

# The role of olfaction in dietary preferences, composition and anthropometric characteristics in the population of Dalmatia

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**UNIVERSITY OF SPLIT  
SCHOOL OF MEDICINE**

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**THE ROLE OF OLFACTION IN DIETARY PREFERENCES AND  
COMPOSITION AND ANTHROPOMETRIC CHARACTERISTICS  
IN THE POPULATION OF DALMATIA**

**Diploma thesis**

**Academic year:**

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**Ivana Kolčić, MD, PhD**

**Split, June 2017**

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## **1. Introduction**

Obesity has become a growing epidemic in developed countries and causes a variety of diseases. In the United States it is linked to almost 300 000 deaths each year and the costs of the consequences of obesity are around \$117 billion (1). One of the many investigated factors associated with obesity is the smell perception ability. A difference in smell (and taste) perception between obese and normal weight individuals has been suggested to cause differences in food choices. Therefore further investigation of the association between alteration in olfactory perception and body mass index (BMI) should be done in order to prevent severe cases of obesity and to advance the development of anti-obesity drugs (2).

The olfactory system in the body serves as an internal sensor and, as all body systems, olfaction is affected by hunger states and plays an important role in many daily functions; olfactory perception influences the food intake, the perception of the environment, as well as mating and the social communication (3,4). Olfaction, one of the chemical senses, has a very important role in daily functioning in humans, since it conveys information on nutritious value of the foods (flavour), mediates safety, sensation of pleasure, but also the overall well-being (5).

Compared to simple eyeglasses for visually impaired people, impaired sense of smell cannot be corrected. The question coming up is: how important is olfaction? In several studies people with acquired olfactory disorders typically complained about difficulties in cooking and a low interest in eating (4). People who were born without a sense of smell in the form of an isolated congenital anosmia (ICA) typically do not complain about a reduced quality of life. However, the incidence in household accidents and depression is higher in people with ICA (4).

Studies suggest that in mammals, breast-feeding is depending on the newborn's ability to find the mother's nipple by olfaction. Rabbits for example do not have any chance of surviving if they are anosmic (4).

Animal models reveal that olfactory perception is decreased by satiation and increased by fasting (6). Further studies in humans have shown that in comparison to moderately obese people ( $BMI > 30 \text{ kg/m}^2$ ), morbidly obese individuals ( $BMI > 40 \text{ kg/m}^2$ ) present with a lower olfactory perception, especially in odour detection as well as in identification (7). The hunger hormone ghrelin is secreted when the stomach is empty and it increases the human response to smelling sensation. Ghrelin concentrations are decreased in obesity, and reduced concentrations are related to smell impairment in obese subjects (7). Also in further studies it was shown that patients with olfactory loss reported alteration of dietary behaviours (8). Many factors appear to have an impact on the results of olfactory loss in term of changes in

diet. Patients reported to eat less outside of their homes, eat more spicy, and drink and eat less sweet food and beverages (8).

Another factor that seemingly plays an important role in perception of body odour is the major histocompatibility complex (MHC) genotype (9). With the help of MHC fit partners can be detected. In a study where women rated body odors of T-shirt worn by men who had a different MHC alleles from themselves as more pleasant than the body odors of T-shirts worn by men with similar MHC alleles (9). The sense of smell has been reported to play a large role in sexual relationships; men with congenital anosmia reported fewer sexual relationships than men in the same age (9). Not only men, but also women born without a sense of smell revealed to feel less secure about sexual relationships compared to the control group (9).

Eating and drinking play a central part in human culture, regardless of the countries or social status and the smell of sense contributes to a good quality of life (6). Olfactory disorders have been connected with depression and social isolation. Hence one can conclude that olfactory loss diminishes the quality of life, safety and health (6).

Despite its major role in human quality of life, the sense of smell has not been studied as much as other senses (10), e.g. vision and hearing and therefore in this study we will further investigate the role of olfaction in the diet composition and relate this to the anthropometric characteristics in the population of Dalmatia.

### **1.1. Anatomy of olfaction**

Olfaction is the sensation of odors that results from the detection of odorous substances aerosolized in the environment (11). The olfactory nerve is the first cranial nerve (CN I). The cell bodies of the olfactory receptor neurons are found in the olfactory organ, in the olfactory epithelium/mucosa, that is located in the roof of the nasal cavity and along the nasal septum and medial wall of the superior nasal concha (11).

The central processes of the olfactory receptor neurons ascend through foramina in the cribriform plate of the ethmoid to reach the olfactory bulbs in the anterior cranial fossa.

These nerves synapse on neurons in the bulbs, and the processes of these neurons follow the olfactory tracts to the primary and associated areas of the cerebral cortex (11).

The anatomy of the nasal cavity is presented in Figure 1.



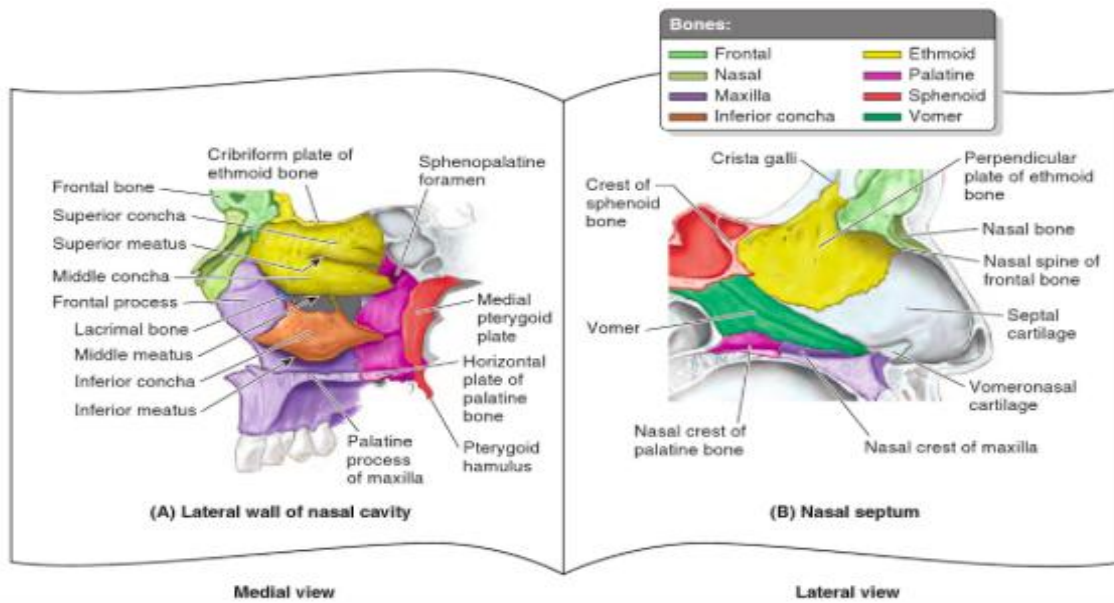


Figure 1. Lateral and medial (septal) walls of right side of nasal cavity. (11)

Olfactory receptor neurons function as both receptors and conductors. The apex of the neurons contains fine olfactory cilia, which are covered by a film of watery mucus. The olfactory glands of the epithelium secrete this mucus. The cilia are excited by molecules of an odiferous gas drained in the fluid (11).

At the base of the bipolar olfactory receptor neurons of the nasal cavity about 20 olfactory nerves arise which present the right or left olfactory nerve (CN I).

The olfactory nerves emerge from the forebrain (prosencephalon) and contain only sensory fibers that play an important role in the special sense of smell (11).

## 1.2. Physiology of olfaction

Olfaction is the sense that is most poorly understood as it has yet to be studied in more depth. The reason for this is that olfaction is subjective and it is hard to compare with lower animals as they have a much lower threshold for odorous stimuli (12).

In order to be able to study the olfactory sense it is important to understand the mechanism of excitation of the olfactory cells. Firstly, the odorant substance activates the receptor proteins, which then activates the G-protein complex. Then, inside the olfactory cell membrane adenylyclase is activated. The activated cyclase converts many molecules of intracellular adenosine-tri-phosphate (ATP) into cyclic adenosine monophosphate (cAMP). This cAMP then activates more molecules which open sodium channels which leads to Na<sup>+</sup> influx and therefore causes depolarization (12). By this mechanism the olfactory neurons are sensitive to

even the slightest amount of odorant (12). The mechanism of excitation of the olfactory cells is schematically presented in Figure 2.

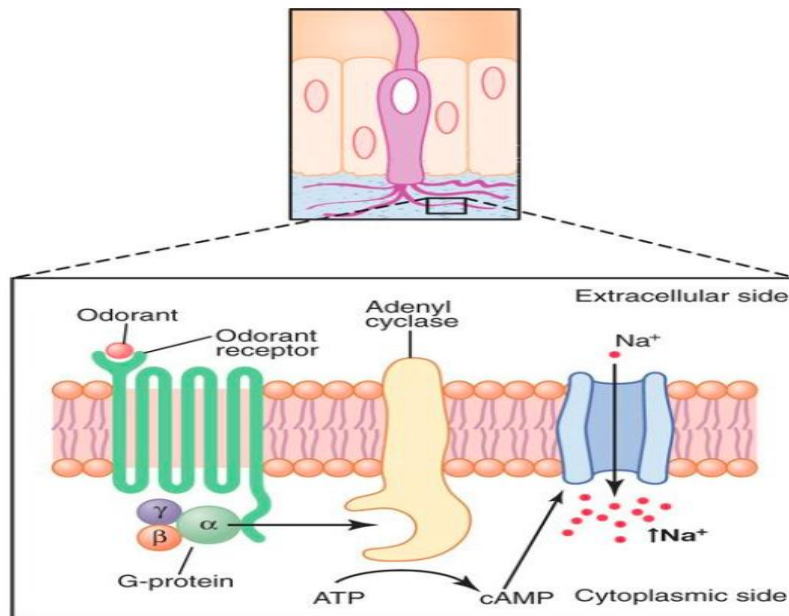


Figure 2. Summary of olfactory signal transduction (12)

### 1.2.1. Olfactory sensations

In the first second after stimulation, the olfactory receptors adapt about 50%. After this time, they adapt only little and very slowly (12). The smell sensations adjust within a minute after entering a strongly odorous atmosphere. As the psychological adaptation is much larger than the adaptation of the receptors themselves, it is clear that most of the additional adaptation happens within the central nervous system (12). On the basis of psychological studies, one attempt is to classify these primary sensations of smell in the following seven sensations: camphoraceous, musky, floral, pepper minty, ethereal, pungent, putrid (12). Other psychological studies distinguish between ten different sensations; fragrant, woody, non-citrus fruity, sharp, chemical, pepper minty, sweet, popcorn, sickening and lemon (13).

Further studies searching for the primary sensations of smell suggest at least 100 primary sensations of smell (13). The reason for this is, as mentioned above, the highly subjective characteristic of olfaction and also odour blindness has been studied in some people for more than 50 substances. Some studies suggest that there may be as many as 1000 different types of odorant receptors (13).

### **1.2.2. Examination of the olfactory nerve**

Asking the patient to identify different but common odors, such as coffee or peppermint, tests the olfactory nerve function. The function of the nerve is assumed to be normal, even if the patient cannot identify the odour correctly but is able to detect it (14). It is important to test each nostril separately. Alcohol should not be used because it is an irritant and those may be detected independently of olfactory receptors, namely trigeminal nerve (14).

### **1.3. Olfactory disorders**

A significant number of the population is affected by olfactory impairments, with 5% of the general population being anosmic and 15% considered being hyposmic (6).

Olfactory disorders can clinically be divided into three categories (12):

1. Anosmia (inability to detect odors)
2. Hyposmia (decreased sensitivity)
3. Dysosmia (distorted identification of smell)

Variants of dysosmia are parosmia, phantosmia and agnosia. Parosmia (troposmia, cacosmia) is an altered and falsified perception of smell. This is usually unpleasant, but does not necessarily have to be, and typically perceived as a burned, rotting, faecal, or chemical smell, which is due to an inability of the brain to properly identify an odour's normal smell (12). Another variant of dysosmia is phantosmia, in which there is a conceived odor when in fact no odorant is present (12).

The unpleasant smell of halogenated volatile agents during anaesthesia can be altered via induction of troposmia. In a study performed at the preoperative visits on the pediatric ward, the anaesthesiologist told the child, that the unpleasant smell could be magically changed into whatever the patient wished for. In fact, it was shown that this worked and that troposmia can be induced (15).

In phantosmia there is a decreased number of functioning olfactory neurons, therefore the odorant is characterized incompletely. It can also be related to either an abnormal or inhibitory signal from the primary olfactory neurons that lead to this central process. Endoscopic transnasal operations have the advantage of treating phantosmia and sometimes allowing a return of olfactory ability after the operation (16).

Kallmann-syndrome (olfactogenital syndrome) is a genetic congenital condition, which is characterized by a lack of an olfactory sense (anosmia) or a reduced olfactory sense

(hyposmia) (17). It is associated with central hypogonadism and neurological deficits and is a form of hypogonadotropic hypogonadism. The patient typically presents with a failure of start of puberty or failure to complete puberty or a history of undescended testis and an inability to smell. Other factors that can lead to a decreased olfactory perception are head trauma, surgery of the brain or subarachnoid haemorrhage. These may alter the brain parenchyma and cause anosmia (16).

Conductive defects can be the result of inflammatory processes that alter the olfactory sensation. Allergic, acute or toxic rhinitis may lead to mucosal disease and despite interventions the smell sensation is altered. The most common cause of nasal masses that block the nasal cavity, are nasal polyps. The odorants cannot reach the olfactory epithelium (18).

#### **1.4. Factors influencing the sense of smell**

Hyperosmia is an increased perception of smell and should also be included in this paragraph although it is very rare. A lower threshold for odour usually causes it. There is an abnormally increased signal at any point between the olfactory receptors and the olfactory cortex. Hyperosmia is classically associated with pregnancy and hyperemesis gravidarum (19). However, it is not clear whether this phenomenon reflects true hypersensitivity or simply reactivity. Other causes may be genetic, environmental or the result of benzodiazepine withdrawal syndrome (19).

Aging alters the olfactory sense. The number of fibers in the olfactory bulb decreases the older we get and therefore older persons perceive smell differently and less intensely than younger individuals (19). Age is the strongest factor that has an impact on olfactory decline in healthy normal elderly people, even more than cigarette smoking (20). Between 65 and 80 years of age about half of the population has significant deficits in the ability to smell. Over the age of 80 nearly 75% experience problems in smelling (20). The cause for this age-related smelling loss is related to, among other things, ossification and closure of the foramina of the cribriform plate, or development of neurodegenerative diseases or repeated damage to the olfactory receptors from viral and other events in life (19,20).

Other factors that influence olfactory perception are emotions. The olfactory bulb has direct connections to the amygdala and hippocampus, which are strongly implicated to play a role in emotion and memory (21). Hence olfaction is of such an importance in triggering emotions and memories, especially when comparing it to visual, auditory and tactile information, which do not pass through these brain areas (21). Also posttraumatic stress

disorder (PTSD) can be evoked by odors. The patients have e.g. disturbing memories, or feelings of guilt when smelling a specific odour (21).

Furthermore, studies have shown, that the odour perception is influenced by the menstrual cycle phase and also by the duration of oral contraception intake, meaning that the odour perception can be altered by hormonal changes (22). Most studies show that there is an increased sensitivity for some odors around ovulation or midluteal phase, while there is a number of studies portraying greater sensitivity during the first phase of the cycle (follicular phase) or even during menstruation (22). The complexity of this topic is being underlined by the fact, that some studies show a decreased sensitivity during menstruation. Especially, females taking oral contraceptives for a longer time, have a better olfactory performance (22).

### **1.5. Sense of smell and health outcomes**

Many neurodegenerative diseases, such as Alzheimer's disease (AD), Parkinson's disease (PD) and other neurologic diseases, such as Huntington disease, multiple sclerosis and motor neuron disease, present with hyposmia. The loss of smell is a cardinal feature of PD and AD and the neurologist should be alert if a patient presents with a recent olfactory dysfunction, though most patients are not even aware of their loss of smell before it is tested and confirmed by their neurologists (18). Nearly 90% of early-stage Parkinson's patients present with an olfactory loss. The reason for this is that there is a decreased activation of central odor processing structures (20). The medication (e.g. dopamine agonists) in PD does not improve the olfactory function of the patient. The preclinical period in AD and PD is often marked with hyposmia and may precede the classical symptoms (18,20). There is a variation in the magnitude and prevalence of the loss of smell among the neurodegenerative diseases. For example, in patients with multiple sclerosis the olfactory dysfunction is proportional to the plaques in the subfrontal and subtemporal lobes (20,23). In variant Creutzfeldt-Jacob disease some patients present with olfactory loss. It is believed that the prion proteins involve the olfactory tract, in a way that the route of infection is the olfactory pathway and via this route the infection is spread (14,18,20,23).

Acute and chronic liver disorders are frequently associated with hyposmia, which can be improved by vitamin A intake (24). In epilepsy early threshold studies of patients reported an increased sensitivity to odors, prior to an ictal event. Antiseizure medications may influence these thresholds, so that in medicated patients the perception of olfaction remains normal (23).

Individuals with schizophrenia show an association between impaired odor identification and social dysfunction (25).

### **1.6. The roles of the human sense of smell**

The sense of smell is mainly associated with eating behaviour, awareness of environmental risks and social behaviour. The olfactory sense is one of the oldest senses; permitting the organisms with olfactory receptors to identify food, finding a mating partner and recognizing dangers. Olfaction is one of the most important ways of interacting with the surrounding.

The olfactory sensory system warns us of leaking gas, fire, microbial risks such as faeces, decay or spoiled foods. It influences our eating behaviour and therefore plays an important role in diet composition (9,23,26).

Therefore, the impact of the olfactory sense on human behaviours is enormous. It has determinant roles in the evolution of human biosphere, in the way of preparing food and in the social behaviour. The odour can also allow recognizing different diseases, e.g. the fruity smelling breath in diabetic ketoacidosis (27). The appetite and food perception is regulated by olfaction. An unbalanced nutritional status and poor food intake seem to be related to an olfactory impairment (9). Furthermore, the major histocompatibility complex (MHC) genotype and body odors can play a critical role in mate selection, not only by avoiding inbreeding, but also by detecting fit mating partners (9).

### **1.7. The role of the sense of smell in diet composition**

People are influenced by certain smells of foods, which evoke hunger and then are strongly driven by the olfactory system to eat this special food (26). The olfactory system drives behavioural decisions about food choice and consumption, and could therefore be linked to obesity (26). In obesity there is an imbalance in the utilization of glucose and insulin, among other energy important molecules, which are detected by the olfactory bulb. In mice it was shown that those on a high-fat diet, independent of the severity of adiposity, had a change in the general neuroarchitecture of the olfactory systems (28). There was also a clear reduction in olfactory discrimination in which obese mice had at least 20% reduced

performance than mice maintained on a low cholesterol diet (28). Also, a chronic exposure to fat impairs the action potential firing of the mitral cells of the olfactory bulb (28).

Hunger can alter the odour perception. Recent evidence suggests that hunger state can similarly affect food odour pleasantness. In rats, decrease of energy is linked to changes in olfactory bulb activity and olfactory sensitivity (2). Also during fasting the identification of food odors is higher than in the satiation period and the thresholds are significantly lower during fasting than in satiation period (3).

Olfactory food cues, meaning smelling a specific odor prior eating, influences the appetite. The appetite increases for congruent products and decreases for incongruent products. This phenomenon is called sensory-specific appetite (10). A continuous exposure to food odors e.g. pizza-odour increases the appetite and craving for that type of food, or any savoury foods that were smelled in reserved eaters (10).

Individuals placed in a fruity odorous room, are more likely to choose fruity desserts than individuals placed in a neutral unscented room. Food odors increase the appetite for products with a similar taste or energy density (10). These effects may be used to stimulate appetite in undernourished individuals. However, the exposure to food odors can promote overeating and could contribute to obesity (10).

### **1.8. The association of olfaction and anthropometric characteristics**

In earlier studies, a relationship between olfactory disturbances and a high Body Mass Index ( $BMI > 45 \text{ kg/m}^2$ ) have been reported. Currently, 1 in 20 Americans have a  $BMI > 40 \text{ kg/m}^2$ . This makes further investigating of olfactory acuity in morbidly obese individuals significantly important. A lower BMI, in this context, should be achieved in order to preserve the olfactory sense and hence a better life quality (6).

A poor odour perception can lead to alterations in food consumption, low food appreciation and a poor nutritional status (29). Recent studies revealed that individuals with increasing BMI had a higher preference for flavour-amplified yoghurt suggesting a relationship between BMI and odour perception (29). An increase in visceral fat has been shown to be related to a decrease in olfactory capacity (2).

Anorexia nervosa is a psychiatric disorder characterized by a very low weight due to a fear of weight gain. In two studies, underweight and weight-recovered patients with anorexia nervosa showed a higher sensitivity to a wide-ranging selection of sensory stimuli than

control participants and the self-reported sensory sensitivity was related to difficulties in emotional regulation (30,31). Another study exhibited a stronger olfactory sensitivity in patients with first-episode anorexia nervosa and in recovered patients, although only patients with first-episode anorexia nervosa and without a comorbid depression showed a superior odor identification (32).

Contrary to the previous findings, some studies did not identify the association between BMI and olfaction perception (33). In conclusion, further studies are needed in order for us to understand better the association between anthropometric factors and odour perception.



## **2. Aims and Hypotheses**

## **2.1. Aims**

The primary aim of this study was to assess the association between the ability to correctly identify odors and anthropometric characteristics in a large population-based sample. Additional aims were to assess the association between the ability to correctly identify odors and dietary preferences and diet composition.

## **2.2. Hypotheses**

1. Examinees with better olfactory performance will have better anthropometric indices, especially smaller BMI
2. Older age and male gender are associated with a decrease in the ability of correct odour identification
3. Olfaction abilities are correlated with the dietary preferences and diet composition

### **3. Material and Methods**

According to the epidemiological design, this is a cross-sectional study. This study was performed within the existing project “Pleiotropy, genetic networks and pathways in isolated human populations: 10,001 Dalmatian” (HRZZ 8875). The ethical approval for this study was obtained by the University of Split Medical School (2181-198-03-04/10-11-0008).

### **3.1. Subjects**

The study sample included the examinees from the city of Split (N=237), and two settlements on the Island of Korcula, Smokvica (N=918) and Blato (N=945), creating a total sample size of 2,100 examinees.

The convenient sampling based on voluntary response was undertaken during May 2013 in Split, during the period of April till December 2012 in Smokvica and during September 2013 – April 2014 in Blato, Korcula. Every adult inhabitant (age  $\geq 18$  years) from these settlements had the opportunity to participate, after the advice given by their local general practitioner. Additionally, examinees were recruited via public media advertisement, like Radio and newspapers adds.

### **3.2. Measurements**

Before any measurements every examinee signed the informed consent. The information obtained for the purpose of this study include anthropometric measurements, odor identification measurements, and a number of information obtained by the use of a questionnaire.

#### **3.2.1. Anthropometric measurements**

Anthropometric indices included in this study were weight, height, BMI, waist circumference, hip circumference, waist-to-hip ratio, brachial width and neck circumference.

Weight and height were measured using a scale and the stadiometer incorporated in one instrument (Seca GMBH & Co., Model 704) which was regularly calibrated. Weight was measured in kilograms and to one decimal point, while height was measured in millimeters. During this procedure the examinees were wearing their underwear.

The abdomen and waist circumferences were using the standard protocol. The measurements were using a flexible but non-elastic measuring tape, divided in millimeters, while the subjects were dressed in the underwear. The abdominal circumference was measured in the point of the end of the expiration, on the site corresponding to the mean distance between the lower part of the rib arch and the upper limit of the pelvic bone (lat. *crista iliaca*), while taking the most prominent diameter of the abdomen in the case of protruding abdomen beyond the chest level. During the measurement of the hip circumference the examinee was standing with the feet closely to each other and the measuring position corresponded to the position of the *trochanter major* of the femur and covering the largest buttocks diameter, while keeping the measuring tape in the parallel position with the floor.

BMI was calculated using the formula:

$$\text{BMI} = \text{weight (kg)} / \text{body mass}^2 \text{ (m)}$$

Waist-to-hip ratio was calculated using the formula:

$$\text{WHR} = \text{waist circumference (cm)} / \text{hip circumference (cm)}$$

Brachial width was measured on the right arm using a dial caliper, placed to gently touch medial and lateral epicondyle. The measurement was done three time consecutively, and the average value was used in the analysis.

Neck circumference was measured using the same tape as used for waist and hip circumference, which was positioned in the mid-point of the neck, in the position of the greatest diameter of the neck.

### **3.2.2. Odor identification measurement**

The screening odor identification test (12 Sniffin' Sticks test, Burghart Messtechnik, Germany) was used to assess the olfactory abilities of the examinees. This is widely used and validated test (34). It consists of 12 odors, which are presented using a felt-tip pens. The odors were: orange, leather, cinnamon, mint, banana, lemon, anise, coffee, clove, pineapple, rose and fish. The test was performed by using random odors, which were presented in from of both nostrils of about 3 seconds each. The subject had to choose an odor from four alternatives, even in the case a subject could not recognize which odor it was (multiple-forced-choice). The sum of correctly identified odors was calculated and used in the analysis.

### 3.2.3. Questionnaire

The self-administered questionnaire consisted of several parts. Demographic questions included age and gender. Socioeconomic data included the information about the years of formal schooling and 16 item material status (yes/no answer for having: water supply, two TVs, washrooms with toilet, dishwasher, bathroom, computer, central or gas heating, library of more than 100 books, wooden floors, art objects, phone, car, DVD player, vacation house/other apartment, freezer, boat), so the values could range from 0 to 16. Medical history questions on chronic diseases included the previous diagnosis of hypertension, coronary heart disease, cerebrovascular insult, Schizophrenia, bipolar disorder, malignant tumor, diabetes type 2, gout, glaucoma, arthritis, renal disease, stomach ulcer and asthma. The sum of these diagnosed chronic disease was used in the analysis.

Behavioral risk factors included smoking, physical activity, alcohol consumption and dietary habits as well as food preferences. Regarding the smoking, an examinee could say he/she is an active smoker, ex-smoker (ceased more than 1 year ago) or never smoked. Physical activity level was assessed for the working part of the day and the leisure part of the day, and the combination of these answers yielded the overall level of physical activity (options were intensive, moderate, light). A subject was rated as having intensive physical activity if intensive physical activity was reported during any part of the day, the same as for moderate physical activity. Alcohol consumption was expressed as the total amount of units of alcohol consumed over a period of one week, including beer, wine, bevanda (a mixture of wine and water) and hard liquor.

The overall dietary habits were estimated using a food-frequency questionnaire (54 questions in total). These data were used to calculate the Mediterranean Diet Serving Score, using a validated approach described in the literature (35). This index includes 14 groups of foods that are the basic components of a Mediterranean diet and it was used before for the assessment of the Mediterranean diet compliance in the same population of Dalmatia (36).

Additionally, dietary preferences were assessed for bacon, pork chops, broccoli, ice cream, milk chocolate, cakes, sweet foods, salty foods, bitter foods, spicy foods, vegetables and fruit on a 9-point Likert scale, where 1 was denoted as 'I do not like it at all', 5 meant 'Medium level of liking', while 9 was represented with the statement 'I like it very much'.

### 3.3. Statistical analysis

Descriptive analysis included the presentation of data as absolute numbers and percentages for categorical and ordinal variables, while medians and interquartile range (IQR) were used in the case of a non-normal distribution of a numeric variable or a mean and standard deviation (SD) were used in the case of a normally distributed numeric variable. The distribution of numeric variables was tested using a Kolmogorov-Smirnov test.

The bivariate statistical analysis was performed using a Chi-square test, Kruskal-Wallis test, ANOVA test and Spearman Rank correlation test.

Finally, a multivariate binary logistic regression analysis was used. For this regression model the outcome (dependent) variable was considered positive in case a subject had a  $BMI \geq 30 \text{ kg/m}^2$ , while the covariates (independent variables) were age, gender, education, material status, chronic diseases (as an ordinary variable), smoking, alcohol intake, physical activity (as an ordinary variable), Mediterranean diet score and odor identification ability.

The statistical analysis was performed using the SPSS software (IBM SPSS Statistics, v19.0), and the P value significance threshold was set to  $<0.05$ .

## **4. Results**



The final sample included in this study consisted of 2100 examinees and 237 (11.3%) were from Split, 918 from Smokvica (43.7%) and 945 came from Blato (45.0%). Demographic, socioeconomic and life-style characteristics of the sample according to the place of residence are shown in Table 1. We found no differences in gender composition in the three studied populations ( $P=0.543$ ; Table 1). Also, it was shown that the alcohol intake did not differ in the three studied populations. All other characteristics were found to be statistically different (Table 1). The subjects from Split were on average the oldest while at the same time they had the smallest prevalence of chronic diseases, with 60% of the examinees in Split sample had no chronic disease, compared to 52% in Smokvica and 47% in Blato (Table 1). Examinees from Split had the least current smokers; 27%, compared to 28.1% in Smokvica and 29.9% in Blato ( $P<0.001$ ; Table 1). On the other hand, examinees from Split had the least examinees who reported intensive physical activity (2.5%), while the highest prevalence was recorded in Smokvica (12.5%) ( $P<0.001$ ; Table 1). Average Mediterranean Diet Serving Score (MDSS) was lowest in Blato (Table 1).

Table 1. Demographic, socioeconomic and life-style characteristics of the sample according to the place of residence

|  | Split<br>N=237 | Smokvica<br>N=918 | Blato<br>N=945 | P value |
|--|----------------|-------------------|----------------|---------|
| Gender; n (%)                                      |                |                   |                |         |
| Female   | 150 (63.3)     | 573 (62.4)        | 613 (64.9)     | 0.543   |
| Male   | 87 (36.7)      | 345 (37.6)        | 332 (35.1)     |         |
| Age (years);<br>median (IQR)                       | 59.1 (18.1)    | 56.5 (22.4)       | 54.0 (25.5)    | <0.001  |
| Education (years<br>of schooling);<br>median (IQR) | 12.0 (4.0)     | 12.0 (4.0)        | 12.0 (2.0)     | <0.001  |
| Material status;<br>median (IQR)                   | 12.0 (3.0)     | 11.0 (3.0)        | 10.0 (4.0)     | <0.001  |
| Chronic diseases;<br>n (%)                         |                |                   |                |         |
| None   | 144 (60.8)     | 474 (51.6)        | 447 (47.3)     | <0.001  |
| One  | 58 (24.5)      | 243 (26.5)        | 248 (26.2)     |         |
| Two  | 30 (12.7)      | 139 (15.1)        | 128 (13.5)     |         |
| Three or<br>more                                   | 5 (2.1)        | 62 (6.8)          | 122 (12.9)     |         |
| Alcohol intake<br>(units); median<br>(IQR)         | 7.0 (20.0)     | 7.0 (23.0)        | 7.0 (20.0)     | 0.055   |
| Smoking; n (%)                                     |                |                   |                |         |
| Current<br>smokers                                 | 64 (27.0)      | 256 (28.1)        | 278 (29.9)     | <0.001  |
| Ex-smokers   | 81 (34.2)      | 182 (20.0)        | 207 (22.2)     |         |
| Never smoked                                       | 92 (38.8)      | 473 (51.9)        | 446 (47.9)     |         |
| Physical activity;<br>n (%)                        |                |                   |                |         |
| Light  | 89 (37.6)      | 178 (19.8)        | 178 (19.3)     | <0.001  |
| Medium   | 142 (59.9)     | 607 (67.7)        | 675 (73.2)     |         |
| Intensive  | 6 (2.5)        | 112 (12.5)        | 69 (7.5)       |         |
| Mediterranean<br>diet score;<br>median (IQR)       | 11.0 (5.0)     | 11.0 (5.0)        | 10.0 (4.0)     | <0.001  |

Anthropometric characteristics and odor identification of the sample according to the place of residence are shown in Table 2. Subjects in Smokvica had the highest BMI (27.2 kg/m<sup>2</sup>), subjects from Split had an average BMI of 26.8 kg/m<sup>2</sup>, while the examines from Blato were shown to have the lowest BMI (26.3 kg/m<sup>2</sup>) (P=0.001; Table 2).

There was no statistically significant difference in the waist circumference in the three studied populations (for females P=0.201; for males P=0.288; Table 2), as well as for the neck circumference (for females P=0.458; for males P=0.147; Table 2). In the case of hip circumference, waist-to-hip ratio, brachial circumference and brachial width there was a statistically significant difference in both women and men (Table 2). However, odor

identification performance did not differ between subjects from three studied populations (for females  $P=0.505$ ; for males  $P=0.948$ ; Table 2).

Table 2 Anthropometric characteristics and odor identification of the sample according to the place of residence

|  | Split<br>N=237 | Smokvica<br>N=918 | Blato<br>N=945 | <i>P</i> value |
|--|----------------|-------------------|----------------|----------------|
| BMI (kg/m <sup>2</sup> );<br>median (IQR)          | 26.8 (5.5)     | 27.2 (5.7)        | 26.4 (5.6)     | 0.001          |
| Waist<br>circumference<br>(cm); median<br>(IQR)    |                |                   |                |                |
| Female   | 90.7 (17.1)    | 90.0 (16.3)       | 90.3 (16.0)    | 0.201          |
| Male   | 98.0 (12.2)    | 98.0 (13.0)       | 99.0 (11.5)    | 0.288          |
| Hip<br>circumference<br>(cm); median<br>(IQR)      |                |                   |                |                |
| Female   | 104.3 (11.0)   | 101.0 (10.4)      | 103.0 (10.0)   | <0.001         |
| Male   | 105.0 (7.0)    | 101.5 (10.0)      | 103.0 (10.0)   | <0.001         |
| WHR; mean (SD)                                     |                |                   |                |                |
| Female   | 0.86 (0.07)    | 0.88 (0.08)       | 0.88 (0.08)    | 0.003          |
| Male   | 0.93 (0.07)    | 0.96 (0.07)       | 0.95 (0.07)    | 0.006          |
| Brachial<br>circumference<br>(cm); median<br>(IQR) |                |                   |                |                |
| Female   | 30.6 (4.9)     | 29.5 (4.5)        | 30.0 (4.4)     | <0.001         |
| Male   | 33.0 (4.3)     | 32.0 (4.3)        | 33.0 (4.2)     | <0.001         |
| Brachial width<br>(cm); median<br>(IQR)            |                |                   |                |                |
| Female   | 6.5 (0.6)      | 6.4 (0.7)         | 6.5 (0.5)      | 0.032          |
| Male   | 7.2 (0.6)      | 7.5 (1.1)         | 7.5 (0.6)      | 0.001          |
| Neck<br>circumference<br>(cm); mean (SD)           |                |                   |                |                |
| Female   | 35.0 (3.5)     | 35.0 (4.0)        | 35.0 (4.0)     | 0.458          |
| Male   | 41.0 (4.0)     | 41.0 (4.0)        | 41.0 (4.0)     | 0.147          |
| Correct odor<br>identification;<br>median (IQR)    | 10.0 (2.0)     | 10.0 (3.0)        | 10.0 (3.0)     |                |
| Female   | 10.0 (2.0)     | 10.0 (2.0)        | 10.0 (2.0)     | 0.505          |
| Male   | 10.0 (3.0)     | 9.0 (3.0)         | 9.0 (3.0)      | 0.948          |

IQR – Interquartile range

Table 3 demonstrates the correlation between anthropometric indices and age and correct odor identification using Spearman Rank correlation test. We found a negative correlation between odor identification and age ( $Rho=-0.377$ ,  $P<0.001$ ), age and education ( $Rho= -0.284$ ,  $P<0.001$ ), education and all of the anthropometric indices (Table 3). We found a positive correlation between correct odor identification and education ( $Rho=0.247$ ,  $P<0.001$ ) and material status ( $Rho=0.247$ ,  $P<0.001$ ), while the negative correlation was found between odor identification and waist circumference ( $Rho=-0.210$ ,  $P<0.001$ ), waist-to-hip ratio ( $Rho=-0.305$ ,  $P<0.001$ ), brachial width ( $Rho=-0.174$ ,  $P<0.001$ ) and neck circumference ( $Rho=-0.222$ ,  $P<0.001$ ) (Table 3). Contrary to these findings, all anthropometric characteristics were positively correlated to age (Table 3).

Table 4 shows the correlation between different foods preferences, anthropometric indices and age and correct odor identification. The results indicate a positive correlation between correct odor identification and the liking of bacon ( $Rho=0.070$ ,  $P<0.002$ ), ice-cream ( $Rho=0.079$ ,  $P<0.001$ ), milk chocolate ( $Rho=0.088$ ,  $P<0.001$ ), cakes ( $Rho=0.062$ ,  $P=0.005$ ), sweet foods ( $Rho=0.099$ ,  $P<0.001$ ), salty foods ( $Rho=0.149$ ,  $P<0.001$ ), spicy foods ( $Rho=0.079$ ,  $P<0.001$ ) and vegetables ( $Rho=0.051$ ,  $P=0.021$ ), , whereas all these food preferences were negatively correlated with age (Table 4).

Table 3. Correlation between anthropometric indices and age and odor identification using Spearman Rank correlation test

|                     | Age    | Education | Material status | Alcohol intake | MDSS    | BMI      | Waist circ. | Hip circ. | WHR      | Brachial circ. | Brachial width | Neck circ. | Odor identification |
|---------------------|--------|-----------|-----------------|----------------|---------|----------|-------------|-----------|----------|----------------|----------------|------------|---------------------|
| Age                 | -      | -0.284**  | -0.106**        | 0.059**        | 0.234** | 0.315**  | 0.370**     | 0.138**   | 0.406**  | 0.141**        | 0.209**        | 0.266**    | -0.377**            |
| Education           | <0.001 | -         | 0.315**         | 0.029          | -0.013  | -0.179** | -0.200**    | -0.040    | -0.243** | -0.071**       | -0.079**       | -0.125**   | 0.247**             |
| Material status     | <0.001 | <0.001    | -               | 0.129**        | 0.093** | -0.019   | -0.024      | 0.026     | -0.048*  | 0.055*         | 0.024          | -0.013     | 0.116**             |
| Alcohol intake      | 0.008  | 0.203     | <0.001          | -              | -0.044* | 0.120**  | 0.199**     | 0.033     | 0.273**  | 0.164**        | 0.404**        | 0.388**    | -0.071**            |
| MDSS                | <0.001 | 0.558     | <0.001          | 0.047          | -       | 0.038    | 0.003       | 0.020     | -0.008   | -0.042         | -0.016         | -0.081**   | -0.028              |
| BMI                 | <0.001 | <0.001    | 0.380           | <0.001         | 0.085   | -        | 0.793**     | 0.698**   | 0.515**  | 0.690**        | 0.404**        | 0.589**    | -0.140**            |
| Waist circ.         | <0.001 | <0.001    | 0.270           | <0.001         | 0.908   | <0.001   | -           | 0.686**   | 0.796**  | 0.685**        | 0.538**        | 0.697**    | -0.210**            |
| Hip circ.           | <0.001 | 0.067     | 0.247           | 0.146          | 0.363   | <0.001   | <0.001      | -         | 0.160**  | 0.695**        | 0.314**        | 0.419**    | 0.007               |
| WHR                 | <0.001 | <0.001    | 0.030           | <0.001         | 0.707   | <0.001   | <0.001      | <0.001    | -        | 0.378**        | 0.499**        | 0.636**    | -0.305**            |
| Brachial circ.      | <0.001 | 0.001     | 0.013           | <0.001         | 0.054   | <0.001   | <0.001      | <0.001    | <0.001   | -              | 0.527**        | 0.638**    | -0.041              |
| Brachial width      | <0.001 | 0.009     | 0.421           | <0.001         | 0.599   | <0.001   | <0.001      | <0.001    | <0.001   | <0.001         | -              | 0.729**    | -0.174**            |
| Neck circ.          | <0.001 | <0.001    | 0.565           | <0.001         | <0.001  | <0.001   | <0.001      | <0.001    | <0.001   | <0.001         | <0.001         | -          | -0.222**            |
| Odor identification | <0.001 | <0.001    | <0.001          | 0.001          | 0.199   | <0.001   | <0.001      | 0.764     | <0.001   | 0.059          | <0.001         | <0.001     | -                   |

Rho coefficients of correlation (Spearman Rank correlation test) are presented in the upper right corner, while *P* values are placed in the lower left corner; \*\*Correlation is significant at the 0.01 level (2-tailed); \*Correlation is significant at the 0.05 level (2-tailed)

MDSS – Mediterranean diet serving score; WHR – waist-to-hip ratio

Table 4. Correlation between foods preferences, age and odor identification using Spearman Rank correlation test

|                     | Age    | Educational status | Material status | MDSS   | Bacon  | Pork chops | Broccoli | Ice cream | Milk chocolate | Cakes  | Sweet foods | Salty foods | Bitter foods | Spicy foods | Vegetables | Fruit  | Odor identification |
|---------------------|--------|--------------------|-----------------|--------|--------|------------|----------|-----------|----------------|--------|-------------|-------------|--------------|-------------|------------|--------|---------------------|
| Age                 |        | -0.284             | -0.106          | 0.234  | -0.127 | -0.163     | 0.176    | -0.196    | -0.207         | -0.084 | -0.199      | -0.313      | -0.080       | -0.151      | 0.080      | 0.087  | -0.377              |
| Education           | <0.001 |                    | 0.315           | -0.013 | 0.034  | -0.092     | -0.014   | 0.028     | 0.068          | 0.029  | 0.051       | 0.186       | 0.077        | 0.108       | -0.051     | -0.032 | 0.247               |
| Material status     | <0.001 | <0.001             |                 | 0.093  | -0.001 | -0.041     | 0.052    | <0.001    | 0.004          | 0.009  | 0.024       | 0.059       | 0.077        | 0.057       | 0.039      | 0.047  | 0.116               |
| MDSS                | <0.001 | 0.558              | <0.001          |        | -0.036 | -0.135     | 0.264    | 0.019     | -0.051         | -0.030 | -0.035      | -0.051      | 0.057        | -0.024      | 0.250      | 0.275  | -0.028              |
| Bacon               | <0.001 | 0.133              | 0.963           | 0.103  |        | 0.304      | 0.001    | 0.216     | 0.232          | 0.242  | 0.168       | 0.211       | -0.012       | 0.046       | 0.035      | 0.063  | 0.070               |
| Pork chops          | <0.001 | <0.001             | 0.065           | <0.001 | <0.001 |            | -0.059   | 0.170     | 0.189          | 0.145  | 0.126       | 0.201       | 0.057        | 0.090       | 0.019      | -0.006 | -0.011              |
| Broccoli            | <0.001 | 0.536              | 0.021           | <0.001 | 0.981  | 0.008      |          | 0.098     | 0.012          | 0.056  | 0.040       | 0.001       | 0.091        | 0.065       | 0.421      | 0.331  | 0.006               |
| Ice cream           | <0.001 | 0.215              | 0.992           | 0.402  | <0.001 | <0.001     | <0.001   |           | 0.459          | 0.434  | 0.420       | 0.185       | -0.043       | 0.006       | 0.165      | 0.218  | 0.079               |
| Milk chocolate      | <0.001 | 0.002              | 0.851           | 0.022  | <0.001 | <0.001     | 0.588    | <0.001    |                | 0.482  | 0.482       | 0.194       | -0.037       | -0.004      | 0.092      | 0.131  | 0.088               |
| Cakes               | <0.001 | 0.200              | 0.692           | 0.176  | <0.001 | <0.001     | 0.012    | <0.001    | <0.001         |        | 0.595       | 0.161       | -0.078       | -0.056      | 0.100      | 0.140  | 0.062               |
| Sweet foods         | <0.001 | 0.024              | 0.283           | 0.123  | <0.001 | <0.001     | 0.075    | <0.001    | <0.001         | <0.001 |             | 0.345       | -0.007       | 0.028       | 0.144      | 0.169  | 0.099               |
| Salty foods         | <0.001 | <0.001             | 0.008           | 0.023  | <0.001 | <0.001     | 0.978    | <0.001    | <0.001         | <0.001 | <0.001      |             | 0.237        | 0.310       | 0.080      | 0.020  | 0.149               |
| Bitter foods        | <0.001 | 0.001              | 0.001           | 0.010  | 0.608  | 0.011      | <0.001   | 0.058     | 0.101          | 0.001  | 0.771       | <0.001      |              | 0.486       | 0.067      | 0.035  | 0.043               |
| Spicy foods         | <0.001 | <0.001             | 0.012           | 0.288  | 0.044  | <0.001     | 0.004    | 0.800     | 0.867          | 0.013  | 0.221       | <0.001      | <0.001       |             | -0.013     | -0.040 | 0.079               |
| Vegetables          | <0.001 | 0.023              | 0.084           | <0.001 | 0.120  | 0.384      | <0.001   | <0.001    | <0.001         | <0.001 | <0.001      | <0.001      | 0.003        | 0.571       |            | 0.686  | 0.051               |
| Fruit               | <0.001 | 0.159              | 0.035           | <0.001 | 0.005  | 0.781      | <0.001   | <0.001    | <0.001         | <0.001 | <0.001      | 0.362       | 0.119        | 0.072       | <0.001     |        | 0.040               |
| Odor identification | <0.001 | <0.001             | <0.001          | 0.199  | 0.002  | 0.618      | 0.786    | <0.001    | <0.001         | 0.005  | <0.001      | <0.001      | 0.057        | <0.001      | 0.021      | 0.072  |                     |

Rho coefficients of correlation (Spearman Rank correlation test) are presented in the upper right corner, while *P* values are placed in the lower left corner

In Table 5 we present the anthropometric characteristics and odor identification of the sample according to the age group. We showed that all measured anthropometric indices, namely the BMI, waist circumference, WHR, brachial circumference, neck circumference were statistically significantly different between groups, with a prevailing pattern of increase with the increase of age ( $P < 0.001$  for both women and men; Table 5).

For example, women in the youngest age group had the lowest BMI (BMI=22.2 kg/m<sup>2</sup>) and in the oldest age the BMI was the highest (BMI=28.0 kg/m<sup>2</sup>; Table 5). The youngest men had a BMI of 25.8 kg/m<sup>2</sup>, the middle age group's BMI was 28.2 kg/m<sup>2</sup>, while the oldest age group had a slightly lower weight (BMI=28.1 kg/m<sup>2</sup>; Table 5).

The capability to correctly identify odors had the opposite association with age, as the youngest examinees had the highest median of correctly identified odors in both women and men, which was the smallest in the oldest group of both women and men (Table 5). Also, women had on average better odor identification abilities compared to men in youngest and oldest age group, indicated by the median of correctly identified odors (Table 5).



Table 5. Anthropometric characteristics and odor identification of the sample according to the age group

|   | Younger age<br>(18 – 34,9 years)<br>N=334 | Middle age<br>(35,0 – 64,9 years)<br>N=1221 | Older age<br>(≥65,0 years)<br>N=545 | P value |
|---|---|---|-------------------------------------|---------|
| Gender; n (%)                             |   |   |                                     |         |
| Female                                    | 207 (62,0)                                | 801 (65,6)                                  | 328 (60,2)                          | 0,073   |
| Male                                      | 127 (38,0)                                | 420 (34,4)                                  | 217 (39,8)                          |         |
| BMI (kg/m <sup>2</sup> ); median (IQR)    |   |   |                                     |         |
| Female                                    | 22,2 (4,1)                                | 26,1 (5,5)                                  | 28,0 (5,6)                          | <0,001  |
| Male                                      | 25,8 (5,7)                                | 28,2 (4,5)                                  | 28,1 (4,1)                          | <0,001  |
| Waist circumference (cm); median (IQR)    |   |   |                                     |         |
| Female                                    | 80,2 (13,0)                               | 89,9 (14,5)                                 | 96,0 (13,0)                         | <0,001  |
| Male                                      | 89,5 (14,8)                               | 98,4 (12,0)                                 | 101,0 (10,0)                        | <0,001  |
| Hip circumference (cm); median (IQR)      |   |   |                                     |         |
| Female                                    | 97,0 (9,0)                                | 102,2 (10,0)                                | 104,0 (9,0)                         | <0,001  |
| Male                                      | 101,5 (10,8)                              | 104,0 (10,0)                                | 102,0 (8,4)                         | 0,002   |
| WHR; mean (SD)                            |   |   |                                     |         |
| Female                                    | 0,83 (0,06)                               | 0,87 (0,07)                                 | 0,92 (0,08)                         | <0,001  |
| Male                                      | 0,89 (0,06)                               | 0,96 (0,06)                                 | 0,99 (0,06)                         | <0,001  |
| Brachial circumference (cm); median (IQR) |   |   |                                     |         |
| Female                                    | 27,2 (3,6)                                | 30,0 (4,5)                                  | 31,0 (4,4)                          | <0,001  |
| Male                                      | 32,2 (4,4)                                | 33,0 (4,2)                                  | 31,4 (4,3)                          | <0,001  |
| Brachial width (cm); median (IQR)         |   |   |                                     |         |
| Female                                    | 6,3 (0,5)                                 | 6,5 (0,5)                                   | 6,7 (0,6)                           | <0,001  |
| Male                                      | 7,2 (0,7)                                 | 7,5 (0,6)                                   | 7,5 (0,6)                           | 0,007   |
| Neck circumference (cm); mean (SD)        |   |   |                                     |         |
| Female                                    | 33,0 (2,5)                                | 35,0 (3,5)                                  | 37,0 (4,1)                          | <0,001  |
| Male                                      | 39,0 (3,0)                                | 41,5 (3,5)                                  | 41,0 (3,7)                          | <0,001  |
| Correct odor identification; median (IQR) |   |   |                                     |         |
| Female                                    | 11,0 (1,0)                                | 10,0 (2,0)                                  | 9,0 (3,0)                           | <0,001  |
| Male                                      | 10,0 (2,0)                                | 10,0 (2,0)                                  | 8,0 (3,0)                           | <0,001  |

IQR – Interquartile range

Figure 3 shows the association between age and odor identification in women and men. The abilities to correctly identify 12 odors correctly in women and men is similar in the age between 20 and 50, while around 50 years of age a decreasing pattern can be observed, with the biggest decrease after 65 years of age (Figure 3.)

The association between waist-to-hip ratio with odor identification ability showed a negative association and as WHR increased, the ability to correctly recognize odors decreased

in both men and women (Figure 4). In females with a WHR of 1.0 the average of 9 odors were correctly identified, while for men it was 8 odors (Figure 4).

The association between BMI and odor identification ability in women and men is shown in Figure 5, showing a weak association. It can be seen that women with a BMI < 20 kg/m<sup>2</sup> on average identified more than 10 odors correctly, while men with a BMI < 20 kg/m<sup>2</sup> identified an average of a little less than 10 odors correctly (Figure 5). We found that the higher the BMI the less the ability to correctly identify odors, but when the BMI exceeds 30 kg/m<sup>2</sup>, the curve reaches a plateau point in both women and men (Figure 5).

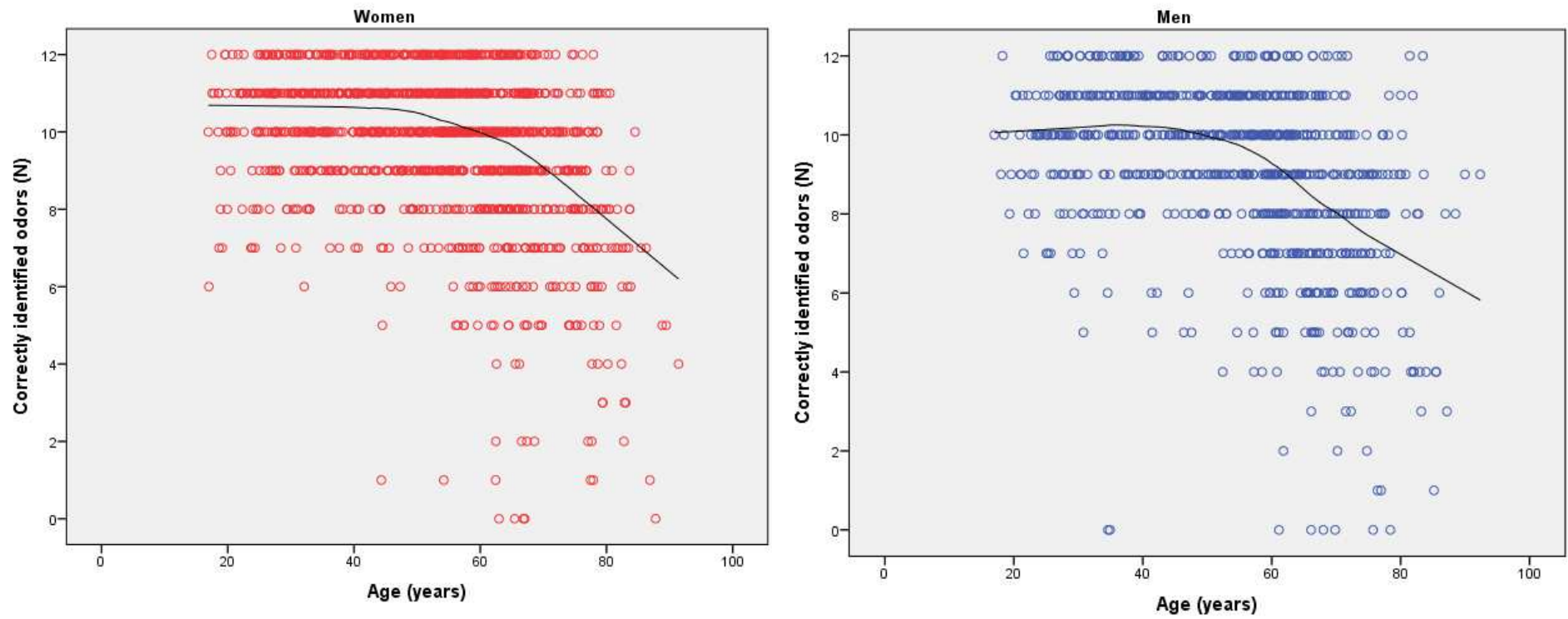


Figure 3. Association between age and odor identification in women and men

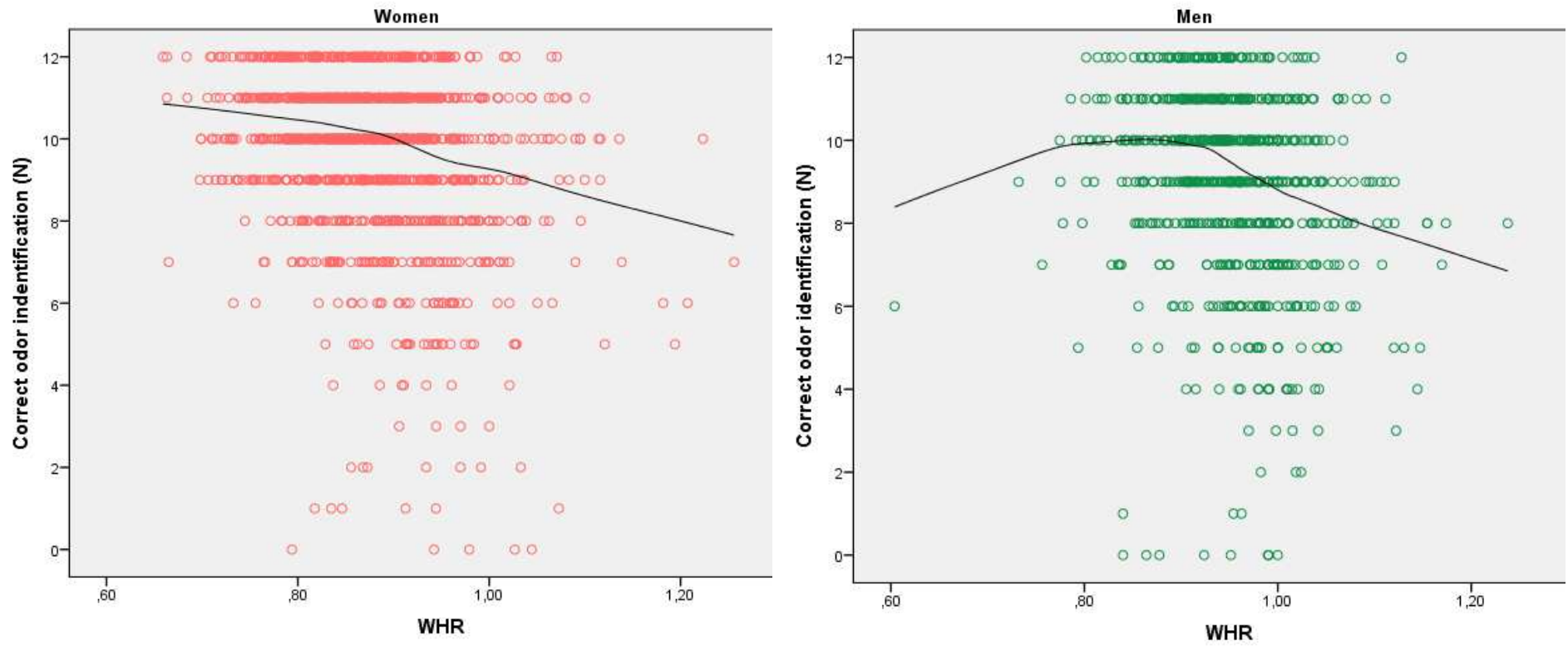


Figure 4. Association between waist-to-hip ratio (WHR) and odor identification in women and men

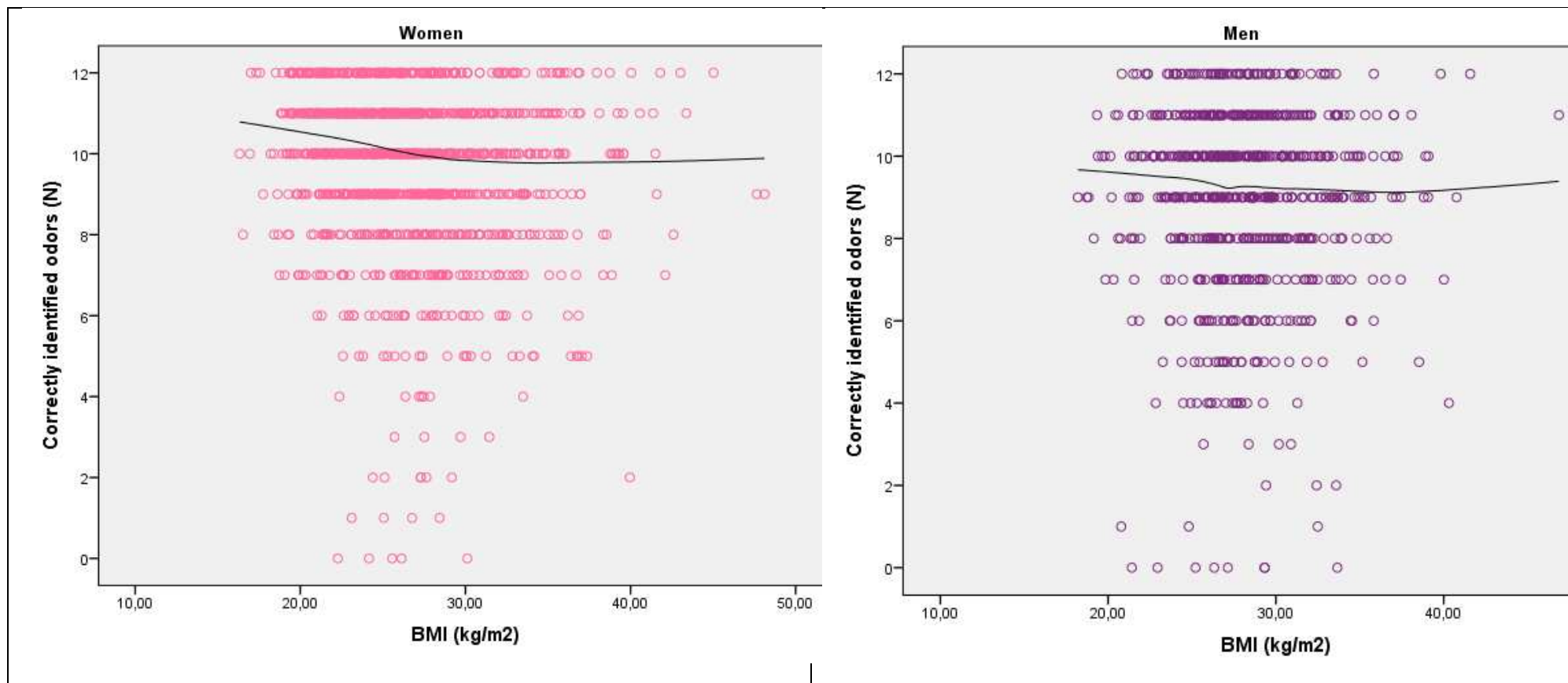


Figure 5. Association between body mass index (BMI) and odor identification in women and men

The results of a binary logistic regression analysis indicated that men had a 3-fold greater probability for having a BMI of  $\geq 30$  kg/m<sup>2</sup> (OR=3.12; 95% CI 2.35-4.15) compared to women. Examinees of older age (OR=1.04; 95% CI 1.03-1.04), better material status (OR=1.07; 95% CI 1.02-1.12) and the presence of one or more chronic diseases were also associated greater probability for having obesity (Table 6). For example, the examinees with a medical history of one chronic disease had a 82% greater probability of having a BMI of  $\geq 30$  kg/m<sup>2</sup> (OR=1.82; 95% CI 1.39-2.36), those with two diseases had 2.2 times greater probability, while examinees with three or more diseases had 2.8 times greater probability of having a BMI of  $\geq 30$  kg/m<sup>2</sup>, compared to examinees without a single chronic disease (Table 6). Smoking was also associated with the odds being obese, in a way that only examinees who used to smoke (ex-smokers) had a greater probability of having a BMI of  $\geq 30$  kg/m<sup>2</sup>, compared to examinees who never smoked (OR=1.50; 95% CI 1.12-2.01) (Table 6). On the other hand, alcohol intake measured in units per week, as well as physical activity level or Mediterranean diet score were not significantly associated with the probability of having a BMI of  $\geq 30$  kg/m<sup>2</sup> (Table 6). The same non-significant association was found for the ability to correctly identify odors and the presence of obesity (OR=1.03; 95% CI 0.97-1.09) (Table 6).

Table 6. Factors associated with BMI  $\geq 30$  kg/m<sup>2</sup> in a binary logistic regression analysis

|                                | OR (95% CI)      | P      |
|--------------------------------|------------------|--------|
| Gender                         |                  | <0.001 |
| Women (referent group)         | 1.000            |        |
| Men                            | 3.12 (2.35-4.15) |        |
| Age                            | 1.04 (1.03-1.04) | <0.001 |
| Education (years of schooling) | 0.92 (0.88-0.96) | <0.001 |
| Material status                | 1.07 (1.02-1.12) | 0.003  |
| Chronic diseases               |                  | <0.001 |
| None (referent group)          |                  |        |
| One                            | 1.82 (1.39-2.39) | <0.001 |
| Two                            | 2.22 (1.53-3.23) | <0.001 |
| Three or more                  | 2.76 (1.67-4.55) | <0.001 |
| Smoking                        |                  | 0.006  |
| Never smoked (referent)        | 1                |        |
| Current smokers                | 0.92 (0.72-1.18) | 0.505  |
| Ex-smokers                     | 1.50 (1.12-2.01) | 0.007  |
| Alcohol intake                 | 0.99 (0.99-1.00) | 0.318  |
| Physical activity              |                  | 0.536  |
| Intensive (referent)           | 1                |        |
| Medium                         | 0.79 (0.50-1.23) | 0.288  |
| Light                          | 0.88 (0.59-1.30) | 0.521  |
| Mediterranean diet score       | 1.00 (0.97-1.03) | 0.991  |
| Correct odor identification    | 1.03 (0.97-1.09) | 0.390  |





The results of the presented study showed a relationship between age and all of the anthropometric indices with olfactory function. In accordance with other studies, olfaction diminished noticeably with age. Besides, a relationship between BMI and olfaction was established. But in a multivariate analysis, while taking into account the influence of age, gender and other possible risk factors, the connection between the ability for correct odor identification and BMI was not statistically significant.

Furthermore, the association between anthropometric characteristics, namely BMI, and age observed in simple correlation, was mediated by age. This makes age a confounding factor in the association between BMI and odor identification abilities in the studied population. Without taking into account of age effect, examines with a BMI > 30 kg/m<sup>2</sup> were found to have a decrease in olfactory function, in both males and females. This type of negative association was found for the odor identification and waist circumference, waist-to-hip ratio, brachial width and neck circumference, all of which were also associated with a higher BMI in the studied population. A study published in 2015 showed, that body weight affects gustatory and olfactory perception in healthy adults and an increasing BMI was associated with a decrease in olfactory and taste sensitivity (37). But, this study performed more extensive olfactory performance testing, measuring odor thresholds, odor discrimination and odor identification and their main result stems from threshold difference, while neither olfactory discrimination or olfactory identification were associated with BMI (37).

Additionally, a study from 2017, presented that chemosensory dysfunction, meaning smell and taste dysfunction, was related with higher serum total cholesterol concentrations among Chinese adults (38). Nevertheless, it is not clear, if obesity influences the loss in olfactory function, or if olfactory function influences obesity.

A difference in smell (and taste) perception between obese and normal weight individuals has already been suggested to cause differences in food choices (2). Interestingly, we found not only the BMI and odor play a role in determining what to eat, also the age correlated strongly with different food preferences. The older examinees were, they expressed lower liking of different foods, e.g. salty foods, bacon, ice cream and milk chocolate. At the same time, the liking of, e.g. bacon and ice cream correlates with the correct odor identification.

As for the results regarding age-related differences in the ability to identify odors, our study revealed the same pattern like previous studies (34,39). We observed an age-related decrease in odor identification in subjects older than 50, and especially older than 65 years of age. Examinees in the age between 20 and 50 showed a similar ability to identify odors.

Previous studies have detected an age-related increase in the olfactory abilities of children (39). Children can detect, discriminate, and respond to odors better and that they can do it from the very beginning of their lives. Young adults and children do not differ much in their ability to identify odors, but in the age of 4-10 years, the abilities to name and recognition and knowledge of the odors are less developed (39). In our study we did not include this age group.

It is important to mention that age is the strongest factor, which has an impact on olfactory decline. Between 65 and 80 years of age about half of the population has significant deficits in the ability to smell (20).

We showed that females performed slightly better on the odor identification scale than males. Previous studies have also shown this phenomenon, alongside that the odor perception is being influenced by the menstrual cycle phase and also by the duration of oral contraception intake (22). Females taking oral contraceptives for a longer time had a better olfactory performance (22), which could be the reason why in our study the females had on average better odor identification abilities compared to men.

Interestingly, we discovered that if examinees' BMI exceeds  $30 \text{ kg/m}^2$ , the odor identification reaches a plateau point in both women and men. This is interesting as earlier studies have differed between the ability of odor identification in moderately obese and morbidly obese subjects, stating that morbidly obese individuals present with a lower olfactory perception (7). Moreover, recent studies discovered that individuals with increasing BMI had a higher preference for flavour-amplified yoghurt suggesting a relationship between BMI and odor perception (30), stating that these obese examinees had a higher odor perception. This issue needs to be further investigated in order to make a suitable conclusion.

A factor not included in our study was the biological control of appetite (40). Biological inputs regulate the appetite and hence also regulate the body weight. Each person has an individual variability in the tendency of becoming obese or losing weight, depending on the biological components of appetite regulation (40). The biology of our body delivers neuroendocrine inputs that affect hunger, satiety, and it determines any changes in our further nutrition (40). Factors that predispose an individual toward a high fat diet can be either inborn or a consequence of not being exposed to healthy foods in early childhood (40). The society should provide and ensure a healthy nutrition in children with consideration of individual variation, which could help in preventing obesity.

The most effective treatment options for patients with severe obesity are bariatric surgery (41). In a study from 2016, patients following Roux-en-Y gastric bypass (RYGB) and

sleeve gastrectomy (SG), the majority of the patients described food dislikes, appetite changes and taste changes (41). Interestingly, alterations in smell were more usual post- RYGB (41%) than post-SG (28%), This shows the link between weight gain and weight loss and alterations in taste and smell sensitivity (41).

Interestingly, reduced subjective taste and smell following GI surgery were first described in normal weight patients as a temporary complication following gastrectomy and oesophagectomy for GI malignancies recommending that these changes are not limited to people with obesity (41).

The limitations of this study include the use of cross-sectional design, in which we cannot distinguish temporal component of causality. Also, only odor identification test was used, which may not be robust enough to find those fine differences of olfactory impairment between people with normal and increased anthropometric indices. The strength of this study was a large sample size and examinees, which were recruited from general population, and not from clinics for whom greater extent of impaired olfaction can be expected.

The results of this study have identified a positive correlation between age and odor identification in bivariate analysis, which was not confirmed in multivariate analysis. Olfactory dysfunction may still contribute to the development of overweight and obesity, but this needs to be studied further.

## **6. Conclusion**

A higher BMI and age were both correlated with olfactory dysfunction. The higher the BMI, the worse the ability for correct odor identification, but only up to a BMI of 30 kg/m<sup>2</sup>. Furthermore, the older examinees were, the higher all of their anthropometric characteristics were, except of their ability of odors identification. But in a multivariate analysis, while taking into account the contribution of age, gender and other possible risk factors, the association between the ability for correct odor identification and BMI was not statistically significant. Future research could investigate this matter further, while measuring olfactory abilities in a more precise and in-depth approach, to be able to answer this research question whether olfactory dysfunction could be a risk factor for obesity development.

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**Title:** The role of olfaction in dietary preferences, composition and anthropometric characteristics in the population of Dalmatia

**Objectives:** To assess the association between the ability to identify odors and anthropometric characteristics, as well as dietary preferences and diet composition in a large population-based sample.

**Materials and Methods:** Examinees from the city of Split, and two settlements on the Island of Korcula (Smokvica and Blato) were included in this cross-sectional study. Anthropometric indices included in the analyses were BMI, waist circumference, waist-to-hip ratio, brachial width and neck circumference. Dietary preferences were assessed for bacon, pork chops, broccoli, ice cream, milk chocolate, cakes, sweet foods, salty foods, bitter foods, spicy foods, vegetables and fruit on a Likert scale. Mediterranean dietary score was calculated to obtain the overall dietary pattern. The statistical analysis was performed using a Chi-square test, Kruskal-Wallis test, ANOVA test, Spearman Rank correlation test, and finally, a multivariate binary logistic regression analysis, where the outcome was a  $BMI \geq 30$  kg/m<sup>2</sup>, and covariates included age, gender, education, material status, chronic diseases, smoking, alcohol intake, physical activity, Mediterranean diet score and odor identification ability.

**Results:** There was a negative correlation between the ability of correct odour identification and age (Rho=-0.377, P<0.001), as well as with BMI (Rho=-0.140, P<0.001), waist circumference (Rho=-0.210, P<0.001), waist-to-hip ratio (Rho=-0.305, P<0.001), brachial width (Rho=-0.174, P<0.001) and neck circumference (Rho=-0.222, P<0.001). Additionally, all anthropometric characteristics were positively and significantly correlated with age. Results indicated a positive correlation between correct odor identification and the liking of bacon (Rho=0.070, P<0.002), ice-cream (Rho=0.079, P<0.001), milk chocolate (Rho=0.088, P<0.001), cakes (Rho=0.062, P=0.005), sweet foods (Rho=0.099, P<0.001), salty foods (Rho=0.149, P<0.001), spicy foods (Rho=0.079, P<0.001) and vegetables (Rho=0.051, P=0.021), whereas all these food preferences were negatively correlated with age. In a logistic regression model the association of obesity and odor identification abilities were attenuated (OR=1.03; 95% CI 0.97-1.09), while only age, gender, education, material status, the presence of chronic diseases and ex-smoking status remained to be associated with obesity.

**Conclusion:** We found that age and all of the anthropometric indices were associated with olfactory function in a bivariate analysis. But, after controlling for confounding factors, namely age and gender, this association for BMI disappeared.



**Naslov:** Uloga osjeta njuha u prehranbenim preferencijama, obrascu prehrane i antropometrijskim osobinama u populaciji Dalmacije

**Ciljevi:** Utvrditi postoji li povezanost između sposobnosti prepoznavanja mirisa i antropometrijskih obilježja, kao i prehranbenih preferencija i sastava prehrane u velikom uzorku iz opće populacije.

**Materijali i metode:** U ovo presječno istraživanje uključeni su ispitanici iz grada Splita te dva naselja na otoku Korčuli (Smokvica i Blato). Antropometrijska obilježja uključivala su indeks tjelesne mase (ITM), opseg struka, omjer opsega struka i kukova, širina lakta i opseg vrata. Prehranbene preferencije su procijenjene za slaninu, svinjetinu, brokule, sladoled, mliječnu čokoladu, kolače, slatku hranu, slanu hranu, goru hranu, začinjenu hranu, povrće i voće koristeći Likertovu ljestvici. Indeks mediteranske prehrane izračunat je kako bi se dobio opći obrazac prehrane. Statistička analiza provedena je korištenjem hi-kvadrat testa, Kruskal-Wallisov testa, ANOVA testa, Spearman Rank korelacijskog testa i binarne logističke regresije, gdje je ishod bio  $BMI \geq 30 \text{ kg/m}^2$ , a kovarijate su uključivale dob, spol, obrazovanje, materijalni status, kronične bolesti, pušenje, unos alkohola, tjelesnu aktivnost, mediteransku prehranu i sposobnost identifikacije mirisa.

**Rezultati:** Pronađena je negativna korelacija između sposobnosti točne identifikacije mirisa i dobi ( $R = -0,377$ ;  $P < 0,001$ ), kao i ITM-a ( $R = -0,140$ ;  $P < 0,001$ ), opsega struka ( $R = -0,210$ ;  $P < 0,001$ ), omjera opsega struka i kukova ( $R = -0,305$ ;  $P < 0,001$ ), širine lakta ( $R = -0,174$ ;  $P < 0,001$ ) i opseg vrata ( $R = -0,222$ ;  $P < 0,001$ ). Osim toga, sve antropometrijske karakteristike pozitivno su i značajno bile povezane s dobi. Rezultati su ukazali na pozitivnu korelaciju između sposobnosti točne identifikacije mirisa i preferencije za slaninu ( $R = 0,070$ ;  $P < 0,002$ ), sladoled ( $R = 0,079$ ;  $P < 0,001$ ), mliječnu čokoladu ( $R = 0,088$ ;  $P < 0,001$ ), kolače ( $R = 0,062$ ;  $P = 0,005$ ), slatku hranu ( $R = 0,099$ ;  $P < 0,001$ ), slanu hranu ( $R = 0,149$ ;  $P < 0,001$ ), ljutu hranu ( $R = 0,079$ ;  $P < 0,001$ ), povrće ( $R = 0,051$ ;  $P = 0,021$ ), dok su sve te preferencije bile negativno povezane s dobi. U multivarijatnom logističkom regresijskom modelu povezanost između sposobnosti točne identifikacije mirisa i pretilosti je atenuirana ( $OR = 1,03$ , 95% CI 0,97-1,09), dok su samo dob, spol, obrazovanje, materijalni status, prisutnost kroničnih bolesti i status bivšeg pušača bili statistički značajno povezan s pretilosti.



**Zaključak:** Utvrđeno je da su dob i sva antropometrijska obilježja ispitanika bili povezani s osjetom mirisa u bivarijatnoj analizi. No, nakon što se isključio učinak varijabli zabune, posebice dobi i spola, ova je povezanost za ITM je nestala.



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