειρά των ονομάτων στις επιστημονικές δημοσιεύσεις ή επιστημονικές ανακοινώσεις θα αποφασίζεται από κοινού από εμένα και τον κύριο επιβλέποντα της εργασίας, πριν αρχίσει η εκπόνησή της. Η απόφαση αυτή θα πιστοποιηθεί εγγράφως μεταξύ εμού και του κ. επιβλέποντα.

Τέλος, δηλώνω ότι γνωρίζω τους κανόνες περί λογοκλοπής και πνευματικής ιδιοκτησίας και ότι θα τους τηρώ απαρέγκλιτα καθ' όλη τη διάρκεια της φοίτησης και κάλυψης των εκπαιδευτικών υποχρεώσεων που προκύπτουν από το ΠΜΣ/τμήμα, αλλά και των διαδικασιών δημοσίευσης που θα προκύψουν μετά την ολοκλήρωση των σπουδών μου.

4 Ιουνίου 2012

Η δηλούσα

Χόρτη Μαρία

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Appendix D: Meeting diary

Ονοματεπώνυμο φοιτήτριας: .....**Χόρτη Μαρία**.....

Συνάντηση 1η

Ημερομηνία: 15/3/2011 Ώρα:.19:00 Υπογραφή Επιβλέποντος: .....

Σκοπός: Θέμα και σχεδιασμός διατριβής Υπογραφή φοιτητή:.....

Επόμενοι Στόχοι: Σύνταξη φόρμας έγγραφης συγκατάθεσης, Πρόταση προς επιτροπή βιοηθικής, μελέτη βιβλιογραφίας

Συνάντηση 2η

Ημερομηνία:.29/3/2011 Ώρα:.12:00 Υπογραφή Επιβλέποντος: .....

Σκοπός: Πρόταση προς επιτροπή βιοηθικής Υπογραφή φοιτητή: .....

Επόμενοι Στόχοι: Σχεδιασμός και οργάνωση πειραματικού μέρους

Συνάντηση 3η

Ημερομηνία:.3/5/2011 Ώρα:.11:30 Υπογραφή Επιβλέποντος: .....

Σκοπός: Οργάνωση πειραματικού μέρους Υπογραφή φοιτητή:

Επόμενοι Στόχοι: Δημιουργία φορμών αποτελεσμάτων, ανεύρεση εθελοντών, παραγγελία ηλεκτρονικών τσιγάρων, προμήθεια και έλεγχος οργάνων (σπιρόμετρο, καπνόμετρο, αναλυτής FeNO)

Συνάντηση 4η

Ημερομηνία: 14/9/2011 Ώρα:17:00 Υπογραφή Επιβλέποντος: .....

Σκοπός: Οργάνωση πειραματικού μέρους Υπογραφή φοιτητή: ….....

Επόμενοι Στόχοι: Προετοιμασία χώρου για μετρήσεις (περιβαλλοντικός θάλαμος), Πιλοτικές δοκιμές, Αναλώσιμα οργάνων και εργαστηριακών εξετάσεων

Συνάντηση 5η

Ημερομηνία: 29/9/2011 Ώρα: 09:00 Υπογραφή Επιβλέποντος: ….....

Σκοπός: Πιλοτικές δοκιμές – έναρξη πειράματος Υπογραφή φοιτητή: .....

Επόμενοι Στόχοι: Ανεύρεση εθελοντών, συνεννόηση με εργαστήριο, ημερολόγιο/ χρονοδιάγραμμα κλινικών και εργαστηριακών μετρήσεων

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Συνάντηση 6η

Ημερομηνία:13/10/2011 Ώρα:17:00 Υπογραφή Επιβλέποντος:….....

Σκοπός: Πρόοδος μετρήσεων Υπογραφή φοιτητή: .....

Επόμενοι Στόχοι: Ολοκλήρωση μετρήσεων, τήρηση χρονοδιαγράμματος

Συνάντηση 7η

Ημερομηνία: 14/11/2011 Ώρα:18:00 Υπογραφή Επιβλέποντος: .....

Σκοπός: Στατιστική ανάλυση δεδομένων Υπογραφή φοιτητή: .....

Επόμενοι Στόχοι: Αποστολή εργαστηριακών δειγμάτων σε Πανεπιστήμιο Κρήτης, έναρξη συγγραφής άρθρου προς δημοσίευση

Συνάντηση 8η

Ημερομηνία: 8/12/2011 Ώρα:11:30 Υπογραφή Επιβλέποντος: .....

Σκοπός: Άρθρο προς δημοσίευση Υπογραφή φοιτητή: .....

Επόμενοι Στόχοι: Οριστική μορφή άρθρου προς δημοσίευση, συγγραφή περιλήψεων για αποστολή σε πανευρωπαϊκό συνέδριο, έναρξη συγγραφής μεταπτυχιακής διατριβής

Συνάντηση 9η

Ημερομηνία: 8/1/2012 Ώρα:17:00 Υπογραφή Επιβλέποντος: .....

Σκοπός: Συγγραφή μεταπτυχιακής διατριβής Υπογραφή φοιτητή:.....

Επόμενοι Στόχοι: Συγγραφή μεταπτυχιακής διατριβής εντός χρονοδιαγράμματος

Συνάντηση 10η

Ημερομηνία:24/5/2012 Ώρα:11:00 Υπογραφή Επιβλέποντος .....

Σκοπός: Παρουσίαση μεταπτυχιακής διατριβής Υπογραφή φοιτητή: .....

Επόμενοι Στόχοι: ολοκλήρωση μεταπτυχιακού προγράμματος

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