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Doctoral Dissertation

Prevalence of multimorbidity in the Cypriot population and its relationship with Mediterranean Diet and quality of sleep; a cross-sectional study (2018-2019)

Maria Kyprianidou

Limassol, 04/21

Approval Form

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Prevalence of multimorbidity in the Cypriot population and its relationship with Mediterranean Diet and quality of sleep; a cross-sectional study (2018-2019)

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ABSTRACT

Introduction: Multimorbidity is defined as the co-existence of two or more chronic conditions. As life expectancy is increasing so does the prevalence of multimorbidity. Identifying the factors associated with the presence of multimorbidity is important. Furthermore, limited evidence exists on the association of Mediterranean Diet or of quality of sleep with the development of multimorbidity in an individual. The aim of this PhD dissertation work was: a) to estimate the prevalence of multimorbidity in Cyprus and identify the most prevalent diseases; b) to evaluate the level of adherence to the Mediterranean Diet in the adult general population of Cyprus and investigate its relationship with multimorbidity; and c) to assess the quality of sleep in Cyprus and examine its association with multimorbidity.

Methods: This is a cross-sectional study and a stratified sampling procedure was implemented. A representative sample of individuals over 18 years old was surveyed during 2018-2019 in the five government-controlled municipalities of the Republic of Cyprus. Demographic data, dietary information, data on sleep quality, smoking, physical activity, stress, and quality of life, as well as the presence of chronic, clinical, and mental conditions were collected using a validated questionnaire. Diseases were classified according to the International Classification of Diseases, 10th Revision (ICD-10).

Results: The mean age of the n=1140 participants was 41 ± 17 years old, 56% of them were women, 76% lived in an urban area, 54% were married, 64% had completed a higher education, and 50% had a yearly average income in the range €6,500 - €19,500. The age and sex standardized prevalence of multimorbidity was 28.6%. Multimorbidity was associated with age ($p<0.01$), with the highest rate observed among people aged 65 years old or older (68.9%). Multimorbidity was higher in women than men (28.2% vs. 22.5%, $p<0.01$) but similar in urban and rural regions (26.4% vs. 23.8%, $p=0.40$). The most prevalent chronic diseases among people with multimorbidity were hyperlipidemia (44.7%), followed by hypertension (37.5%), gastric reflux (23.9%), and thyroid diseases (22.2%), while the most common combinations of diseases were in the circulatory and endocrine systems. The profile of the multimorbid individual indicated this to be a person at an older age, with a higher BMI, being a current smoker, and having a higher salary. The average Mediterranean Diet score was 15.5 ± 4.0 with men and residents of rural

regions being more adherent to the Mediterranean Diet, compared to women and residents of urban regions, respectively ($p<0.05$). Being in the higher tertile of adherence to the Mediterranean Diet was associated with lower odds of multimorbidity, compared to the lower tertile, and this result was statistically significant even after adjusting for age, sex, smoking habits, and physical activity (adjusted OR=0.68, 95% CI: 0.46, 0.99). The median Pittsburgh Sleep Quality score of the participants was 5 (q1=3, q3=7) with the maximum score being 17. Women, residents of Paphos, and married people had a poorer quality of sleep ($p<0.05$). Having a better quality of sleep was associated with lower odds of multimorbidity, even after adjusting for demographics, socioeconomic and lifestyle factors (adjusted OR=2.21, 95% CI: 1.55, 3.16).

Conclusions: More than one quarter of the general population of Cyprus has multimorbidity, and this rate is almost 70% among the elderly, with multimorbidity being relatively common even in younger ages too. Adherence to the Mediterranean Diet and better quality of sleep were associated with lower risk of multimorbidity. The results of the study underline the need for prevention strategies and health awareness programs for the entire population, including in relation to dietary and sleeping habits. Prevention programs and public health guidelines in Cyprus and elsewhere should take these results into account and public health guidelines should be developed in regards to the importance of adherence to the Mediterranean Diet and good quality of sleep, highlighting their association with multimorbidity. Further research on multimorbidity should be carried out, including in specific subgroups of the population.

Keywords: multimorbidity, Mediterranean Diet, sleep, epidemiology, chronic diseases

ΠΕΡΙΛΗΨΗ

Εισαγωγή: Η πολυνοσηρότητα ορίζεται ως η συνύπαρξη δύο ή περισσότερων χρόνιων ασθενειών. Καθώς το προσδόκιμο ζωής αυξάνεται, το ίδιο ισχύει και για τον επιπολασμό της πολυνοσηρότητας. Ο εντοπισμός των παραγόντων που σχετίζονται είτε με υψηλή είτε με χαμηλή πολυνοσηρότητα στον πληθυσμό είναι σημαντικός. Υπάρχουν περιορισμένες ενδείξεις σχετικά με τη συσχέτιση της Μεσογειακής διατροφής με την ύπαρξη πολυνοσηρότητας σε ένα άτομο. Οι στόχοι αυτής της διδακτορικής διατριβής ήταν: α) να εκτιμηθεί ο επιπολασμός της πολυνοσηρότητας στην Κύπρο και να εντοπιστούν οι πιο συχνές χρόνιες ασθένειες, β) να εξεταστεί η απήχηση της Μεσογειακής διατροφής στον ενήλικο γενικό πληθυσμό της Κύπρου και η σχέση της με την πολυνοσηρότητα, και γ) να υπολογιστεί η ποιότητα του ύπνου στην Κύπρο και να αξιολογηθεί η σχέση της με την πολυνοσηρότητα.

Μέθοδοι: Η μελέτη ήταν συγχρονική και εφαρμόστηκε στρωματοποιημένη δειγματοληψία. Ένα αντιπροσωπευτικό δείγμα ατόμων άνω των 18 ετών ερευνήθηκε κατά την περίοδο 2018-2019 στις πέντε επαρχίες της Κυπριακής Δημοκρατίας που βρίσκονται υπό τον έλεγχο της Κυπριακής κυβέρνησης. Δημογραφικά στοιχεία, πληροφορίες για τη διατροφή, δεδομένα για την ποιότητα του ύπνου, το κάπνισμα και τη σωματική δραστηριότητα, καθώς και η παρουσία χρόνιων, κλινικών και ψυχικών ασθενειών συλλέχθηκαν χρησιμοποιώντας ένα επικυρωμένο ερωτηματολόγιο. Οι ασθένειες ταξινομήθηκαν σύμφωνα με τη διεθνή ταξινόμηση των ασθενειών, 10η αναθεώρηση (ICD-10).

Αποτελέσματα: Η μέση ηλικία των 1140 συμμετεχόντων ήταν 41 ± 17 έτη, 56% από αυτούς ήταν γυναίκες, 76% ήταν κάτοικοι αστικής περιοχής, 54% ήταν παντρεμένοι, 64% είχαν ανώτερη εκπαίδευση και το 50% είχαν ετήσιο μέσο εισόδημα €6,500-€19,500. Ο τυποποιημένος ως προς την ηλικία και το φύλο επιπολασμός της πολυνοσηρότητας ήταν 28.6%. Η πολυνοσηρότητα σχετίζεται με την ηλικία ($p < 0.01$), με το υψηλότερο ποσοστό να παρατηρείται σε άτομα ηλικίας 65 ετών και άνω (68.9%). Η πολυνοσηρότητα ήταν υψηλότερη στις γυναίκες παρά στους άνδρες (28.2% έναντι 22.5%, $p < 0.01$), ενώ τα ποσοστά ήταν παρόμοια στις αστικές και στις αγροτικές περιοχές (26.4% έναντι 23.8%, $p = 0.40$). Οι πιο διαδεδομένες χρόνιες ασθένειες μεταξύ ατόμων με πολυνοσηρότητα ήταν η υπερλιπιδαιμία (44.7%), ακολουθούμενη από υπέρταση

(37.5%), γαστρική παλινδρόμηση (23.9%) και ασθένειες του θυρεοειδούς (22.2%), ενώ οι πιο συνηθισμένοι συνδυασμοί ασθενειών ήταν στο κυκλοφορικό και ενδοκρινολογικό σύστημα. Το προφίλ του ατόμου με πολυνοσηρότητα δείχνει ένα άτομο μεγαλύτερης ηλικίας, με υψηλότερο δείκτη μάζας σώματος, που είναι καπνιστής και έχει υψηλότερο μισθό. Η μέση βαθμολογία της Μεσογειακής Διατροφής ήταν 15.5 ± 4.0 με τους άνδρες και τους κατοίκους των αγροτικών περιοχών να έχουν μεγαλύτερη συμμόρφωση στη Μεσογειακή Διατροφή σε σύγκριση με τις γυναίκες και τους κατοίκους των αστικών περιοχών, αντίστοιχα ($p<0.05$). Το να έχει ένα άτομο μεγαλύτερη συμμόρφωση στη Μεσογειακή Διατροφή σχετίζεται με χαμηλότερες πιθανότητες πολυνοσηρότητας και αυτό το αποτέλεσμα ήταν στατιστικά σημαντικό ακόμη και μετά την προσαρμογή των αποτελεσμάτων για την ηλικία, το φύλο, τις συνήθειες καπνίσματος και τη σωματική δραστηριότητα (OR = 0.68, 95% CI: 0.46, 0.99). Η μέση βαθμολογία ποιότητας ύπνου των συμμετεχόντων ήταν 5 (q1=3, q3=7) με τη μέγιστη βαθμολογία να είναι 17. Οι γυναίκες, οι κάτοικοι της Πάφου και οι παντρεμένοι είχαν χαμηλότερη ποιότητα ύπνου ($p <0.05$). Η καλύτερη ποιότητα ύπνου συσχετίστηκε με χαμηλότερες πιθανότητες πολυνοσηρότητας, ακόμη και μετά την προσαρμογή για δημογραφικούς και κοινωνικοοικονομικούς παράγοντες καθώς και τρόπο ζωής (OR = 2.21, 95% CI: 1.55, 3.16).

Συμπεράσματα: Περισσότερο από το ένα τέταρτο του γενικού πληθυσμού της Κύπρου έχει πολυνοσηρότητα και το ποσοστό αυτό είναι σχεδόν 70% μεταξύ των ατόμων άνω των 65 ετών. Η πολυνοσηρότητα είναι σχετικά συχνή ακόμη και σε νεότερες ηλικίες. Η συμμόρφωση στη Μεσογειακή διατροφή και η καλύτερη ποιότητα του ύπνου σχετίζονται με χαμηλότερο κίνδυνο πολυνοσηρότητας. Τα αποτελέσματα της μελέτης υπογραμμίζουν την ανάγκη για στρατηγικές πρόληψης και προγράμματα ευαισθητοποίησης για την υγεία για ολόκληρο τον πληθυσμό. Προγράμματα πρόληψης και οδηγίες πρακτικής δημόσιας υγείας στην Κύπρο και αλλού θα πρέπει να λάβουν υπόψη τα παραπάνω αποτελέσματα και θα πρέπει να αναπτυχθούν κατευθυντήριες γραμμές για τη δημόσια υγεία υπογραμμίζοντας τη σημασία της τήρησης της Μεσογειακής διατροφής και της καλής ποιότητας του ύπνου και της συσχέτισης τους με την πολυνοσηρότητα.

Λέξεις κλειδιά: πολυνοσηρότητα, Μεσογειακή διατροφή, ύπνος, επιδημιολογία, χρόνιες παθήσεις

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LIST OF ABBREVIATIONS

BMI:	Body Mass Index
CHI2:	Chi-squared test
CI:	Confidence Interval
CNBC:	Cyprus National Bioethics Committee of Cyprus
CVD:	Cardiovascular diseases
EGPRN:	European General Practice Research Network
EQ-5D:	Euro Quality of Life
FFQ:	Food Frequency Questionnaire
GIS:	Geographic Information Systems
IPAQ:	International Physical Activity Questionnaire
MedDietScore:	Mediterranean Diet score
N:	No
OR:	Odds Ratio
PSQI:	Pittsburgh Sleep Quality Index
PSS-14:	Perceived Stress Scale – 14
Q_1:	1st quartile
Q_2:	2nd quartile
Q_3:	3rd quartile
RR:	Relative Risk
SD:	Standard Deviation
VAS:	Visual Analogue Scale
WHO:	World Health Organization
Y:	Yes

1 Chapter 1 - Introduction

1.1 Multimorbidity

During the last decade, there has been an increasing interest in the clinical importance of multimorbidity, which is defined as the co-existence of two or more chronic conditions [1]. More specifically, multimorbidity is described as any combination of a chronic disease with at least one other disease (acute or chronic) or biopsychosocial factor (associated or not) or somatic risk factor [2]. Hence, multimorbidity, or multiple co-morbidity, or multiple chronic conditions, is a term that means co-occurring diseases.

The idea of multimorbidity was first described in 1970 by P. Brandlmeier [3], in an effort to examine all conditions as a whole in an individual [4], in addition to the definition and concept of comorbidity. Since then, there were many terms used to denote comorbidity, such as multimorbidity, morbidity burden, and the medical and social complexity of the patient [5], without, however, meaning the same thing. Comorbidity defines the combination of additional diseases beyond an index disorder [6], which indicates that the main interest is on the index condition and the possible effects of other disorders on the prognosis of that disease. In 2008, the World Health Organization (WHO) defined multimorbidity as "being affected by two or more chronic health conditions" in order to explain the idea of multimorbidity, with the aim to focus on people's overall health status [7,8]. Multimorbidity seemed to be a concept that could function as a driving force for general practice and long-term care [8].

In one of the first reviews that aimed to clarify the definition of multimorbidity, the European General Practice Research Network (EGPRN) found that more than one hundred definitions existed [5], hence, EGPRN outlined the definition and the concept of multimorbidity, which was also supported by a systematic review [9]. According to that description, multimorbidity is defined as any combination of a chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor. In this definition, any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption, and the patient's coping strategies may function as modifiers of the effects of multimorbidity. Three major definitions are used in the literature based on 1) the number (commonly two or three) of concurrent diseases in the same individual, 2) cumulative indices evaluating both number

and severity of the concurrent diseases, and 3) the simultaneous presence of diseases/ symptoms, cognitive and physical functional limitations [10]. The first definition is mostly used in epidemiological studies; the second one is frequently used in clinical studies where the goal is to identify individuals who may benefit from specific interventions; and the third one is used in studies, which consider symptoms, cognitive and physical dysfunctions and psychological problems, in addition to the co-occurrence of the diseases.

Multimorbidity is a relatively common condition which affects 18-30% of adults of all ages [1,11]. Estimates of multimorbidity vary from 10% to over 90% [12,13]. A systematic review found that the prevalence of multimorbidity ranged from 3.5% to 98.5% in primary care setting and 13.1% to 71.8% nationally [14]. This wide variation is partly due to dissimilar definitions, including the number of chronic conditions considered, and the data sources and data collection methods used (for example, self-reported questionnaires, questionnaires with medical history obtained from a health professional, and pharmacy databases to identify different conditions). Apart from these, the variation in the prevalence of multimorbidity could be the result of differences in demographic characteristics, in recruitment methods, and sample sizes. In addition, some studies focused only on specific chronic or mental health diseases, or the presence of two or more chronic diseases from a smaller number of diseases [14]. More specifically, an epidemiologic study in Australia [13] reported that the prevalence of multimorbidity was 37.1% and that this did not differ between sexes and that the most common morbidity combinations were arthritis/ chronic back pain with vascular disease (15.0%), mental health problem with vascular disease (10.6%), and arthritis/ chronic back pain with mental health problem (10.6%). These combinations are consistent with the most prevalent combinations found in another study in the Swiss Sentinel Surveillance Network [15] with the exception of arthritis/ chronic pain combined with mental health problem; instead, this study found that the third most prevalent combination was conditions of the metabolic and endocrine systems.

In another study, the prevalence of multimorbidity in South Asian adults was reported to be only 9.4% and the analysis for different age groups showed that the prevalence in people younger than 60 years old was 10% and in people older than 60 years old it was 37% [16]. Studies in several western countries showed that many people living with chronic diseases have in fact two or more chronic diseases [12]. Similarly, a

large, nationally representative, study in Scotland demonstrated that across 40 chronic conditions, there were more people with multimorbidity than with a single disease [17]. In Southern China, an epidemiologic study [18] found that more than one in ten of the total study population had two or more chronic conditions and that the prevalence of multimorbidity increased with age, which is consistent with reports from other studies as well [19,20]. A cross-sectional study, conducted in a practice-based research network, found that multimorbidity is a prevalent problem in primary care practice [21], a finding with implications for health care delivery and payment, quality assessment, and research. Median prevalence across practices ranged from 35.8% for hypertension to 0.23% for Parkinson disease, with wide variability among practices for all conditions.

Furthermore, in Alberta, a western province of Canada, a cross-sectional survey [22] found that the overall age and sex standardized prevalence of multimorbidity was 19.0%. The authors reported that of those participants with multimorbidity, 70.2% were less than 65 years old, and that the most common combination of chronic conditions was chronic pain and arthritis. Finally, the Swiss Fire project [20], which examined the prevalence of multimorbidity using three different definitions, found that the prevalence estimates were similar under the three different definitions (13%, 14%, and 15%) and that the most prevalent conditions were hypertension, back syndrome, type II diabetes, and degenerative joint disease.

Several factors have been identified as contributing to the multimorbidity burden, including socio-demographic factors, such as age [23–30], gender [18], education [31], and socio-economic status [17,32,33], body mass index (BMI) [32], quality of life [34], physical activity [32], smoking [35], as well as other psychological and environmental factors [14]. The onset of multimorbidity may occur 15-20 years earlier in individuals living in deprived areas as a result of poor quality of life, psychological distress, worsening functional capacity, longer hospital days, and more post-operative complications leading to higher costs of care [36]. In addition, people in deprived areas are at an increased risk for poor health outcomes, such as hospital re-admission, institutionalization, and mortality [37,38]. Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty. Cardiometabolic multimorbidity, which is defined as the co-existence of at least two conditions of diabetes, coronary heart disease, and stroke, has also been shown to be quite common in the general population [36,39]. Metabolic syndrome, which is a term

describing the condition where a combination of diabetes, hypertension, and obesity exists, is associated with the risk of cardiometabolic multimorbidity and multimorbidity in more general.

Furthermore, multimorbidity is quite common in the elderly, among whom the prevalence was estimated to be 60% in some populations [11,14]. However, even in younger ages the prevalence of multimorbidity is relatively high and it has been reported that almost 50% of the people with multimorbidity are in fact younger than 65 years old [17]. Globally, the proportion of people aged 60 years old and older has steadily increased from 8.1% in 1960 to 10% in 2000 [10]. WHO indicates that the average life expectancy has increased from 2000 to 2019 more than 6 years. Specifically, in 2000 the life expectancy was 66.8 years while in 2019 the life expectancy was 73.4 years. As the average life expectancy is increasing worldwide so does multimorbidity since the number of years living with disability due to various chronic conditions, such as angina, arthritis, asthma, chronic back pain, diabetes, oral diseases, hearing problems, tuberculosis, and visual impairments, is also rising [40,41], mainly due to population growth and aging of the population worldwide [40]. Given that chronic illnesses are the leading cause of morbidity worldwide with several diseases being related to aging [14] and the fact that the World Health Organization (WHO) estimates that by 2030 life expectancy will be even higher than today, multimorbidity is emerging as a new global health challenge.

Multimorbidity is associated with reduced quality of life [14] and it can limit access to therapies and operative interventions [42], as well as increase disabilities and mortality [11,32,43]. A systematic review reported that the majority of the studies considered found a significant effect of multimorbidity on disability, quality of life, and health care utilization [10]. On the other hand, multimorbidity increases the risk of hospital admission, the length of stay and readmission, dependency, polypharmacy, and mortality [32,44]. More specifically, multimorbid individuals have a greater need of using multiple medications which is associated with other contrary effects and longer and more regular hospitalization [45,46].

Knowledge of multimorbidity in a given population has important implications for prevention, diagnosis, treatment, and prognosis strategies, as the appropriate management of long-term disorders is a key challenge for health systems internationally. Consequently, identifying the factors associated with the likelihood of multimorbidity is

important. Apart from the factors mentioned before as significant predictors, it is also possible that other factors, such as adherence to the Mediterranean Diet and quality of sleep, may also be connected with the development of multimorbidity in an individual.

1.2 Mediterranean Diet

Dietary habits can affect an individual's health throughout life. A healthy diet is preventive of several non-communicable diseases and conditions [47]. It has been reported that a diet which includes a high consumption of fruits and vegetables, whole grains, and fish [48], and a low consumption of animal fat lowers the risk of obesity and cardiovascular diseases[49], as well as neoplastic diseases [50].

The effect of diet on human health has been the subject of investigation in many epidemiological studies and the Mediterranean Diet is the most extensively studied dietary pattern. In the Mediterranean region, olive oil, which is very important to human health, is the main source of dietary fat [48] and it is usually accompanied by the consumption of large portions of vegetables, in the form of cooked foods or salads (i.e. Greek salad). Wheat, olives, and grapes, as well as their derivatives are also important components of the Mediterranean Diet [48]. Furthermore, for residents of the Mediterranean region, fish consumption is an essential part of their diet [51].

The Mediterranean Diet was first described by Ancel Keys in the 1950s. The Mediterranean dietary pattern is usually presented in the form of a pyramid [52]. At the top of that pyramid, there are the foods which should be consumed rarely and at the base the foods which should be consumed most frequently. The pyramid suggests the appropriate servings for each food category as well and it defines that one serving is approximately equal to one half of the proportions as defined in the Greek market regulations (set to approximately half the quantity served in a Greek restaurant). Thus, one serving is equal to one slice of bread (25 g), 100 g potatoes, half a cup (i.e. 50-60 g) of cooked rice or pasta, a cup of raw leafy vegetables or half a cup of other vegetables, cooked or chopped (i.e. approximately 100 g for most vegetables), one apple (80 g), one banana (60 g), one orange (100 g), 200 g of melon or watermelon, 30 g of grapes, one cup of milk or yogurt, 30 g of cheese, 1 egg, approximately 60 g of cooked lean meat or fish and one cup (i.e. 100 g) of cooked dry beans. So, the Mediterranean Diet pattern includes at the base the daily consumption of non-refined cereals and products, such as whole grain bread, pasta,

rice (8 servings), fruits (4-6 servings), vegetables including wild greens (2-3 servings), daily consumption of oil in cooking as the main added lipid, and nonfat or low fat dairy products, such as milk, cheese, yoghurt (1-2 servings) [48]. In the intermediate positions of the pyramid, there is the weekly consumption of foods, including potatoes (4-5 servings), olives, pulses and nuts (>4 servings), sweets (1-3 servings), eggs (1-3 servings), fish (4-5 servings), and poultry (1-3 servings). At the top, there is the monthly consumption of red meat and meat products (4-5 servings). Apart from the above, the Mediterranean Diet pattern is characterized by a moderate consumption of wine such as 1 to 2 glasses per day, usually accompanying the meals. Furthermore, it promotes the daily physical activity, drinking plenty of water and avoiding salt, replacing it with herbs, including basil, oregano, thyme etc. Hence, the Mediterranean Diet is characterized by a high intake of olive oil, fruit, nuts, vegetables, and cereals, a moderate intake of fish and poultry, a low intake of dairy products, red meat, processed meats, and sweets, and wine in moderation consumed with meals [53].

The relationship of the Mediterranean Diet with human health and particularly cardiovascular diseases (CVD) [54,55], other metabolic morbidities [49], some types of cancer [56], and psychological and neurological disorders [57] has also been examined. Increased levels of obesity, CVD, and diabetes [58] have been observed over the past couple of decades, matched with a transition in dietary patterns, including reduced levels of adherence to the Mediterranean Diet. A randomized clinical trial in Lyon, France [59] assigned the experimental group to a diet similar to the Cretan diet, which includes foods high in α-linolenic acid and olive oil and a low consumption of red meat and dairy products. The control group was assigned to a diet similar to a low fat diet as recommended by the American Heart Association. The authors reported a 70% reduction in the risk of death and of recurrent cardiovascular disease in the participants on the Mediterranean Diet in comparison to the control group, after five years. Moreover, it has been reported that the Mediterranean Diet is protective against cardiovascular disease, coronary heart disease, and stroke [54,55,60–62]. A meta-analysis showed that adherence to the Mediterranean Diet was associated with a reduced risk of metabolic syndrome [63] and the same study also argued for its protective role on the different components of metabolic syndrome, namely waist circumference, high-density lipoprotein cholesterol, triglycerides, systolic and diastolic blood pressure, and glucose. Furthermore, an

epidemiological study in Greece [64] showed that the Mediterranean Diet was associated with a statistically significant reduction in total mortality. Apart from the beneficial effects of the Mediterranean Diet on cardiovascular disease, coronary heart disease, stroke, and metabolic syndrome, Willett WC [65] argued that, together with regular physical activity and not smoking, 90% of Type II diabetes cases could be avoided by healthy food choices that are consistent with the traditional Mediterranean Diet. Another epidemiological study [66] examined the association of Mediterranean Diet with medical multimorbidity and depressive symptoms among elderly participants. The study showed that the Mediterranean Diet was involved in the regulation of physical and mental health of elderly people and suggested that it may contribute to protecting elderly from higher levels of poly-pathology.

In summary, Mediterranean Diet, defined as the traditional dietary pattern found in Mediterranean countries with production of olives, such as Greece, Southern Italy and Spain [67], meets many criteria of a healthy diet [68] and is highly beneficial to any individual.

1.3 Quality of sleep

Sleep is described as "a reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment and is a complex mixture of behavioral as well as physiologic processes" [69]. It is an important part of our existence and postural recumbence, behavioral quiescence, closed eyes, and other indicators are the common components which are usually present during sleep [69].

Poor sleep is a major public health concern and a common medical condition with serious adverse consequences [70]. The recommended duration of sleep is 8.5-9.5 hours for adolescents (10-17 years old) and 7-9 hours for individuals older than 18 years old [70,71]. Sufficient sleep enhances memory [72] and it has been associated with self-rated happiness [73], as well as with good academic performance [72,74]. On the other hand, poor sleep has been shown to affect the endocrine, immune, and nervous systems and increases someone's cardio-metabolic risk as it is associated with obesity, diabetes, impaired glucose tolerance, and hypertension [75,76].

Many studies have demonstrated a high prevalence of sleep disturbances among older adults [77–81] which are associated with different chronic diseases, including heart disease, diabetes, and depression [81–88]. Furthermore, it seems that aging is related with

changes in certain sleep parameters. Specifically, aging decreases the total sleep time and sleep efficiency, the slow wave sleep, and the rapid eye movements sleep and increases the time awake after sleep onset, the number of arousals from sleep, and sleep latency [89]. At the same time, insufficient sleep is common among different age groups [90] and nowadays it seems that younger people too have difficulties with their sleep due to several factors, including shift work, prolonged working hours, irregular sleep schedules [75] and the use of electronics (i.e., mobile phones, tablets etc.). Quality of sleep is affected by sleep disorders, such as insomnia, sleep-disordered breathing, circadian rhythm disorders [75], and obstructive sleep apnoea. Moreover, socioeconomic factors [91–94], physical activity [95] and dietary habits [96,97], pathological factors, as well as psychosocial factors [89], can also affect sleep and they are associated with certain primary sleep disorders.

Some epidemiological studies [98,99] have examined the association between obstructive sleep apnoea and multimorbidity and found that obstructive sleep apnoea is often associated with severe multimorbidity. In addition, epidemiological studies reported associations between insomnia and medical conditions in elderly people [100]. The consequences of sleep quality are quite prevalent, and they take a toll on nearly every key indicator of public health: mortality, morbidity, performance, accidents and injuries, functioning and quality of life, family well-being, and health care utilization.

1.4 Cyprus

The latest survey in 2019 of the Statistical Service of Cyprus, a high-income country in the Eastern Mediterranean, reported that 47.7% of the Cypriot population aged 15 years old and older have one chronic disease which indicates an increase compared to the corresponding percentage in 2014 (42.5%). More specifically, 16.2% of individuals aged 15-24 years old reported having one chronic disease, with the percentage increasing as the age increases. In individuals 25-34 years old the percentage was 22.2%, in those aged 35-44 years old it was 32%, in those aged 45-54 years old 55.4%, in those aged 55-64 years old 76.3%, in those aged 65-74 years old 89.5%, and in those aged 75 years old or older 94.3%.

Moreover, in the latest survey of the Statistical Service of Cyprus it was reported that the prevalence of specific chronic diseases in the last 12 months in Cypriots aged 15 years old and older was as follows: 18.9% for hypertension, 17.6% for hyperlipidemia,

15.3% for back pain chronic diseases, 9.8% for neck chronic diseases, 9.6% for joint diseases (excluding arthritis), 7% for diabetes (excluding gestational diabetes), 5.1% for osteoporosis, 4.7% for depression, and 2.8% for having a heart attack. Among individuals with hypertension, hyperlipidemia, and heart attack, there were more men than women while for back pain chronic diseases, neck chronic diseases, joint diseases, diabetes and depression, there were more women than men. However, there is no data available about individuals who have more than one morbidities.

According to the latest WHO data (2018), the life expectancy at birth in Cyprus is 82.2 years (83.1 years for women and 78.4 years for men), which is among the highest in the EU, giving Cyprus a World Life Expectancy ranking of 28. At the same time, Cyprus has a high prevalence of smoking (39% in men vs. 17% in women) (WHO, 2019) and overweight/ obese people (60% vs. 38% for men and women, respectively) (EUROSTAT, 2014). Hence, the Cypriot population has several characteristics, which could be associated with the occurrence of a number of chronic diseases.

In relation to the Mediterranean Diet, the latest study in Cyprus which investigated the adherence of the Cypriot population to the Mediterranean Diet was in 2005 [101]. The study reported that the adherence to the Mediterranean Diet was higher in the elderly and that more than 90% of the participants in that age group followed the Mediterranean Diet pattern for at least 30-40 years of their life. Apart from this, the latest survey of the Statistical Service of Cyprus in 2019 found that 56.6% of men aged 15 years old and older consumed fruits at least once a day, while the corresponding percentage among women was 63.1%. Regarding the consumption of vegetables, the study reported that 44.6% of men and 51.5% of women consumed vegetables at least once a day. However, there is no updated data about adherence to Mediterranean Diet in the general adult population of Cyprus as well as its association with multimorbidity.

Similarly, there is no data about the Cypriot population's sleep quality. A recent cross-sectional study [102] reported that 50% of men and 18% of women in the general population of Cyprus were in an intermediate to high risk for obstructive sleep apnoea. Nevertheless, there is no information about the overall quality of sleep in the Cypriot population in general, or within different age groups and sexes. In addition, not much is known about the association of quality of sleep and multimorbidity.

1.5 Research gaps

As mentioned above, in Cyprus there is a lack of information about multimorbidity, the relevant risk factors, and the characteristics of individuals with the condition. Moreover, there is no recent data about the adherence to Mediterranean Diet in the general adult population of Cyprus, including in different age groups, males and females, and all the geographical areas of Cyprus, as well as its association with multimorbidity. Finally, there is a gap in research knowledge in terms of the Cypriot population's sleep quality and there is further a lack of evidence of the association of quality of sleep and multimorbidity.

1.6 Aims

The first goal of this dissertation work was to assess the prevalence of multimorbidity in the adult general population of Cyprus and create the profile of the multi-morbid individual. Furthermore, our study aimed to identify the most common diseases and the most frequent combinations of diseases in the Cypriot population. Given the lack of knowledge about the prevalence of multimorbidity in the Cypriot population, this would be important to assess, as individuals with multiple chronic conditions have more health needs, which should be recognized by the health system. As previously mentioned the assessment of multimorbidity prevalence and its related factors in a population has important implications for the prevention, diagnosis, treatment, and public health strategies, hence there is a need for generating relevant data.

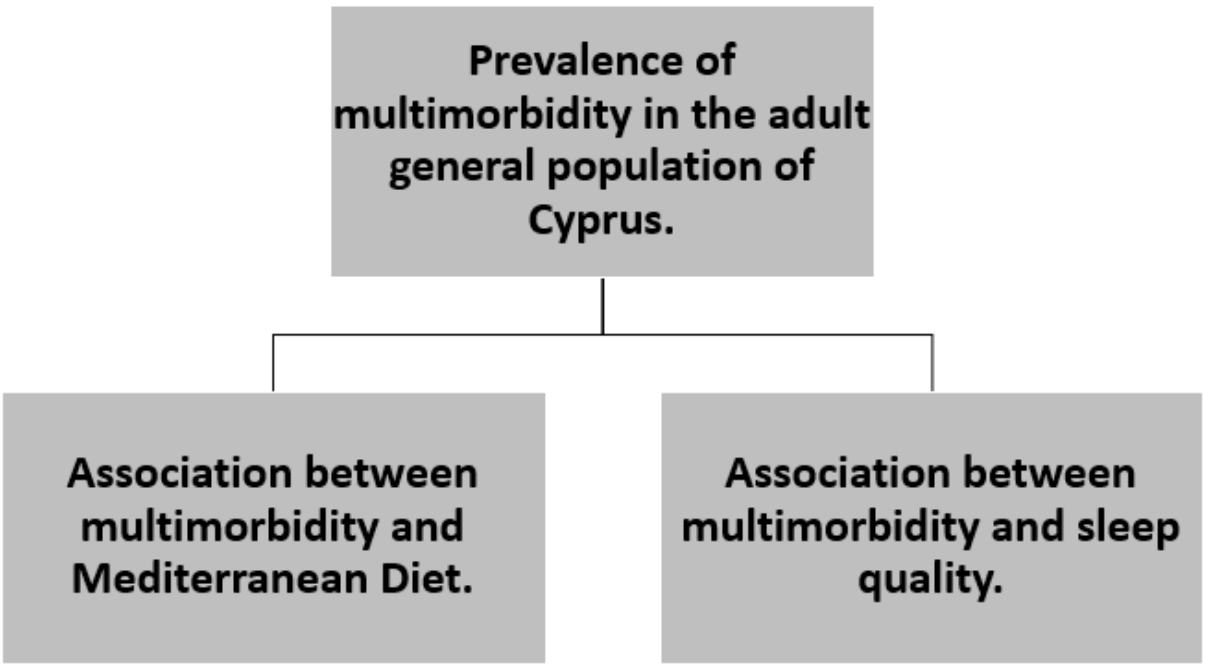
Another goal of the study was to evaluate the association of Mediterranean Diet with multimorbidity as, to the best of our knowledge, this has not been previously examined. The examination of the association of Mediterranean Diet and multimorbidity may have important implications not only in the Cypriot population but elsewhere as well. Hence, the second aim of the dissertation was to examine the adherence of the adult general population of Cyprus to the Mediterranean Diet and assess the relationship between this adherence and multimorbidity. As mentioned in section 1.2, it appears that the level of adherence to the Mediterranean Diet has been reduced over the past couple of decades and there has been a transition in dietary patterns from a more traditional Mediterranean Diet to a more western Diet. Moreover, there is no recent information

about the adherence of the Cypriot population to the Mediterranean Diet and given the fact that the Mediterranean Diet is a healthy diet with many beneficial effects on human health, that knowledge would be important.

Finally, sleep quality influences many key indicators of public health, including morbidity [75]. Given the clinical significance of multimorbidity and the importance of sleep in a specific population, the third objective of the study was to assess the quality of sleep in the adult general population of Cyprus and examine the relationship between quality of sleep and multimorbidity. Some epidemiological studies [98,99] have examined the association between specific sleep disturbances and multimorbidity, however, there is no evidence for the relationship between quality of sleep and multimorbidity. In addition, there is no data about the quality of sleep in the Cypriot population and since quality of sleep plays an important role to every key indicator of public health, that estimation would be important.

The goals of the study are presented in Figure 1.1.

Figure 1.1: Aims of the study.



1.7 Outline

The rationale and the objectives of this work are explained in Chapter 1. Furthermore, Chapter 1 provides some background information on multimorbidity based on a review of the literature, which also includes epidemiologic information about multimorbidity prevalence, Mediterranean Diet, and quality of sleep.

Chapter 2 provides the research methodology of the study, including details about the study design, sample size calculation, setting, sampling and data collection, and ethics approval. It defines the main outcome and the main exposures of interest (Mediterranean Diet and sleep quality) and it outlines other important characteristics of interest. Chapter 2 also includes information about the statistical analysis followed for the calculation of the prevalence of multimorbidity, of the most common chronic diseases and the most common combinations of chronic diseases, the assessment of the adherence to the Mediterranean Diet and its association with multimorbidity, and the assessment of the quality of sleep and its association with multimorbidity.

Chapter 3 focuses on the results of the first aim of this work, which involves the assessment of the prevalence of multimorbidity, of the most common chronic diseases and of the most common combinations of chronic diseases. It describes the participants' characteristics overall, by sex, and by the four age groups of the study, and it reports on the prevalence of multimorbidity, the most common diseases, and the most frequent combinations of diseases in the Cypriot population, as well as on the distribution of multimorbidity.

Chapter 4 provides the results on the assessment of the adherence to the Mediterranean Diet and its association with multimorbidity – the second aim of this dissertation. It describes the adherence of the population to the Mediterranean Diet, it evaluates the association of Mediterranean Diet with multimorbidity, and it further explains how Mediterranean Diet is associated with specific chronic diseases.

Chapter 5 describes the results of the third aim of this work, which is the assessment of the quality of sleep in the Cypriot adult population. It examines how different characteristics are associated with quality of sleep and it addresses the association of quality of sleep with multimorbidity and with particular chronic conditions.

Chapter 6 includes a discussion of the results. It compares the study with other similar studies elsewhere and it outlines the general implications, as well as the impact and significance of the work.

Chapter 7 provides a conclusion, describes the study's major limitations and strengths, and discusses the implications and the future directions.

Finally, an Appendix is provided at the end of the dissertation, which includes additional figures and tables, as well as the different tools and measures used in this study, such as the questionnaire of the study.

2 Chapter 2 - Research Methodology

2.1 Study Design

This was a cross-sectional study. Cross-sectional studies could be used to estimate a population parameter like prevalence of some disease in a community or the average value of some quantitative variable in a population, commonly for the purposes of public health planning. Cross-sectional studies may be also used to examine associations between outcomes and exposures, which may exist, and that information could potentially be used for generating other hypotheses for future research, such as for randomized clinical trials investigating causal relationships among exposures and outcomes. Cross-sectional studies are conducted at a specific point in time, so they can be thought of as a "snapshot" of the outcome of interest and any exposures or risk factors or characteristics associated with it. The data collected in this type of study include characteristics of the study participants, such as demographic information, exposures or risk factors that may be associated with the outcome, as well as information and details about the study outcome.

The aim of our study was to assess the prevalence of multimorbidity in the Cypriot population and several subgroups of the population at a given point in time and evaluate its association with Mediterranean diet and quality of sleep, hence, a cross-sectional study design was considered appropriate.

2.2 Sample size calculation

The sample size needed for the study was calculated using the following formula [103,104]:

$$n = \frac{z^2 \times P(1-P)}{d^2}$$

Where:

n = required sample size

z = value from a standard Normal distribution corresponding to an α level of confidence

P = expected prevalence

d = precision needed

The level of confidence usually aimed for is 95% with most researchers presenting results with a 95% confidence interval (CI), hence the corresponding z used under a 95% CI was 1.96. In addition, we need to know the expected prevalence and this could be estimated from previous studies, if available, or from a smaller pilot study which can be used to calculate the corresponding P [104]. Based on a literature review on the topic, the prevalence of multimorbidity varies between 25%-50%. Moreover, we also conducted a pilot study with a sample of 100 individuals and we found that the prevalence of multimorbidity was 30%. Therefore, we used an expected prevalence prevalence equal to 0.30 for our sample size calculation. Finally, though there are no clear guidelines for choosing an appropriate precision d, some authors recommend selecting a precision of around 5% if the prevalence of the disease is going to be between 10% and 90%, which is also what we used here.

In addition to estimating the prevalence of multimorbidity in the Cypriot population in general, another goal of the study was the estimation of the prevalence of multimorbidity separately for specific age groups given the age distribution of the general population of Cyprus. Based on the literature, we found that the prevalence of multimorbidity varies between 10%-15%, 20%-30%, 30%-65%, and 65%-75% [18,20,21,28,55,104–107] in the four age groups which was used in the study (18-24, 25-44, 45-64, and 65+ years old), respectively. Using the anticipated population proportion table [108] and assuming a prevalence P estimated to within d points with 95% confidence [108] we found that the most appropriate sample sizes for the four different age groups were 138-196, 384-504, 350-380, and 200-243, for 18-24, 25-44, 45-64, and 65+ years old groups of the study, respectively. We used different precisions for each age group given the prevalence in each age group and Cypriot population distribution. Hence, we used a precision of 5% in the age groups 25-44 and 45-64 years old, a precision of 4% in the age group 18-24 years old, and a precision of 6% in the 65 years old and older group. Based on the prevalence in each age group from the pilot study (11% in the 18-24 years old group, 22% in the age group 25-44, 36% in the 45-64 age group, and 70% in the 65+ age group) and the corresponding precisions in each age group we calculated the necessary sample size in each age group separately using the formula $n = \frac{z^2 \times P(1-P)}{d^2}$, with z equal to 1.96.

The resulting sample sizes were 146, 420, 360 and 220 in each of the 18-24, 25-44, 45-64 and 65+ age groups, respectively. Thus, the required total sample size to estimate the prevalence of multimorbidity using a 95% confidence interval (CI) was the sum of the sample sizes of the four age groups which was *n*=1,145.

2.3 Setting

The referent population included all men and women over 18 years old, living in the five government-controlled municipalities of the Republic of Cyprus (Nicosia, Limassol, Larnaca, Paphos, and Ammochostos). Individuals living in nursing homes or those institutionalized were excluded. In order to ensure that data was collected during all seasons of the year, as the questionnaire had elements that could be affected by seasonality, we chose to perform the administration of the questionnaire over a whole year. Data collection took place between May 2018 and June 2019. We collected a similar number of questionnaires each month and since the total sample size of the study was 1145 we collected approximately 95 questionnaires per month.

2.4 Sampling

A stratified sampling procedure, on a feasibility basis, was implemented to ensure that the sample matched the Cypriot population in three key demographic characteristics, namely age, sex, and region. Using the latest census data available for Cyprus (2011), the referent population was divided to the five municipalities of Cyprus, corresponding to the 5 government controlled geographical areas. Then, the population was further divided according to type of residence (urban or rural, as provided by the National Bureau of Statistics), sex (men, women), and age group (18-24, 25-44, 45-64, 65+ years old). The effort was to recruit within the age groups 18-24, 25-44, 45-64 and 65+, for men-women, and urban-rural areas, within each of the 5 municipalities, according to the size of the population.

More specifically, we first obtained the total number of people in each of the 16 subgroups for each geographical area of Cyprus as indicated in ***Table 2.1***. The subgroups were as follows: in urban areas; men 18-24 years old, men 25-44 years old, men 45-64 years old, men 65+ years old, women 18-24 years old, women 25-44 years old, women 45-64 years old, women 65+ years old and similarly in rural areas; men 18-24 years old,

men 25-44 years old, men 45-64 years old, men 65+ years old, women 18-24 years old, women 25-44 years old, women 45-64 years old, women 65+ years old.

Table 2.1: Cypriot population in each of the 16 subgroups of the study based on the census of the Cypriot population in 2011.

Province	**Urban/Rural**	**Sex**	**Age group**			
			18-24	**25-44**	**45-64**	**65+**
Overall	Total	Total	88400	265538	206164	111767
		Men	45364	124926	100404	51689
		Women	43036	140612	105760	60078
	Urban	Total	59486	185320	138940	71848
		Men	30284	86595	66703	32990
		Women	29202	98725	72237	38858
	Rural	Total	28914	80218	67224	39919
		Men	15080	38331	33701	18699
		Women	13834	41087	33523	21220
Nicosia	Total	Total	34518	107809	79108	42897
		Men	17827	50891	37916	19549
		Women	16691	56918	41192	23330
	Urban	Total	24603	80956	58654	31479
		Men	12581	37820	27652	14332
		Women	12022	43136	31002	17147
	Rural	Total	9915	26853	20454	11400
		Men	5246	13071	10264	5217
		Women	4669	13782	10190	6183
Limassol	Total	Total	24746	73482	58199	32180
		Men	12507	34239	28375	14652
		Women	12240	39243	29824	17528
	Urban	Total	19312	57788	44442	22963
		Men	9753	26896	21436	10427
		Women	9567	30892	23006	12536
	Rural	Total	5426	15694	13757	9217
		Men	2753	7343	6939	4225

		Women	2673	8351	6818	4992
Larnaka	Total	Total	15683	44103	34432	18318
		Men	8033	20948	16950	8564
		Women	7650	23155	17482	9754
	Urban	Total	9167	26597	20138	10779
		Men	4709	12414	9780	4950
		Women	4458	14183	10358	5829
	Rural	Total	6516	17506	14294	7539
		Men	3324	8534	7170	3614
		Women	3192	8972	7124	3925
Paphos	Total	Total	8476	25991	22935	12993
		Men	4372	12192	11405	6334
		Women	4104	13799	11530	6659
	Urban	Total	6396	19979	15706	6627
		Men	3241	9465	7835	3281
		Women	3155	10514	7871	3346
	Rural	Total	2080	6012	7229	6366
		Men	1131	2727	3570	3053
		Women	949	3285	3659	3313
Ammochostos	Total	Total	4977	14153	11490	5397
		Men	2625	6656	5758	2590
		Women	2351	7497	5732	2807
	Rural	Total	4977	14153	11490	5397
		Men	2625	6656	5758	2590
		Women	2351	7497	5732	2807

We then computed the corresponding percentages in each of those 16 subgroups (***Table 2.2***) by first dividing the total number of people in each of the age groups of the study with the total Cypriot population (671,869). Then we divided the total number of men and women separately with the total number of each age group to find the corresponding percentages of both sexes in the four age groups of the study. For each province, we divided the total number of individuals in each age group with the overall total number of individuals in each age group. For instance, in order to find the percentage

of individuals aged 18-24 years old overall living in Nicosia, we divided the total number of individuals aged 18-24 years old living in Nicosia (34,518) with the total number of individuals aged 18-24 years old (88,400). In addition, we found the percentages of each age group in urban and rural areas, by diving the total number of individuals of a specific age group living in urban and rural area with the total number of that specific age group. For example, in order to find individuals aged 18-24 years old living in urban area in Nicosia, we divided the total number of individuals aged 18-24 years old living in urban area (24,603) with the total number of individuals aged 18-24 years old (34,518). We performed the same procedure for each age group, sex and region in the five provinces of Cyprus, separately (***Table 2.2***).

This way we calculated the percentage of men/ women in each of the four age groups (18-24, 25-44, 45-64, 65+) in rural and urban areas of each province and after this was done we computed the sample size needed with respect to each age, sex, geographical area, and residency (for example, the sample size for residents aged 18-24 years old of urban regions in Nicosia was $\frac{24603}{671869} \times 1145 = 41$) (***Table 2.3***). Using this stratified random sampling approach, we ensure a representative sample of the entire population with respect to age group, sex, geographical area, and residency.

Table 2.2: Cypriot population (%) in each of the 16 subgroups of the study based on the census of the Cypriot population in 2011.

Province	**Urban/ Rural**	**Sex**	**Age group**			
			18-24	**25-44**	**45-64**	**65+**
Overall	Total	Total[1]	$\frac{88400}{671869}\times 100 = 13$	$\frac{265538}{671869}\times 100 = 39$	$\frac{206164}{671869}\times 100 = 31$	$\frac{111767}{671869}\times 100 = 19$
		Men[2]	$\frac{45364}{88400}\times 100 = 51$	$\frac{124926}{140612}\times 100 = 47$	$\frac{100404}{206164}\times 100 = 49$	$\frac{51689}{111767}\times 100 = 46$
		Women[2]	$\frac{43036}{88400}\times 100 = 49$	$\frac{140612}{140612}\times 100 = 53$	$\frac{105760}{206164}\times 100 = 51$	$\frac{60078}{111767}\times 100 = 54$
	Urban	Total[3]	$\frac{59486}{455594}\times 100 = 13$	$\frac{185320}{455594}\times 100 = 41$	$\frac{138940}{455594}\times 100 = 30$	$\frac{71848}{455594}\times 100 = 16$
		Men[2]	$\frac{30284}{59486}\times 100 = 51$	$\frac{86595}{185320}\times 100 = 47$	$\frac{66703}{138940}\times 100 = 48$	$\frac{32990}{71848}\times 100 = 46$
		Women[2]	$\frac{29202}{59486}\times 100 = 49$	$\frac{98725}{185320}\times 100 = 53$	$\frac{72237}{138940}\times 100 = 52$	$\frac{38858}{71848}\times 100 = 54$
	Rural	Total[4]	$\frac{28914}{216275}\times 100 = 13$	$\frac{80218}{216275}\times 100 = 37$	$\frac{67224}{216275}\times 100 = 31$	$\frac{39919}{216275}\times 100 = 19$
		Men[2]	$\frac{15080}{28914}\times 100 = 52$	$\frac{38331}{80218}\times 100 = 48$	$\frac{33701}{67224}\times 100 = 50$	$\frac{18699}{39919}\times 100 = 47$
		Women[2]	$\frac{13834}{28914}\times 100 = 52$	$\frac{41087}{80218}\times 100 = 48$	$\frac{33523}{67224}\times 100 = 50$	$\frac{21220}{39919}\times 100 = 53$
	Total	Total[5]	$\frac{34518}{88400}\times 100 = 39$	$\frac{107809}{265538}\times 100 = 40$	$\frac{79108}{206164}\times 100 = 38$	$\frac{42897}{111767}\times 100 = 39$

Nicosia		Men[2]	$\frac{17827}{34518}\times 100 = 52$	$\frac{50891}{107809}\times 100 = 47$	$\frac{37916}{79108}\times 100 = 48$	$\frac{19549}{42897}\times 100 = 46$
		Women[2]	$\frac{16691}{34518}\times 100 = 48$	$\frac{56918}{107809}\times 100 = 53$	$\frac{41192}{79108}\times 100 = 52$	$\frac{23330}{42897}\times 100 = 54$
	Urban	Total[6]	$\frac{24603}{34518}\times 100 = 71$	$\frac{80956}{107809}\times 100 = 75$	$\frac{58954}{79108}\times 100 = 74$	$\frac{31479}{42897}\times 100 = 73$
		Men[2]	$\frac{12581}{24603}\times 100 = 51$	$\frac{37820}{80956}\times 100 = 47$	$\frac{27652}{58954}\times 100 = 47$	$\frac{14332}{31479}\times 100 = 46$
		Women[2]	$\frac{12022}{24603}\times 100 = 49$	$\frac{43136}{80956}\times 100 = 53$	$\frac{31002}{58954}\times 100 = 53$	$\frac{17147}{31479}\times 100 = 54$
	Rural	Total[6]	$\frac{9915}{34518}\times 100 = 29$	$\frac{26853}{107809}\times 100 = 25$	$\frac{20454}{79108}\times 100 = 26$	$\frac{11400}{42897}\times 100 = 27$
		Men[2]	$\frac{5246}{9915}\times 100 = 53$	$\frac{13071}{26853}\times 100 = 49$	$\frac{10264}{20454}\times 100 = 50$	$\frac{5217}{11400}\times 100 = 46$
		Women[2]	$\frac{4669}{9915}\times 100 = 47$	$\frac{13782}{26853}\times 100 = 51$	$\frac{10190}{20454}\times 100 = 50$	$\frac{6183}{11400}\times 100 = 54$
	Total	Total[5]	$\frac{24746}{88400}\times 100 = 28$	$\frac{73482}{265538}\times 100 = 28$	$\frac{58199}{206164}\times 100 = 28$	$\frac{32180}{111767}\times 100 = 29$
		Men[2]	$\frac{12507}{24746}\times 100 = 51$	$\frac{34239}{73482}\times 100 = 47$	$\frac{28375}{58199}\times 100 = 49$	$\frac{14652}{32180}\times 100 = 46$
		Women[2]	$\frac{12240}{24746}\times 100 = 49$	$\frac{39243}{73482}\times 100 = 53$	$\frac{29824}{58199}\times 100 = 51$	$\frac{17528}{32180}\times 100 = 54$
		Total[6]	$\frac{19312}{24746}\times 100 = 78$	$\frac{57788}{73482}\times 100 = 79$	$\frac{44442}{58199}\times 100 = 76$	$\frac{22963}{32180}\times 100 = 71$

Limassol	Urban	Men[2]	$\frac{9753}{19312}\times 100 = 50$	$\frac{26896}{57788}\times 100 = 46$	$\frac{21436}{44442}\times 100 = 48$	$\frac{10427}{22963}\times 100 = 45$
		Women[2]	$\frac{9567}{19312}\times 100 = 50$	$\frac{30892}{57788}\times 100 = 54$	$\frac{23006}{44442}\times 100 = 52$	$\frac{12536}{22963}\times 100 = 55$
	Rural	Total[6]	$\frac{5426}{24746}\times 100 = 22$	$\frac{15694}{73482}\times 100 = 21$	$\frac{13757}{58199}\times 100 = 24$	$\frac{9217}{32180}\times 100 = 29$
		Men[2]	$\frac{2753}{5426}\times 100 = 51$	$\frac{7343}{15694}\times 100 = 47$	$\frac{6939}{13757}\times 100 = 50$	$\frac{4225}{9217}\times 100 = 46$
		Women[2]	$\frac{2673}{5426}\times 100 = 49$	$\frac{8351}{15694}\times 100 = 53$	$\frac{6818}{13757}\times 100 = 50$	$\frac{4992}{9217}\times 100 = 54$
Larnaka	Total	Total[5]	$\frac{15683}{88400}\times 100 = 18$	$\frac{44103}{265538}\times 100 = 17$	$\frac{34432}{206164}\times 100 = 17$	$\frac{18318}{111767}\times 100 = 16$
		Men[2]	$\frac{8033}{15683}\times 100 = 51$	$\frac{20948}{44103}\times 100 = 47$	$\frac{16950}{34432}\times 100 = 49$	$\frac{8564}{18318}\times 100 = 47$
		Women[2]	$\frac{7650}{15683}\times 100 = 49$	$\frac{23155}{44103}\times 100 = 53$	$\frac{17482}{34432}\times 100 = 51$	$\frac{9754}{18318}\times 100 = 53$
	Urban	Total[6]	$\frac{9167}{15683}\times 100 = 58$	$\frac{26597}{44103}\times 100 = 60$	$\frac{20138}{34432}\times 100 = 58$	$\frac{10779}{18318}\times 100 = 59$
		Men[2]	$\frac{4709}{9167}\times 100 = 51$	$\frac{12414}{26597}\times 100 = 47$	$\frac{9780}{20138}\times 100 = 49$	$\frac{4950}{10779}\times 100 = 46$
		Women[2]	$\frac{4458}{9167}\times 100 = 49$	$\frac{14183}{26597}\times 100 = 53$	$\frac{10358}{20138}\times 100 = 51$	$\frac{5829}{10779}\times 100 = 54$
	Rural	Total[6]	$\frac{6516}{15683}\times 100 = 42$	$\frac{17506}{44103}\times 100 = 40$	$\frac{14294}{34432}\times 100 = 42$	$\frac{7539}{18318}\times 100 = 41$
		Men[2]	$\frac{3324}{6516}\times 100 = 51$	$\frac{8534}{17506}\times 100 = 49$	$\frac{7170}{14294}\times 100 = 50$	$\frac{3614}{7539}\times 100 = 48$

		Women[2]	$\frac{3192}{6516}\times100=49$	$\frac{8972}{17506}\times100=51$	$\frac{7124}{14294}\times100=50$	$\frac{3925}{7539}\times100=52$
Paphos	Total	Total[5]	$\frac{8476}{88400}\times100=10$	$\frac{25991}{265538}\times100=10$	$\frac{22935}{206164}\times100=11$	$\frac{12993}{111767}\times100=11$
		Men[2]	$\frac{4372}{8476}\times100=51$	$\frac{12192}{25991}\times100=47$	$\frac{11405}{22935}\times100=49$	$\frac{6334}{12993}\times100=47$
		Women[2]	$\frac{4104}{8476}\times100=49$	$\frac{13799}{25991}\times100=53$	$\frac{11530}{22935}\times100=51$	$\frac{6659}{12993}\times100=53$
	Urban	Total[6]	$\frac{6396}{8476}\times100=75$	$\frac{19979}{25991}\times100=77$	$\frac{15706}{22935}\times100=68$	$\frac{6627}{12993}\times100=51$
		Men[2]	$\frac{3241}{6396}\times100=51$	$\frac{9465}{19979}\times100=47$	$\frac{7835}{15706}\times100=49$	$\frac{3281}{6627}\times100=46$
		Women[2]	$\frac{3155}{6396}\times100=49$	$\frac{10514}{19979}\times100=53$	$\frac{7871}{15706}\times100=51$	$\frac{3346}{6627}\times100=54$
	Rural	Total[6]	$\frac{2080}{8476}\times100=25$	$\frac{6012}{25991}\times100=23$	$\frac{7229}{22935}\times100=42$	$\frac{6366}{12993}\times100=49$
		Men[2]	$\frac{1131}{2080}\times100=51$	$\frac{2727}{6012}\times100=49$	$\frac{3570}{7229}\times100=50$	$\frac{3053}{6366}\times100=48$
		Women[2]	$\frac{949}{2080}\times100=49$	$\frac{3285}{6012}\times100=51$	$\frac{3659}{7229}\times100=50$	$\frac{3313}{6366}\times100=52$
	Total	Total[5]	$\frac{4977}{88400}\times100=5$	$\frac{14153}{265538}\times100=5$	$\frac{11490}{206164}\times100=6$	$\frac{5397}{111767}\times100=5$
		Men[2]	$\frac{2625}{4977}\times100=53$	$\frac{6656}{14153}\times100=47$	$\frac{5758}{11490}\times100=50$	$\frac{2590}{5397}\times100=48$
		Women[2]	$\frac{2351}{4977}\times100=47$	$\frac{7497}{14153}\times100=53$	$\frac{5732}{11490}\times100=50$	$\frac{2807}{5397}\times100=52$

Ammochostos						
	Rural	Total[6]	$\frac{4977}{88400}\times 100 = 5$	$\frac{14153}{265538}\times 100 = 5$	$\frac{11490}{206164}\times 100 = 6$	$\frac{5397}{111767}\times 100 = 5$
		Men[2]	$\frac{2625}{4977}\times 100 = 53$	$\frac{6656}{14153}\times 100 = 47$	$\frac{5758}{11490}\times 100 = 50$	$\frac{2590}{5397}\times 100 = 48$
		Women[2]	$\frac{2351}{4977}\times 100 = 47$	$\frac{7497}{14153}\times 100 = 53$	$\frac{5732}{11490}\times 100 = 50$	$\frac{2807}{5397}\times 100 = 52$

[1]Population of each age group divided by the total population of Cyprus (671,869).
[2] Population of each sex divided by the total population of the corresponding age group.
[3]Population of each age group divided by the total population of Cyprus in urban regions (455,594).
[4]Population of each age group divided by the total population of Cyprus in rural regions (216,275).
[5]Population of each age group divided by the total population of the total population in the corresponding age group.
[6]Population of each age group divided by the total population of the total population in the corresponding age group and geographical area.

Table 2.3: Sample size of the study.

Province	Urban/Rural	Sex	Age group			
			18-24	**25-44**	**45-64**	**65+**
Overall	Total	Total	146	420	360	220
		Men	75	198	174	102
		Women	72	222	184	118
	Urban	Total	98	293	243	143
		Men	50	137	116	65
		Women	48	156	127	78
	Rural	Total	48	127	117	77
		Men	25	61	58	36
		Women	23	66	59	41
Nicosia	Total	Total	57	170	138	84
		Men	29	80	66	38
		Women	28	90	72	46
	Urban	Total	41	128	102	62
		Men	21	60	48	28
		Women	20	68	54	34
	Rural	Total	16	42	36	22
		Men	8	21	18	10
		Women	8	21	18	12
Limassol	Total	Total	41	116	102	63
		Men	21	54	50	29
		Women	20	62	52	34
	Urban	Total	32	91	78	45
		Men	16	42	38	20
		Women	16	49	40	25
	Rural	Total	9	25	24	18
		Men	5	12	12	8
		Women	4	13	12	10
Larnaka	Total	Total	26	70	60	36
		Men	13	33	29	17
		Women	13	37	31	19
	Urban	Total	15	42	35	22
		Men	8	20	17	10
		Women	7	22	18	12
	Rural	Total	11	28	25	14
		Men	6	14	12	7
		Women	5	14	13	7
Paphos	Total	Total	14	41	40	27
		Men	7	19	20	13
		Women	7	22	20	14
	Urban	Total	11	32	20	14
		Men	6	15	10	7
		Women	4	17	10	7

	Rural	Total	3	9	20	13
		Men	2	4	10	6
		Women	1	5	10	7
Ammochostos	Total	Total	8	22	20	10
		Men	4	10	10	5
		Women	4	12	10	5
	Rural	Total	8	22	20	10
		Men	4	10	10	5
		Women	4	12	10	5

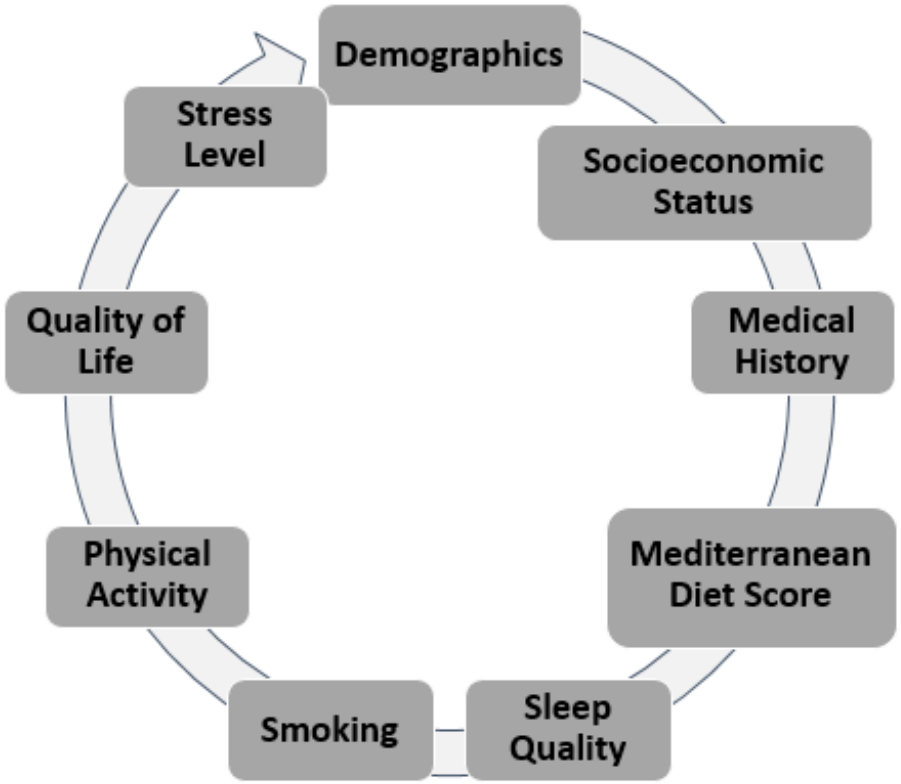
Relevant training was provided to the researchers who would help with the field work, including guidance on the instructions to be given to the participants and possible clarifications that may be needed. The trained researchers, worked in groups of two and approached people in all geographical areas of Cyprus. Recruitment occurred in public places such as kiosks, supermarkets, malls, cafes, restaurants, village squares, busy sidewalks, universities, public services, and in houses throughout urban and rural areas of Cyprus; Nicosia (43% of the total Cypriot population), Limassol (27%), Larnaca (15%), Paphos (10%), and Ammochostos (5%).

To account for potential biases during the enrollment of the participants, the sampling, although on a feasibility basis, was unrestricted by any conventional selection rules or procedures, and an effort was made to be as random as possible. For instance, we chose public places with individuals from all ages (more than 18 years old) in all geographical areas of Cyprus. In addition, we recruited participants at different times during the day, and not for example only in the morning or only in the afternoon, as well as on all days of the week, including weekends. We also tried to collect data from all the urban and rural regions of the five geographical areas of Cyprus in a representative way. Finally, we avoided places where it is expected that there would be more people with chronic diseases, such as restaurants and cafes next to hospitals and nursing homes.

2.5 Data collection

A questionnaire (Appendix) was used to collect data. The questionnaire had different sections, namely sections on personal information, medical history, dietary habits, quality of sleep, smoking and physical activity, as well as on quality of life and stress (***Figure 2.1***).

Figure 2.1: Section of the study questionnaire.



Under the personal information section we collected information on socio-demographic characteristics (i.e., age (in years), sex, residence (province as well as urban/ rural), marital and educational status, and annual income).

The medical history part included a detailed list of 47 chronic diseases or conditions (***Table 2.4***) as well as the option of providing a chronic disease other than those in the list. The 47 diseases or conditions which were included in the study were compiled from the literature and specifically from other epidemiological studies that investigated previously the prevalence of multimorbidity in different populations. The medical history part included also questions applicable only to women regarding previous pregnancies, use of contraceptive pills, menstruation, and menopause.

Table 2.4: The 47 chronic diseases or conditions were included in the study.

Disease	Code	Description
Hyperlipidemia	E78.5	Unspecified, a disorder of lipoprotein metabolism other lipidemias.
Hypertension	I10	Essential (primary) hypertension, high blood pressure, hypertension (arterial) (benign) (essential) (malignant) (primary) (systemic).
Thyroid diseases	E02, E03.8, E03.9, E05.90, E07.9	Subclinical iodine-deficiency hypothyroidism; other specified hypothyroidism; hypothyroidism, unspecified; thyrotoxicosis, unspecified without thyrotoxic crisis or storm; disorder of thyroid, unspecified.
Gastric reflux	K21	Gastro-esophageal reflux disease with esophagitis.
Polycystic ovarian syndrome	E28.2	Polycystic ovarian syndrome, Ovarian dysfunction.
Asthma	J45	Asthma.
Irritating Bowel syndrome	K58	Irritable bowel syndrome, irritable colon, spastic colon.
Depression	F33	Major depressive disorder, recurrent.
Angina	I20.9	Angina pectoris, unspecified.
Atrial fibrillation	I48.91	Unspecified atrial fibrillation.
Chronic hepatitis	K73	Chronic hepatitis, not elsewhere classified.
Cirrhosis	K74.60	Unspecified cirrhosis of liver.
Type 1 diabetes mellitus	E10	Type 1 diabetes mellitus.
Type 2 diabetes mellitus	E11	Hyperosmolar hyperglycemic state.
Crohn's disease	K50	Regional enteritis.
Chronic Bronchitis	J41, J42	Simple and mucopurulent chronic bronchitis, Unspecified chronic bronchitis
Chronic Obstructive Pulmonary Disease	J44.9	Chronic obstructive pulmonary disease, unspecified

Chronic sinusitis	J32	Chronic sinusitis
Inflammatory bowel disease/ chronic enteritis/ ulcerative colitis	K50-K52	Non infective enteritis and colitis.
Heart failure	I50	Heart failure.
Coronary heart disease	I25.1	Atherosclerotic heart diseases of native coronary artery.
Colon cancer	C18.9	Malignant neoplasm of colon, unspecified.
Melanoma	C43	Malignant melanoma of skin.
HIV	B20	Human immunodeficiency virus [HIV] disease.
Lupus	M32.9	Systemic lupus erythematosus, unspecified.
Multiple sclerosis	G35	Multiple sclerosis.
Leukemia	C95.9	Leukemia, unspecified.
Dementia/Alzheimer disease	G30.9, F03	Alzheimer's disease, unspecified, Unspecified dementia.
Parkinson disease	G20	Parkinson's disease.
Epileptic	G40.909	Epilepsy, unspecified, not intractable, without status epilepticus.
Chronic kidney disease	N18.9	Chronic kidney disease, unspecified.
Urinary cancer	C67	Malignant neoplasm of bladder.
Anorexia/Bulimia	F50.0, F50.2	Anorexia nervosa, unspecified, Bulimia nervosa.
Schizophrenia/Bipolar	F20.9, F31.9	Schizophrenia unspecified, bipolar disorder, unspecified.
Erectile dysfunction	N52.9	Unspecified sexual dysfunction not due to a substance or known physiological condition.
Rheumatoid arthritis	MO6.9	Rheumatoid arthritis, unspecified.

Blindness/Low vision	H54.0	Blindness, both eyes.
Glaucoma/Cataract	H40, H25	Glaucoma, Sentile cataract.
Hearing loss/Deafness	H90, H91	Conductive and sensorineural hearing loss, other and unspecified hearing loss.
Cervical cancer	C53.9	Malignant neoplasm of cervix uteri, unspecified.
Ovarian cancer	C56.9	Malignant neoplasm of unspecified ovary.
Prostate cancer	C61	Malignant neoplasm of prostate.
Breast cancer	C50.9	Malignant neoplasm of breast of unspecified site.

The part on dietary habits included a detailed validated [109] semi-quantitative Food Frequency Questionnaire (FFQ). The FFQ can give an adequate assessment of long-term dietary habits in the general population and it has been used extensively, including for nutritional assessment. An important benefit of the FFQ is the ability to include specific local food groups which can be used to substitute other similar traditional foods of other countries, which is the approach we followed here. This allows for comparisons between countries.

Under the quality of sleep section, a validated version [110] of the Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality. Permission to use this questionnaire as developed for Greece (in Greek) was received from the University of Pittsburgh. The PSQI is useful in identifying "good" and "poor" sleepers in different populations and to identify associations between sleep quality and other variables (i.e., age, sex, medical conditions) [110]. The PSQI is a self-reported questionnaire which examines the quality of sleep and the sleep disturbances during a 1-month interval.

The section on smoking and physical activity comprised of questions about current smoking status and physical activity habits (i.e., type of exercise and duration of exercise). The quality of life section included the EQ-5D-3L questionnaire (Greek version). The EQ-5D-3L responses recorded three levels of severity to assess the quality of life of the participant [111]. The Perceived Stress Scale (version PSS-14) [112] was also used for the evaluation of stress levels. Reliability and validity assessments of the translated

stress questionnaire in Greek have been performed before [113], and we obtained permission to use the questionnaire directly from the authors. PSS-14 measures the perceived stress of the respondent and it consists of 14 closed questions. More details about the questionnaire and the information collected are provided in section 2.7.

A pilot study was performed for validation and fine tuning of the questionnaire on about 10% of the total sample of the study. Any necessary modifications were then made on the questionnaire based on this pilot study. For example, we realized that it was helpful to start the questionnaire via a face-to-face interview for the medical history part of the questionnaire rather than having participants completing it by themselves, so as to clarify for a start that only chronic diseases that have been diagnosed by a doctor should be selected. Moreover, participants had several questions about the chronic diseases, so, with the face-to-face interview any clarification needed was provided to the participant right away ensuring the reliability of the responses. We also realized during the pilot study that some of the participants did not understand that for the Food Frequency Questionnaire, the PSQI, and the PSS-14 parts of the questionnaire answers should be given for the last 30 days, hence, the phrase "the last 30 days" was added with capital letters in the corresponding parts of the questionnaire.

After modifying and finalizing the questionnaire, the main part of the data collection started. Urban and rural areas were selected based on the division into rural and urban areas by the Cyprus Agricultural Payments Organization (***Appendix Table 1***).

After explaining to the potential participants the purpose of the study, including the gap in the literature on the prevalence of multimorbidity in Cyprus and its association with potential risk factors, the researchers would point out that the study was approved by the Cyprus National Bioethics Committee (CNBC) (ΕΕΒΚ ΕΠ 2018.01.123) and that their participation would be anonymous as well as that they could stop participating at any time they wanted to. The researchers would then ask for the participants' consent to participate (verbal) and then they would give them the questionnaire of the study for completion. All the details above were also included in the first page of the questionnaire. The researchers would also explain to the study participants that the questionnaire is self-reported except the medical history part, which would be performed with a face-to-face interview.

The final dataset was recorded in Excel on a password protected laptop which was stored in the building of the Cyprus International Institute for Environmental and Public Health at Cyprus University of Technology with the only persons having access to it being the supervisor of the study Dr. Costas Christophi (Associate Professor of Biostatistics and Epidemiology) and the PhD candidate, Maria Kyprianidou.

2.6 Ethics approval

This study was conducted according to the Declaration of Helsinki guidelines and all procedures involving research study participants were approved by the Cyprus National Bioethics Committee (CNBC) (ΕΕΒΚ ΕΠ 2018.01.123) (***Appendix***). The application submitted to the CNBC outlined the study objectives and outcomes, the data collection process and data management, the use of the data, and the expected benefits. The questionnaire of the study was also submitted with the application to the CNBC.

2.7 Participants' characteristics

2.7.1 Main outcome

The medical history of the participants included the presence, as diagnosed by a physician, of chronic conditions. Diseases were coded according to the International Classification of Diseases, 10th Revision (ICD-10). The medical history considered 47 chronic diseases of all circulatory, digestive/excretory, endocrine, immune, nervous, renal/ urinary, reproductive, respiratory, and skeletal/ muscular systems, as well as neoplasms. Specifically, the categorization of the chronic diseases in human systems was as follows:

- Circulatory system: Hypertension (I10), Hyperlipidemia (E78.5), Angina (I20.9), Coronary Heart Disease (I25.1), Atrial fibrillation (I48.91), Heart failure (I50)
- Digestive/excretory system: Inflammatory bowel disease/chronic enteritis/ulcerative colitis (K50-K52), Irritating Bowel syndrome (K58), Gastric reflux (K21), Crohn's disease (K50), Chronic hepatitis (K73), Cirrhosis (K74.60)
- Endocrine system: Type 1 diabetes mellitus (E10), Type 2 diabetes mellitus (E11), Thyroid diseases (E02, E03.8, E03.9, E05.90, E07.9), Polycystic ovarian syndrome (E28.2)

- Immune system: HIV (B20), Lupus (M32.9), Multiple sclerosis (G35), Leukemia (C95.9), Anemia (D64.9)
- Nervous system: Dementia/Alzheimer disease (G30.9, F03), Depression (F33), Anorexia/Bulimia (F50.0, F50.2), Schizophrenia/Bipolar (F20.9, F31.9), Parkinson disease (G20), Epileptic (G40.909), Blindness/Low vision (H54.0), Glaucoma/Cataract (H40, H25), Hearing loss/Deafness (H90, H91)
- Renal/urinary system: Chronic kidney disease (N18.9)
- Reproductive system: Erectile dysfunction (N52.9)
- Respiratory system: Chronic Bronchitis (J41, J42), Chronic Obstructive Pulmonary Disease (J44.9), Asthma (J45), Chronic sinusitis (J32)
- Skeletal/muscular system: Rheumatoid arthritis (M06.9)
- Neoplasms: Colon cancer (C18.9), Melanoma (C43), Urinary cancer (C67), Cervical cancer (C53.9), Ovarian cancer (C56.9), Prostate cancer (C61), Breast cancer (C50.9)

The question used to obtain the medical history of the participants was: "Have you ever been diagnosed by a physician with any of the following chronic diseases? Choose all that apply". Multimorbidity was defined as the concurrent presence of two or more chronic conditions in an individual. The no multimorbidity group included participants with no disease or with only one disease reported.

2.7.2 Main exposures of interest

2.7.2.1 Mediterranean diet score

The dietary assessment was based on a validated semi-quantitative Food Frequency Questionnaire (FFQ) [47]. The questionnaire contained extensive information on the dietary habits of the participants and it included the consumption of 11 food groups: non-refined cereals (i.e. whole grain dread, rice cereals), fruits (i.e. banana, summer and winter fruits), vegetables (i.e. tomatoes, cucumbers), legumes, potatoes, fish (i.e. small and big fish), red meat and processed meats (i.e. beef, pork, chicken, sausages), poultry, full fat dairy products (i.e. milk/yoghurt, cheese), as well as olive oil and alcohol intake. Apart from these, the food frequency questionnaire included questions about the consumption of olives, mayonnaise, sunflower, margarine, butter, and organic products. In addition, there were questions about fast-food consumption, if participants eat breakfast or snacks, number of meals, and food supplements consumption (i.e. vitamins).

Adherence to the Mediterranean diet was evaluated on the basis of the MedDietScore [48] which has a range of 0 - 55, with higher values indicating greater adherence to the Mediterranean diet. For the consumption of items presumed to be close to this pattern, scores were assigned as 0, 1, 2, 3, 4, and 5 when a participant reported no consumption, never/ rarely, 1-3 times/month, 1-2 times/week, 3-6 times/week, 1 time/day, and more than 2 times/day, respectively. For the consumption of foods presumed to be away from this pattern, scores were assigned in the reverse order. The sum of the individual scores on the 11 food items considered provides the final MedDietScore.

2.7.2.2 Sleep quality assessment

Several questionnaires that assess sleep quality exist. Firstly, there are some post-sleep questionnaires which may reflect more accurately the night-to-night variations that occur in sleep quality, but they do not provide information about the frequency or duration of sleep problems. Secondly, there are some survey-type questionnaires which, however, may not provide information on the severity of a problem at the present time. In our study, we used the Pittsburgh Sleep Quality Index (PSQI) which was developed in order to provide a brief, clinically useful assessment of a variety of sleep disturbances that may affect sleep quality, and to provide a reliable, valid, and standardized measure of sleep quality, to distinguish "good" and "poor" sleepers, while providing an index that is easy for participants to use and for clinicians and researchers to interpret. The PSQI assesses sleep quality during the previous month which is somewhere in the middle between post-sleep and survey-type questionnaires. This is something that has the advantage that duration of 2-3 weeks is often used clinically to differentiate transient from persistent sleep-wake disorders (Consensus Conference on Insomnia, 1984).

We used the PSQI for Greece version which was kindly provided by the University of Pittsburgh. The PSQI consists of 19 self-rated questions and an additional five questions that are rated by the bed-partner or roommate, which are used for clinical information only and are not tabulated in the calculation of the PSQI score. The 19 self-rated questions assess a wide variety of factors relating to sleep quality, including estimates of sleep duration and latency, and of the frequency and severity of specific sleep-related problems. These 19 items are grouped into seven component scores, each weighted equally on a 0-3 scale. These components include subjective sleep quality, sleep

latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction. The seven component scores are then summed to yield a global PSQI score, which has a maximum score of 21, with higher scores indicating worse sleep quality.

2.7.2.3 Other covariates

The first part of the questionnaire collected information on demographic and socio-economic characteristics of the participants. Age, weight, and height were provided in years, in kilograms, and in meters, respectively. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters squared). Obesity was defined as BMI >29.9 kg/m^2, overweight as BMI 25-29.9 kg/m^2, normal as BMI 18.5-24.9 kg/m^2, and underweight as BMI <18.5 kg/m^2, according to the WHO classification. Sex was recorded as men or women. The province was categorized in one of the five geographical areas of Cyprus (Nicosia, Limassol, Larnaka, Paphos, and Ammochostos) and residency was recorded as urban or rural. Marital status was provided as never married, married/ engaged, or separated/ divorced/ widowed. There was also a question about having children or not and if the answer was affirmative then participants had to provide the number of children they have. Education level was classified in three categories, as commonly used in Cyprus, and similar to a study on the Greek population [114], namely: (i) primary education (participants who completed only primary school, i.e. <7 years of schooling); (ii) secondary education (participants who completed middle or high school, i.e. 7-12 years of schooling); (iii) higher education (participants who have a university degree, i.e. >12 years of schooling). Job status was collected in one of 9 available categories: private employee, state employee, farmer, student, unemployed, retired, freelance, housewife, or something else which had to be provided. Financial status was classified based on the annual income as: (i) low (≤ €6,500); (ii) moderate (€6,500 - 19,500); and (iii) high (> €19,500).

Apart from the 47 chronic diseases which were included in the medical history, there were an additional four questions specifically for women. These questions asked whether the participant was pregnant or not, the age of the first menstruation and of menopause in years, and a question about the use of contraceptive pills for which if the answer was yes then the participant had to provide the number of years using contraceptives pills.

In the dietary habits section, apart from the Food Frequency Questionnaire, there was another question about the use of dietary supplements. Specifically, dietary supplements was assessed in three categories: vitamins, proteins, and creatine. If the participants wished to provide something else there was also the option 'Other'.

The next part of the questionnaire included the lifestyle habits of the participants. Current smokers were defined as those who smoked whereas not current smokers included both never and former smokers. We also asked the participants to provide the age at which they started smoking and in the case of past smokers the time they quit smoking. For the evaluation of physical activity, the International Physical Activity Questionnaire (IPAQ) was used as an index of weekly energy expenditure using frequency (times per week), duration (in minutes per time), and intensity of sports or other habits related to physical activity (in expended calories per time). Physical activity was defined as leisure-time activity of a certain intensity and duration, at least once/week during the past year, including "light" (expended calories < 4 Kcal/ min), "moderate" (expended calories 4-7 Kcal/ min), or "vigorous" (expended calories >7 Kcal/ min).

In order to assess quality of life, we used the EQ-5D questionnaire which has five dimensions (mobility, self-care, usual activities, pain/ discomfort, anxiety/ depression), each with three response levels (no problems=1, moderate=2, severe problems=3) (EQ-5D-3L) [115]. The EQ-5D-3L produces a 5-digit health profile which presents the level of reported problems on each of the threedimensions of health, for example 12211. Then, the 5-digit health profile is converted into a single summary number, namely the index value [116]. The maximum score of 1 indicates the best health state. In addition, there was a visual analogue scale (VAS) provided for the participant to indicate his/ her own general health status assessment with 100 indicating the best health status.

Furthermore, we used the Greek version of PSS-14 [117] to estimate the levels of perceived stress, which consists of seven negative and seven positive items (***Appendix Table 2***), each with a possible answer rated on a five-point scale (from 0=never to 4=very often). The highest possible score is 56, since positive questions were rated from 4 to 0 and negative questions were rated in the reverse order. The positive elements evaluate the ability to cope with perceived stressors, whereas the negative ones focus on assessing lack of control as well as negative emotions and reactions. Scores ranging from 0-13, 14-26, and 27-40 are considered low, moderate, and high perceived stress, respectively.

2.8 Statistical analysis

2.8.1 Descriptive analysis

The distributions of continuous variables were assessed for normality using the Shapiro-Wilk test, which indicates if a random sample comes from a normal distribution. The test gives a value for a statistics (W) and small values of W indicate that the sample is not normally distributed. In addition, normality was assessed using histograms and normal probability plots (i.e., QQ plots). Continuous variables with normal distribution (such as age, weight, height, BMI, and quality of life score) were presented as mean ± standard deviation (SD) while continuous variables with skewed distributions (such as Mediterranean diet score and Quality of sleep score) were presented as median (1^{st} quartile, 3^{rd} quartile). Categorical variables (such as age group, sex, geographical area, residency, marital status, educational status, salary category, physical activity level, smoking, obesity group, and quality of sleep levels) were provided as absolute and relative (%) frequencies. The distribution of continuous variables were shown as box plots and of categorical variables as bar charts. A box plot is a graphical method of representing continuous data through their quartiles while a bar chart presents categorical data using rectangular bars with heights proportional to the values that they represent.

Student's t-tests and Kolmogorov-Smirnov tests were used for the comparison of continuous characteristics with normal distributions and with skewed distributions, respectively, between men and women. Specifically, the student's t-test is a parametric statistic which is used to determine if there is a significant difference between the means between two groups of a categorical variable while the Kolmogorov-Smirnov test is a non-parametric alternative for when the underlying distributions are not normally distributed.

The Pearson's chi-squared test of independence was applied to evaluate potential associations between sex and other categorical characteristics (i.e. age groups (18-25, 25-44, 45-64, 65+ years old), geographical area, residency, marital status, educational level, physical activity, type of exercise, hours of exercising, BMI categories, and perceived score categories). The chi-squared test was further applied to evaluate if there was any association between any of the categorical characteristics and multimorbidity groups (yes/ no). Similarly, the student's t-test and the Kolmogorov-Smirnov test were used to

examine if there was any difference between multimorbidity groups in any of the continuous characteristics considered. The student's t-test was used for normally distributed variables while Kolmogorov-Smirnov test was used for non-normally distributed variables.

2.8.2 Prevalence of multimorbidity, of the most common chronic diseases, and of the most common combinations of chronic diseases

We assessed the prevalence of multimorbidity in the general population of Cyprus using age and sex standardized values. Specifically, we estimated the standardized prevalence using the formula $\frac{\sum E_i}{\sum P_i}$ where E_i is the expected number of cases in each age and sex subgroup i (calculated as the product of the crude rate and the size of the population in i which were provided by the Statistical Service of the Republic of Cyprus) and P_i is the number of people in the population in subgroup i. We computed the confidence intervals using the formula $\hat{p} \pm Z_{\alpha/2} \times \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$.

Cyprus is characterized by several geographical disparities in the health care system distribution, in terms of the number of hospitals, health centers (***Appendix Table 2***), physicians' offices, and practicing physicians (***Appendix Table 3***). In order to assess the spatial distribution of multimorbidities in the general population of Cyprus, the parameter of spatial heterogeneity was accounted for and the analysis was based on the districts of Cyprus (Nicosia-the capital area- with total population 332,200; Limassol, 239,400; Larnaca, 144,900; Paphos, 91,300, and Ammochostos, 47,000). Spatial analysis included any of the formal techniques which studies objects using their topological or geographic properties. Geographic Information Systems (GIS) is a geospatial technology with a significant role in area-based epidemiological analysis [118–124]. GIS conduce to mapping and creating of data visualizations, by combining both statistical and geographic data [124]. The data was the spatial layer of districts of Cyprus (polygon entities). All datasets, including the series of statistical data tables and the spatial layer of Cyprus districts, were stored in a common geodatabase [124,125] in GIS environment. A series of GIS-supported procedures were implemented to geocode and aggregate all data by spatial unit (district). Specifically, each district was characterized by a unique code. The code of each district

(polygon entity) was recorded in the corresponding entry of each table that was referred to the specific district. Based on the district code field, all the tables were joined to the districts' spatial layer. As a result, each polygon entity (spatial unit) was attributed with the corresponding statistical data and variables' values. Cyprus districts are spatial units represented by polygons (polygon entities) in the maps. All variables were mapped [126,127] and a series of choropleth maps was created that illustrates the adherence to the Mediterranean diet and multi-morbidities across the districts of Cyprus. Geodatabase, spatial analysis, and mapping were performed using the ArcGIS version 10.4 (ESRI Inc., Redlands, California, USA) and QGIS version 3.10 (ArcGIS: https://desktop.arcgis.com/en/arcmap/, QGIS: https://www.qgis.org/en/site/).

The Student's t-test was used for the comparison of normally distributed variables between the multimorbidity and not multimorbidity groups while for non-normally distributed variables, the Kolmogorov-Smirnov test was used instead. We used box plots to present the distribution of co-morbidities overall and by demographic, socioeconomic and lifestyle characteristics. A categorical variable for multimorbidity level was created in four levels for 0-1, 2, 3, and more than 3 morbidities. Pie charts were also used for presenting the socio-economic characteristics by multimorbidity level. Pie charts are circular statistical graphics which present categorical variables by dividing into slices the categories of the variable to produce a visual of the different groups and the different proportions.

Furthermore, the analysis of variance (ANOVA) technique was used for the comparison of normally distributed variables among multimorbidity levels (0 or 1, 2, 3, and more than 3 morbidities groups) while for non-normally distributed variables, the Kruskal-Wallis test was used instead. ANOVA is a statistical test which evaluates if three or more population means are equal while Kruskal-Wallis test is the non-parametric alternative to the ANOVA test. The Pearson's chi-square test of independence was applied to evaluate if there was any association between any of the categorical characteristics and multimorbidity level groups.

The crude prevalence of all the chronic diseases included in the study are presented as absolute and relative (%) frequencies, by sex and by the four age groups considered. The number of co-morbidities was presented separately in men and women. We used student's t-test to evaluate if the average number of co-morbidities in an individual differs between men and women. The chi-squared test was applied to evaluate if there was any

difference in the distribution of any of the chronic diseases between men and women as well as among the different age groups. Pie charts of the prevalence of the most chronic diseases among multimorbidity and no multimorbidity groups were also drawn.

Radar graph was constructed to present the most commonly occurring combinations of chronic conditions. More specifically, a radar graph is a graphical method of presenting multivariate data in a way of comparing multiple quantitative variables. The graph is very useful for identifying which variables have similar values amongst each variable. In our case we have an eleven-dimensional chart as the number of combinations of human systems was eleven. The radar graph is also known as web chart, spider chart, star chart, irregular polygon, polar chart, or Kiviat diagram, and it is similar to a parallel coordinates plot with the axes arranged radially. Moreover, a bubble graph was constructed to represent the most common combinations of chronic diseases. A bubble graph is another type of a graphical method of representing multivariate data using multiple bubbles in a two-dimensional plot. It is a generalization of the scatter plot, replacing the dots with bubbles, and it is very useful for comparing the associations between data objects in three-numeric-datadimensions, namely, the X-axis data, the Y-axis data, and its size, with larger bubbles indicating larger values.

In addition, discriminant classification analysis, with the calculation of the Wilk's lambda and the Fisher's classification function coefficients, was used to explore the patterns of characteristics of people with multimorbidity. A value of the Wilk's lambda close to 1, indicates better discriminating ability, i.e. that the estimated model has the ability to classify people in the different classes of the outcome (multimorbidity) efficiently. Discriminant analysis is a statistical method which is commonly used to evaluate the association between an outcome and one or more predictors where the outcome is a categorical variable with at least two categories and these categories are mutually exclusive. It is a useful tool when the aim is to predict the group or the category to which an individual or a subject belongs. Our goal here was to identify the characteristics of the individuals who belong in the three multimorbidity groups (2, 3, and more than 3 morbidities) compared to those who belong to the group with 0 or 1 morbidities.

Mixed effects multinomial regression was performed to evaluate the significance of different factors (marital status, educational level, salary categories, physical activity,

smoking, and BMI) on the level of multimorbidity, after accounting for age and sex, within the various sampling regions. Mixed effects multinomial regression models is used for analysis of nominal or ordinal response data [128]. One of the advantages of the technique is the flexibility in the choice of differences used to represent comparisons across the response categories. Maximum marginal likelihood (MML) is used to estimate the corresponding coefficients by using quadrature to numerically integrate over the distribution of random effects.

2.8.3 Adherence to Mediterranean diet and multimorbidity

The tertiles of adherence to a Mediterranean diet were defined based on the observed distribution of MedDietScores as follows: low adherence (score <13), moderate adherence (score 13-17), and high adherence (score >17). Tertiles represent any of the two points that divide an ordered distribution into three parts containing about a third of the distribution each. Normally distributed continuous variables (such as age, weight, height, and BMI) are presented as mean ± SD, non-normally distributed variables are presented as median and quartiles, and categorical variables (such as age group, sex, geographical area, residency, marital status, educational level, salary category, physical activity level, smoking, and obesity group) as absolute and relative (%) frequencies among the three tertiles of the MedDietScore tertiles. Differences in normally distributed variables among the MedDietScore tertiles were assessed using the one-way analysis of variance method, whereas for non-normally distributed variables the non-parametric Kruskal-Wallis test was used instead. The Pearson's chi-squared test was applied to evaluate potential associations between categorical variables and MedDietScore tertiles.

In order to assess the spatial distribution of the adherence to the Mediterranean diet in the general population in Cyprus, the parameter of spatial heterogeneity was accounted for and the analysis was based on the districts of Cyprus (Nicosia, with total population 332,200; Limassol, 239,400; Larnaca, 144,900; Paphos, 91,300; and Ammochostos, 47,000). Spatial analyses and mapping were performed using the ArcGIS version 10.4 (ESRI Inc., Redlands, California, USA). We also used box plots to present the distribution of co-morbidities overall and by Mediterranean diet tertiles (low, moderate, high).

Crude logistic regression models were used to examine the association of the adherence to the Mediterranean diet, separately, on the odds of having more than two chronic conditions. Then, logistic regression models of multimorbidity and adherence to

Mediterranean diet were constructed after adjusting for possible confounders, including age, sex, smoking, and physical activity status. Logistic regression models are used to model the probability of an 'event' where the dependent variable is binary and the two values of the outcome are labeled "0" (non-event) and "1" (event). In the logistic model the logarithm of the odds (log-odds) for the value labeled as "1" is a linear combination of one or more predictors (independent variables) which can be either categorical or continuous variables.

Hierarchical multivariable logistic regression models were used adjusting for social and demographic indicators. Firstly, we adjusted for age and sex, then added lifestyle habits, including smoking habits and physical activity level, and finally socioeconomic and demographic characteristics, including educational and marital status, geographical area, and residency, were added. Odds ratios and the corresponding 95% CIs were reported. Hierarchical logistic regression analysis is useful as the order that the covariates are entered into the regression equation is specified by the analyst. We started with the variable or the group of variables which we want to enter in the model and we perform the logistic regression with those variables as the independent variables. From that model we have the variance accounted for this corresponding group of independent variables and then we applied another regression model adding a new set of independent variables. This way, we have the opportunity to examine the contribution of the second set of variables over and above the first group of independent variables. Interactions terms were tested using the Wald test, and if there was a statistically significant interaction then we used a stratified the analysis. The fit of the model was assessed using the Hosmer-Lemeshow goodness of fit test. The test assesses whether or not the observed event rates match the expected event rates in the subgroups of the study populations.

In order to visually inspect the association of Mediterranean diet and specific chronic diseases, we used box plots to present the Mediterranean diet score over the individuals with and without the specific chronic disease focusing only on the most prevalent ones (i.e., hyperlipidemia, thyroid diseases).

2.8.4 Quality of sleep and its association with multimorbidity

The tertiles of the quality of sleep were defined based on the observed distribution of PSQI scores as follows: good quality of sleep (score <4), moderate quality of sleep (score 4-6), and poor quality of sleep (score >6). Continuous variables with no normal

distribution (i.e. quality of sleep score) are presented as median (1st quartile, 3rd quartile) and categorical variables (such as age group, sex, geographical area, residency, marital status, educational status, salary category, physical activity level, smoking, and BMI groups) as absolute and relative (%) frequencies, by the tertiles of the quality of sleep score. Differences in normally distributed variables and non-normally distributed variables among the quality of sleep score tertiles were evaluated through ANOVA and Kruskal-Wallis test, respectively. The chi-squared test was utilized to evaluate potential associations between categorical variables. Box plots were used for the distribution of co-morbidities overall and by quality of sleep score tertiles.

Multinomial logistic regression was used to examine the association of quality of sleep on multimorbidity level, after accounting for age and sex, as well as separately by sex, controlling for age. Logistic regression models were used to examine the association of quality of sleep with the probability of having more than two chronic conditions after adjusting for possible confounders, including age, sex, smoking, and physical activity status. Interactions terms between quality of sleep tertiles and age as well as sex were tested using the Wald test and in case of significant interactions a stratified analysis was conducted instead. The fit of the model was assessed using the Hosmer-Lemeshow goodness of fit test. Multivariable logistic regression models were used adjusting for social and demographic indicators in a hierarchical way. Firstly, we adjusted for age and sex, then added lifestyle habits, including smoking habits and physical activity level, and then we finally added socioeconomic and demographic characteristics, including educational, marital and salary status, geographical area, and residency.

2.8.5 Adherence to Mediterranean Diet, quality of sleep and multimorbidity

Multinomial logistic regression was used to examine the association of the adherenhe to Mediterranean Diet and quality of sleep on multimorbidity level, after accounting for age and sex, as well as separately by sex, controlling for age. Logistic regression models were used to examine the association of the adherenhe to Mediterranean Diet and quality of sleep with the probability of having more than two chronic conditions after adjusting for possible confounders, including age, sex, smoking, and physical activity status. Interactions terms between quality of sleep tertiles and

Mediterranean Diet adherence were tested using the Wald test.The fit of the model was assessed using the Hosmer-Lemeshow goodness of fit test.

All the statistical analysis were conducted using STATA 14.0 statistical software (Stata Corp, College Station, TX, USA) and R studio statistical software. All statistical tests performed were two-sided with the statistical significance level set at $\alpha=0.05$.

3 Chapter 3 - Prevalence of multimorbidity in Cyprus. The most common chronic diseases and the most common combinations of chronic diseases in Cypriot population.

3.1 Participants characteristics

3.1.1 Overall

The sample is considered representative of the entire population of Cyprus, by a priori weighing the sampling procedure. In order to confirm that the sample matched the Cypriot population in the three key demographic characteristics considered in the study (age, sex, and region), we performed chi-square goodness of fit tests comparing the distribution of the sample size in each key characteristic and the corresponding distribution in the overall Cypriot population. In all the characteristics, the distributions in the sample were similar to the corresponding ones in the Cypriot population (***Table 3.1***) (all p-values > 0.05), hence the sample was considered representative.

The mean age of the participants was 41 ± 17 years old; 15% of the participants were 18-24 years old, 46% were 25-44 years old, 27% were 45-64 years old, and 12% were 65 years old or older (***Table 3.1***). Overall, 56.4% were women, 76.3% lived in an urban area, 54.4% were married, 64.3% had completed a higher education, and 49.7% had a yearly average income of €6,500- €19,500 (***Figure 3.1***). The largest part of the total sample was from the capital of Cyprus, Nicosia (43.3%) while the smallest was from Ammochostos (4.4%), matching the actual distribution of the population of Cyprus. The median number of children of the participants was 1 (q_1=0, q_3=2).

We found that almost half of the participants was physically active and 35.5% were current smokers. The most common type of exercise in our study sample was going to the gym (51%), followed by jogging (14%), swimming (10%), and playing football (10%). Also, the largest percentage of the physically active people exercised 1-3 hours per week (42%), followed by people who exercised 3-6 hours (25%) (***Table 3.1***). The median number of hours per day of sedentary activity was 2.5 (q_1=0, q_3=5).

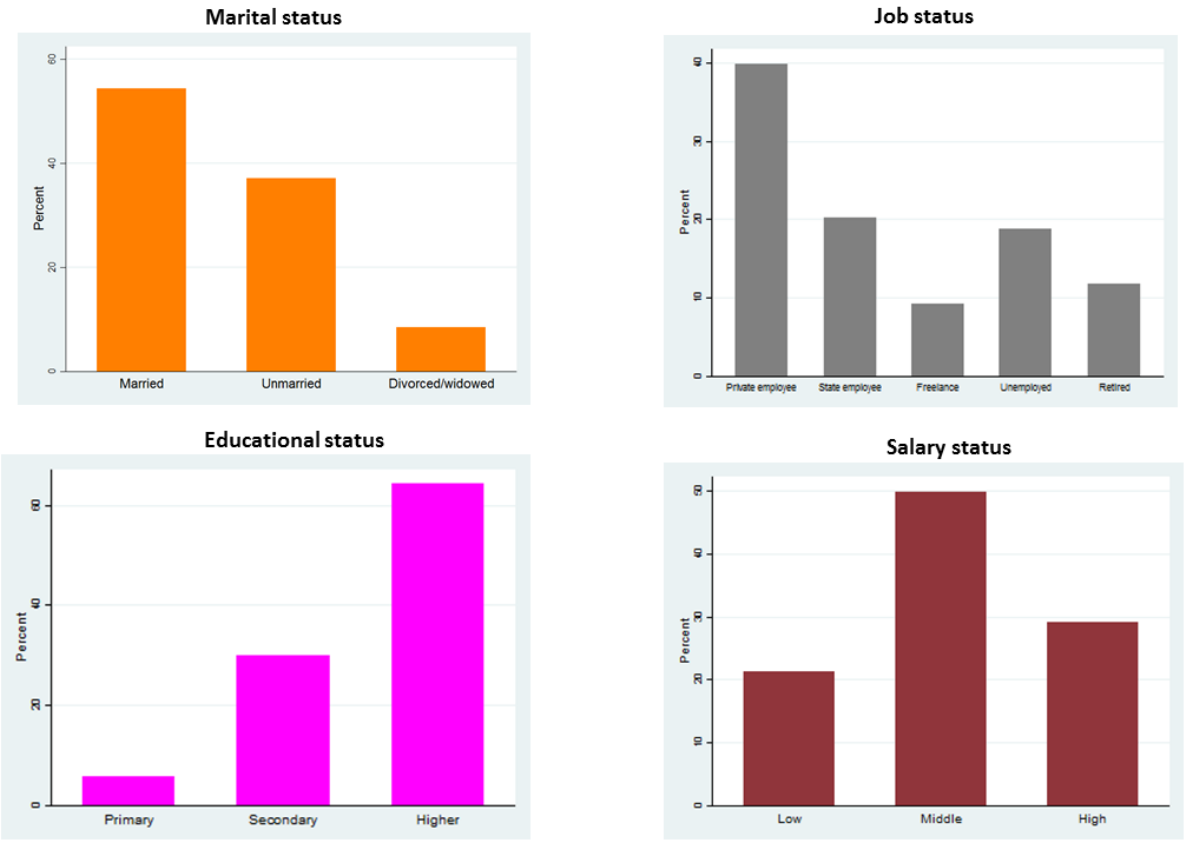
Table 3.1: Characteristics of participants.

Characteristics	**Overall**	**Cypriot population**
Age (years) (mean ± SD)	40.8 ± 16.9	
Age group [N (%)][a]		
18-24	167 (14.7)	88400 (13.2)
25-44	524 (46.0)	265538 (40.0)
45-64	314 (27.5)	206164 (31.0)
65+	135 (11.8)	111767 (15.8)
Sex [N (%)][b]		
Men	497 (43.7)	322383 (48.0)
Women	642 (56.4)	349486 (52.0)
Geographical area [N (%)][c]		
Nicosia	493 (43.3)	264314 (41.0)
Limassol	311 (27.4)	188607 (28.0)
Larnaka	171 (15.0)	112536 (17.0)
Paphos	113 (9.9)	70395 (9.0)
Ammochostos	50 (4.4)	36017 (5.0)
Residency [N (%)][d]		
Urban	864 (76.3)	455594 (70.0)
Rural	269 (23.7)	216275 (30.0)
Marital status [N (%)][d]		
Married	616 (54.4)	
Unmarried	421 (37.2)	
Divorced / Widowed	96 (8.5)	
Educational level [N (%)][d]		
Primary education	66 (5.8)	
Secondary education	338 (29.8)	
Higher education	729 (64.3)	
Salary [N (%)][e]		
Low	241 (21.3)	
Middle	562 (49.7)	
High	328 (29.0)	
Number of children [median (Q1, Q3)][f]	1 (0, 2)	
Physical activity [N (%)][g]		
No	591 (52.2)	
Yes	541 (47.8)	
Type of exercise [N (%)][h]		
Football	48 (10.0)	
Volley	17 (3.5)	
Basketball	17 (3.5)	
Swimming	50 (10.4)	
Martial arts	0 (0.0)	

Gym	244 (50.7)
Track	2 (0.4)
Jogging	67 (13.9)
Bicycle	36 (7.6)
Hours of exercising [N (%)][i]	
Less than 1 hour	107 (15.5)
1-3 hours	287 (41.5)
3-6 hours	175 (25.3)
6-9 hours	86 (12.4)
More than 9 hours	37 (5.3)
Activities (h/d) [median (Q1, Q3)]	
Dance	0 (0, 0)
Walking	0 (0, 1)
Agricultural	0 (0, 0)
Sedentary activity	2.5 (0.5, 5)
Heavy object	0 (0, 0.5)
Current smoker [N (%)][d]	
No	731 (64.5)
Yes	402 (35.5)
BMI (kg/m^2) (mean ± SD)	25.0 ± 4.6
BMI group [N (%)][j]	
Underweight	42 (3.7)
Normal	565 (50.4)
Overweight	362 (32.3)
Obese	152 (13.6)
PSS-14 score (mean ± SD)	21.8 ± 7.8
PSS-14 score group [N (%)][k]	
Low	158 (13.9)
Moderate	642 (56.3)
High	340 (29.8)
EQ-5D score (mean ± SD)	0.8 ± 0.2
General health status self-assessment (mean ± SD)	81.3 ± 15.1

Abbreviations: SD, standard deviation; IQR, interquartile range; [a] N=1140; [b]N=1139; [c]N=1138; [d]N=1133; [e]N=1131; [f]N=1137; [g]N=1132; [h]N=481 (total number of sports who were reported by the participants); [i]N=692 (total number of hours of exercising who were reported by the participants) ; [j]N=1121; [k]N=1084

Figure 3.1: Socio-economic characteristics.



The mean BMI was 25.0 ± 4.6 kg/m^2 with almost half of the study participants (46%) being overweight or obese. Regarding the psychological characteristics, the mean perceived stress score was 22 ± 8 and 56% of the participants were categorized in the moderate stress group. In addition, the EQ-5D and the general health status self-assessment suggest a good quality of life since on average they are close to 1 (0.8 ± 0.2) and 100 (81.3 ± 15.1), respectively. Further details about the participants' main characteristics are presented in ***Table 3.1***.

3.1.2 Characteristics by sex and by age group

The mean age was 40 ± 16 years old among the *n*=642 women of the study compared to 42 ± 18 years old among the *n*=497 men (p=0.04) (***Table 3.2***). The distribution of the age groups was similar in men and women in general with a small difference in the age group of 65 years old and over (15% vs. 10%, respectively) (p=0.05). Men and women were distributed similarly among the five geographical areas of Cyprus (p=0.82) as well as between urban and rural regions (p=0.87).

Table 3.2: Characteristics of participants by sex.

Characteristics	**Sex**		**p-value**	**Cypriot population**	
	Women (N=642)	**Men** (N=497)		**Women** (N=349486)	**Men** (N=322383)
Age (years) (mean ± SD)	39.9 ± 15.9	41.9 ± 18.0	**0.04**[h]		
Age group [N (%)][a]					
18-24	93 (13.5)	74 (14.9)	0.05[g]	43036	45364
25-44	307 (47.7)	218 (43.7)		140612	124926
45-64	182 (28.3)	133 (26.7)		105760	100404
65+	61 (9.5)	73 (14.7)		60078	51689
Geographical area [N (%)][b]					
Nicosia	272 (42.3)	222 (44.7)	0.82[g]	138131	126183
Limassol	174 (27.1)	138 (27.8)		98835	89773
Larnaka	100 (15.5)	71 (14.3)		58041	54495
Paphos	66 (10.3)	47 (9.4)		36092	34303
Ammochostos	31 (4.8)	19 (3.8)		18387	17629
Residency [N (%)][c]					
Urban	488 (76.5)	378 (76.1)	0.87[g]	239022	216572
Rural	150 (23.5)	113 (23.9)		109664	105811
Marital status [N (%)][c]					
Married	352 (55.0)	265 (53.5)	**0.03**[g]		
Unmarried	223 (34.8)	199 (40.2)			
Divorced / Widowed	65 (10.2)	31 (6.3)			
Educational level [N (%)][c]					
Primary education	34 (5.3)	32 (6.5)	**0.02**[g]		
Secondary education	172 (26.9)	166 (33.5)			
Higher education	434 (67.8)	297 (60.0)			
Salary [N (%)][d]					
Low	162 (25.3)	79 (16.0)	**<0.01**[g]		
Middle	331 (51.8)	232 (47.0)			
High	146 (22.9)	183 (37.0)			
Number of children [N (%)][e]	1 (0, 2)	1 (0, 2)	0.65[i]		
Physical activity [N (%)][f]					
No	362 (56.7)	230 (46.6)	**<0.01**[g]		
Yes	276 (43.3)	264 (53.4)			
Type of exercise [N (%)][g]					
Football	1 (0.5)	47 (18.4)	**<0.01**[g]		
Volley	7 (3.2)	10 (3.8)			
Basketball	3 (1.4)	14 (5.4)			
Swimming	26 (11.7)	24 (9.0)			

Martial arts	0 (0.0)	0 (0.0)	
Gym	143 (64.7)	100 (39.0)	
Track	0 (0.0)	2 (0.8)	
Jogging	32 (14.5)	35 (13.6)	
Bicycle	9 (4.0)	26 (10.0)	
Hours of exercising per week [N (%)][h]			
Less than 1 hour	54 (15.9)	126 (35.9)	**<0.01**[g]
1-3 hours	160 (47.2)	99 (28.2)	
3-6 hours	76 (22.5)	49 (14.0)	
6-9 hours	37 (10.9)	53 (15.1)	
More than 9 hours	12 (3.5)	24 (6.8)	
Activities (h/d) [median (Q1, Q3)]			
Dance	0 (0, 0)	0 (0, 0)	0.14[i]
Walking	0 (0, 0.75)	0 (0, 1)	0.50[i]
Agricultural	0 (0, 0)	0 (0, 0)	**<0.01**[i]
Sedentary activity	2 (0, 5)	3 (1, 5.25)	**0.02**[i]
Heavy object	0 (0, 0)	0 (0, 1)	**<0.01**[i]
Smoking status [N (%)][c]			
No	471 (73.6)	259 (52.6)	**<0.01**[g]
Yes	169 (26.4)	233 (47.4)	
BMI (kg/m^2) (mean ± SD)	23.9 ± 4.8	26.4 ± 4.0	**<.01**[h]
BMI group [N (%)][i]			
Underweight	37 (5.8)	5 (1.0)	**<.01**[g]
Normal	396 (62.5)	169 (34.8)	
Overweight	130 (20.5)	232 (47.7)	
Obese	71 (11.2)	80 (16.5)	
PSS-14 score (mean ± SD)	22.9 ± 7.9	20.5 ± 7.7	**<.01**[h]
PSS-14 score group [N (%)][a]			
Low	74 (12.3)	84 (17.4)	**<.01**[j]
Moderate	338 (56.2)	303 (62.9)	
High	189 (31.5)	95 (19.7)	
EQ-5D score (mean ± SD)	0.8 ± 0.2	0.9 ± 0.2	**<.01**[h]
General health status self-assessment (mean ± SD)	80.2 ± 14.7	82.8 ± 15.4	**<.01**[h]

Bold values represent $p < 0.05$; Abbreviations: SD, standard deviation; IQR, interquartile range; [a] N=1140; [b] N=1138; [c]N=1133; [d]N=1131; [e]N=1137; [f]N=1132; [g]N=404 (total number of sports who were reported by the participants); [h]N=1263 (total number of hours of exercising who were reported by the participants); [i]N=1120; [g] Differences were evaluated by the chi-square test; [h] Differences were evaluated by the t- test; [i] Differences were evaluated by the Kolmogorov-Smirnov test; [j] Differences were evaluated by the Kruskal-Walls test.

We also found statistically significant differences ($p<0.05$) in marital status and educational level as well as in yearly average salary groups between men and women and among the age groups (***Table 3.2***). More specifically, a largest percentage of divorced/widowed participants (10%) was reported in women compared to men (6%) while more men were unmarried compared to women (40% vs. 35%) ($p=0.03$).

Among the four age groups, we found that 96% of the individuals aged 18-24 years old were unmarried while in the other three age groups (25-44, 45-64, 65+) the majority of the participants were married ($p<0.01$) (***Table 3.3***). The largest percentage of divorced/widowed participants was identified in the people aged 65 years old and older (22%). Apart from this, we identified a largest percentage of participants who completed a higher education among women compared to men (68% vs. 60%) ($p=0.02$). Regarding the association of educational level and age, no participant aged 18-24 years old was reported as completed only primary education while on the other hand the majority of the participants aged 65 years old have completed only primary education (41%) ($p<0.01$). Moreover, the majority of those who aged 25-64 years old have completed a higher education.

We identified statistically significant differences ($p<0.01$) in men vs. women (***Table 3.2***) and among the four age groups in regards to the type of exercise and the hours of exercising per week (***Table 3.3***). A larger percentage of men noted that they were physically active compared to the corresponding percentage in women (53% vs. 43%). Furthermore, more physically active individuals were identified in 18-24 and 25-44 age groups compared to more than 45 years old age groups ($p<0.01$). In addition, there is a larger percentage of women who exercise in the gym compared to men ($p<0.01$) and in people aged 64 years old and smaller compared to the older group ($p<0.01$). Individuals aged 65 years old and older noted that the type of exercise they do was swimming (58%).

Furthermore, the majority of the women participants exercised 1-3 hours per week (47%) while the majority of the men participants exercised less than 1 hour per week ($p<0.01$). Moreover, a percentage of 11% of the individuals aged 18-24 years old noted that they exercise more than 9 hours per week while the corresponding percentages among the other age groups of the study were 4%, 4%, and 7% for 25-44, 45-64, and 65+ years old, respectively.

The median hours per day of sedentary activity was 2 hours per day for the n=642 women and 3 hours per day for the n=497 men (p=0.02). There are statistically significant (p<0.05) differences between the hours per day of sedentary activity among the four age groups of the study participants, with younger (18-24 years old) and elderly (65+) people having the largest median number of hours per day (p<0.01).

Moreover, men had a larger percentage of smokers (47%) than women (26%) (p<0.01) and it was also observed that 43% of elderly people were current smokers. The mean BMI of the study participants was 23.9 ± 4.8 kg/m^2 and 26.4 ± 4.0 kg/m^2 for women and men, respectively (p<0.01). In addition, the mean BMI of the participants aged 18-24, 25-44, 45-64 and 65+ years old was 23.0 ± 3.8 kg/m^2, 24.3 ± 4.8 kg/m^2, 26.3 ± 4.3 kg/m^2, and 27.3 ± 3.9 kg/m^2, respectively (p<0.01). The majority of women was classified in the category of normal BMI (63%) while the majority of men was classified in the category of overweight (48%) (p<0.01). More than half of the participants aged 18-44 years old had a normal BMI while the majority of those who were more than 45 years old was overweight or obese (p<0.01).

More women had a high perceived stress score compared to men (32% vs 20%) (p<0.01). Moreover, larger perceived stress scores, indicating high stress, were identified in younger ages with the scores decreasing as the age increases (p<0.01) (***Table 3.3***).

Table 3.3: Characteristics of participants by age group (18-24, 25-44, 45-64 and 65+ years old).

Characteristics	**Age group**				**p-value**
	18-24 (N=167)	**25-44** (N=524)	**45-64** (N=314)	**65+** (N=135)	
Geographical area [N (%)][a]					
Nicosia	61 (36.7)	221 (42.1)	148 (47.1)	63 (47.0)	**<0.01**[j]
Limassol	42 (25.3)	132 (25.1)	90 (28.7)	47 (35.1)	
Larnaka	32 (19.3)	85 (16.2)	42 (13.4)	12 (9.0)	
Paphos	28 (16.9)	56 (10.9)	22 (7.0)	7 (5.2)	
Ammochostos	3 (1.8)	30 (5.7)	12 (3.8)	5 (3.7)	
Residency [N (%)][b]					
Urban	121 (72.9)	395 (76.0)	249 (79.3)	99 (74.4)	0.41[j]
Rural	45 (27.1)	125 (24.0)	65 (20.7)	34 (25.6)	
Marital status [N (%)][b]					
Married	6 (3.6)	263 (50.4)	246 (78.6)	101 (76.5)	**<0.01**[j]
Unmarried	159 (95.8)	243 (46.5)	17 (5.4)	2 (1.5)	

Divorced / Widowed	1 (0.6)	16 (3.1)	50 (16.0)	29 (22.0)	
Educational level [N (%)][b]					
Primary education	0 (0.0)	1 (0.2)	11 (3.5)	54 (40.9)	**<0.01**[j]
Secondary education	94 (56.3)	69 (13.2)	130 (41.8)	45 (34.1)	
Higher education	73 (43.7)	453 (86.6)	170 (54.7)	33 (25.0)	
Salary [N (%)][c]					
Low	110 (66.7)	49 (9.4)	45 (14.5)	37 (28.0)	**<0.01**[j]
Middle	55 (33.3)	334 (63.9)	110 (35.4)	63 (47.7)	
High	0 (0.0)	140 (26.7)	156 (50.1)	32 (24.3)	
Number of children [N (%)][d]	0 (0, 0)	0 (0, 1)	2 (2, 3)	2 (2, 3)	**<0.01**[l]
Physical activity [N (%)][e]					
No	64 (39.0)	247 (47.4)	184 (59.0)	96 (71.1)	**<0.01**[j]
Yes	100 (61.0)	274 (52.6)	128 (41.0)	39 (28.9)	
Type of exercise [N (%)][f]					
Football	7 (9.2)	38 (13.7)	3 (3.4)	0 (0.0)	**<0.01**[j]
Volley	5 (5.1)	10 (3.6)	2 (2.3)	0 (0.0)	
Basketball	3 (3.0)	11 (4.0)	3 (3.4)	0 (0.0)	
Swimming	5 (5.1)	8 (2.9)	26 (29.9)	11 (57.9)	
Martial arts	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Gym	56 (57.0)	148 (53.4)	35 (40.2)	5 (26.3)	
Track	1 (1.0)	1 (0.4)	0 (0.0)	0 (0.0)	
Jogging	16 (16.3)	40 (14.4)	10 (11.6)	1 (5.3)	
Bicycle	5 (5.1)	21 (7.6)	8 (9.2)	2 (10.5)	
Hours of exercising per week [N (%)][g]					
Less than 1 hour	17 (13.2)	54 (14.9)	24 (16.2)	12 (30.0)	**<0.01**[j]
1-3 hours	43 (33.3)	173 (47.8)	56 (37.8)	15 (37.5)	
3-6 hours	38 (29.5)	83 (22.9)	39 (26.4)	6 (15.0)	
6-9 hours	17 (13.2)	38 (10.5)	23 (15.5)	4 (10.0)	
More than 9 hours	14 (10.8)	14 (3.9)	6 (4.1)	3 (7.5)	
Activities (h/d) [median (Q1, Q3)]					
Dance	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.08[l]
Walking	0 (0, 1)	0 (0, 0.58)	0 (0, 1)	0 (0, 0.5)	**0.04**[l]
Agricultural	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 1)	**<0.01**[l]
Sedentary activity	3 (0.5, 5)	2 (0.5, 6)	2 (0.33, 5)	3 (1, 4.5)	0.55[l]
Heavy object	0 (0, 0)	0 (0, 0.67)	0 (0, 1)	0 (0, 0)	**<0.01**[l]
Smoking status [N (%)][b]					
No	125 (76.7)	336 (64.4)	193 (61.7)	77 (57.0)	**<0.01**[j]
Yes	38 (23.3)	186 (35.6)	120 (38.3)	58 (43.0)	
BMI (kg/m^2) (mean ± SD)	23.0 ± 3.8	24.3 ± 4.8	26.3 ± 4.3	27.3 ± 3.9	**<.01**[k]
BMI group [N (%)][h]					
Underweight	15 (9.1)	24 (4.7)	3 (1.0)	0 (0.0)	**<.01**[j]

Normal	101 (61.2)	299 (58.1)	127 (41.2)	38 (28.5)	
Overweight	33 (20.0)	146 (28.3)	124 (40.3)	59 (44.4)	
Obese	16 (9.7)	46 (8.9)	54 (17.5)	36 (27.1)	
PSS-14 score (mean ± SD)	23.3 ± 8.0	22.7 ± 7.7	21.0 ± 7.5	18.5 ± 8.2	**<.01**[k]
PSS-14 score group [N (%)][i]					
Low	19 (12.4)	60 (12.1)	41 (13.6)	38 (28.8)	**<.01**[j]
Moderate	81 (52.9)	291 (58.4)	197 (65.5)	73 (55.3)	
High	53 (34.7)	147 (29.5)	63 (20.9)	21 (15.9)	
EQ-5D score (mean ± SD)	0.8 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	0.7 ± 0.2	**<.01**[k]
General health status self-assessment (mean ± SD)	82.4 ± 15.7	82.9 ± 14.4	80.0 ± 14.1	76.7 ± 17.9	**<.01**[k]

Bold values represent p < 0.05; Abbreviations: SD, standard deviation; IQR, interquartile range; [a]N=1138; [b]N=1133; [c]N=1131; [d]N=1137; [e]N=1132; [f]N=404 (total number of sports who were reported by the participants); [g]N=1263 (total number of hours of exercising who were reported by the participants); [h]N=1120; [i]N=1084; [j] Differences were evaluated by the chi-square test; [k] Differences were evaluated by the t- test ; [l] Differences were evaluated by the Kolmogorov-Smirnov test.

3.1.3 Prevalence of multimorbidity, the most common diseases and the most frequent combinations of diseases in the Cypriot population.

3.1.4 Distribution of multimorbidity

The overall age and sex standardized prevalence of multimorbidity was 28.6% (95% CI: 26.0, 31.2). The multimorbidity rate increased significantly with age (*p* for trend <0.01), was higher in women than in men (28% vs. 23%, p<0.01), inoverweight/obese people (p<0.01), among divorced/widowed participants (p<0.01), in people who completed primary school only (p<0.01), among current smokers (p=0.02), and in people who were physically inactive (p<0.01).

Specifically, 8% of people aged 18-24 years old, 16% of people aged 25-44 years old, 33% of people aged 45-64 years old, and 69% of people aged 65 years old and older had 2 or more morbidities (p<0.01). In addition, 32% of married participants had 2 or more morbidities while the corresponding percentages in unmarried and divorced/widowed participants were 12% and 48%, respectively. Regarding the educational level, a high percentage of individuals with multimorbidity (73%) was reported in participants who completed only primary education while on the other hand 74% and 79% of the participants who completed a secondary or a higher education respectively, reported no having multimorbidity (p<0.01) (***Table 3.4***).

Regarding the lifestyle characteristics of the participants, such as physical activity level and smoking status, we found a higher percentage of participants in physically inactive ($p<0.01$) as well as in current smokers ($p=0.02$) having multimorbidity. In addition, a higher percentage of participants having more than 2 morbidities was observed in the overweight and obese categories of BMI compared to the normal and underweight categories ($p<0.01$).

Moreover, we found a higher percentage of multimorbidity in the participants with elevated stress levels (29%) compared to the corresponding percentages in the participants with low (28%) and moderate (24%) stress ($p<0.01$). In addition, we observed a largest value of the quality of life score in individuals with no multimorbidity compared to individuals with multimorbidity ($p<0.01$) (***Table 3.4***).

The mean number of conditions was 1.07 with the largest number of conditions in an individual being 12. In addition, the mean number of the conditions among the n=642 women was 1.1 ± 1.5 with the biggest number of conditions being 9 and the corresponding mean number was 1.0 ± 1.5 with the biggest number being 12 for the n=497 men. Furthermore, the mean age of people with multimorbidity was almost 53 ± 18 years old compared with people without multimorbidity which was only 37 ± 14 years old.

Moreover, most of the elderly people had 2 or more morbidities (68.9%) which was no surprise, however, 33% of the people with multimorbidity was under 45 years old. Regarding the educational status, 72.7% of participants who had completed only primary education had multimorbidity in contrast with the 21.5% of people who had completed a higher education. No significant differences were observed between residents of urban and rural regions, among the five geographical areas of Cyprus, or among the salary categories.

Table 3.4: Characteristics of participants by multimorbidity group.

Characteristics	**Multimorbidity** (N=293)	**No multimorbidity** (N=847)	**p-value**
Age (years) (mean ± SD)	52.9 ± 18.0	36.6 ± 14.2	**<0.01**[j]
Age group [N (%)][a]			
18-24	13 (18.2)	154 (4.4)	**<0.01**[i]
25-44	84 (52.0)	440 (28.7)	
45-64	103 (24.8)	211 (35.2)	
65+	93 (5.0)	42 (31.7)	
Sex [N (%)][b]			
Men	112 (38.2)	385 (45.5)	**0.03**[i]
Women	181 (61.8)	461 (54.5)	
Geographical area [N (%)][c]			
Nicosia	131 (44.7)	362 (42.8)	0.18[i]
Limassol	89 (30.4)	222 (26.3)	
Larnaka	36 (12.3)	135 (16.0)	
Paphos	22 (7.5)	91 (10.8)	
Ammochostos	15 (5.1)	35 (4.1)	
Residency [N (%)][d]			
Urban	228 (78.1)	636 (75.6)	0.39[i]
Rural	64 (21.9)	205 (24.4)	
Marital status [N (%)][d]			
Married	194 (66.9)	422 (50.1)	**<.01**[i]
Unmarried	50 (17.2)	371 (44.0)	
Divorced / Widowed	46 (15.9)	50 (5.9)	
Educational level [N (%)][d]			
Primary education	48 (16.4)	18 (2.1)	**<.01**[i]
Secondary education	87 (29.8)	251 (29.9)	
Higher education	157 (53.8)	572 (68.0)	
Salary [N (%)][e]			
Low	53 (18.2)	188 (22.4)	0.17[i]
Middle	144 (49.3)	418 (49.8)	
High	95 (32.5)	233 (27.8)	
Physical activity [N (%)][f]			
No	184 (63.0)	407 (48.5)	**<.01**[i]
Yes	108 (37.7)	433 (51.5)	
Current smoker [N (%)][d]			
No	172 (58.7)	559 (66.5)	**0.02**[i]
Yes	121 (41.3)	281 (33.5)	
BMI group [N (%)][g]			
Underweight	5 (1.7)	37 (4.4)	**<.01**[i]

Normal	112 (38.9)	453 (54.4)	
Overweight	105 (36.5)	257 (30.9)	
Obese	66 (22.9)	86 (10.3)	
PSS-14 score group [N (%)][h]			
Low	44 (15.8)	114 (14.2)	**<.01[i]**
Moderate	152 (54.5)	490 (60.9)	
High	97 (29.7)	243 (24.9)	
EQ-5D score (mean ± SD)	0.7 ± 0.2	0.9 ± 0.2	**<.01[j]**
General health status self-assessment (mean ± SD)	75.3 ± 16.0	83.4 ± 14.2	**<.01[j]**

Bold values represent p < 0.05; Abbreviations: SD, standard deviation; [a] N=1140; [b]N=1139;[c]N=1138; [d]N=1133; [e]N=1131; [f]N=1132;[g]N=1121;[h]N=1084; [i] Differences between multimorbidity and no-multimorbidity groups of individuals were evaluated by the chi-square test; [j] Differences between multimorbidity and no multimorbidity groups of individuals were evaluated by the t- test.

The prevalence and standardized prevalence of multimorbidity and the mean number of diseases are presented by region in ***Fig 3.2*** which also highlights the presence of general hospitals, health centers, and private physicians' office in Cyprus (as retrieved from the Cyprus Ministry of Health). The data suggests that the prevalence of multimorbidity is inversely correlated with the presence of health centers within a region ($p<0.01$), and positively correlated with the population density of practicing physicians (i.e., physicians per 10,000 population) ($p<0.01$).

The median number of conditions per participant was 1 (quartiles, $q_1 = 0$ and $q_3 = 2$) with the maximum number being 12. ***Figure 3.3*** shows the median number of morbidities, by age group, sex, marital and education status, smoking and physical activity level, as well as obesity group. A higher median number of morbidities was observed in people who completed only primary education and in those aged 65+. A lower number of conditions was identified in people aged 18-44 years old, in men, among unmarried people, among people who completed a higher education, in non-smokers, among physically active people, in underweight and normal BMI categories.

We also identified that among the study participants 11.8% had 2 morbidities, 6.6% had 3 morbidities, 5.3% had 4 morbidities, and 0.03% had 5 morbidities (***Appendix Table 5***). Given that 74.3% had 0 or 1 morbidities, the cumulative frequency until the cut-off of 5 morbidities was 98% and until the largest number of morbidities reported (12), it does not increase sharply.

Figure 3.2: Spatial analysis of multi-morbidities by region of residence and level of urbanity.

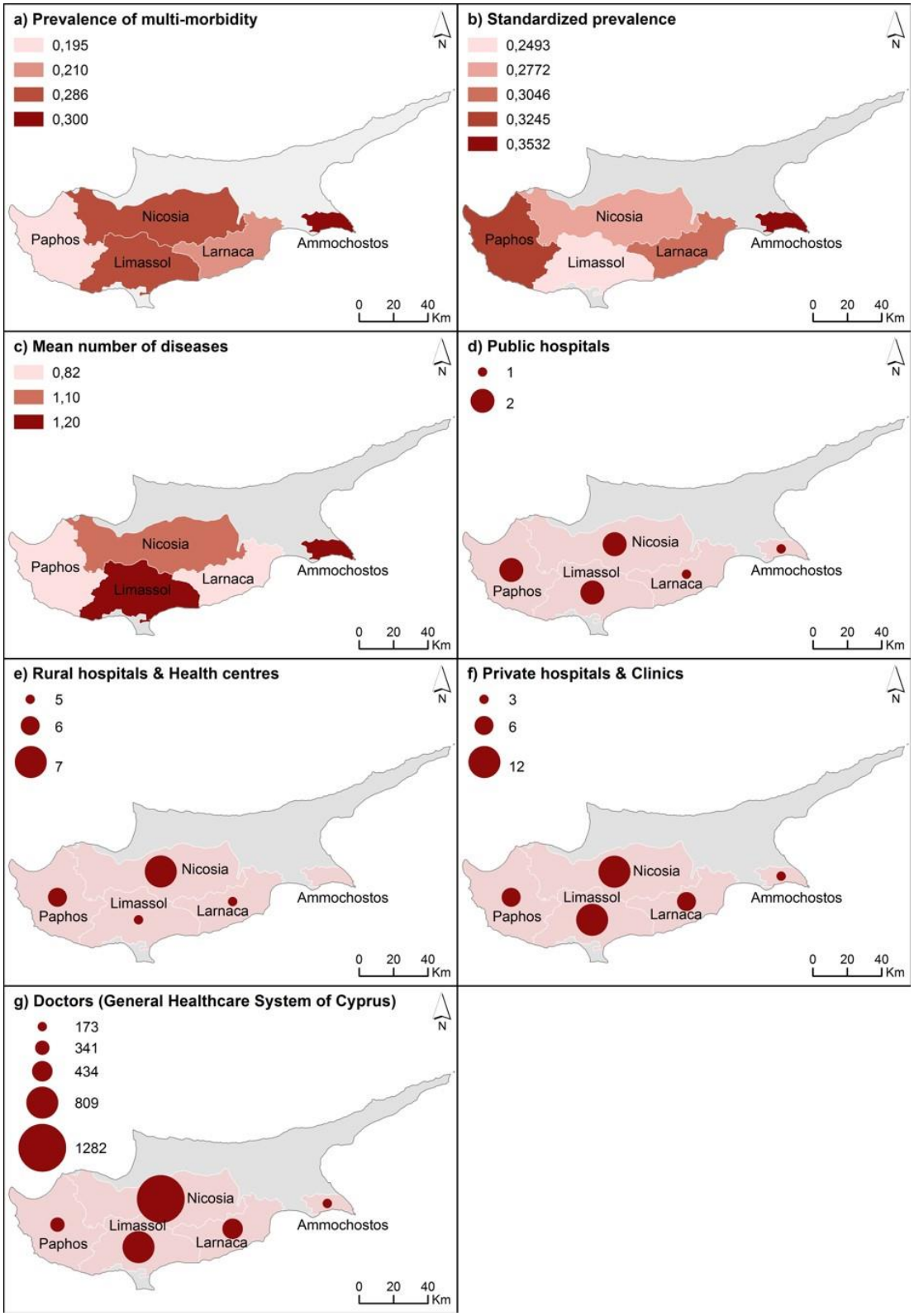


Figure 3.3: Distribution of co-morbidities overall and by age group, sex, marital and educational status, smoking and physical activity level, and obesity status.

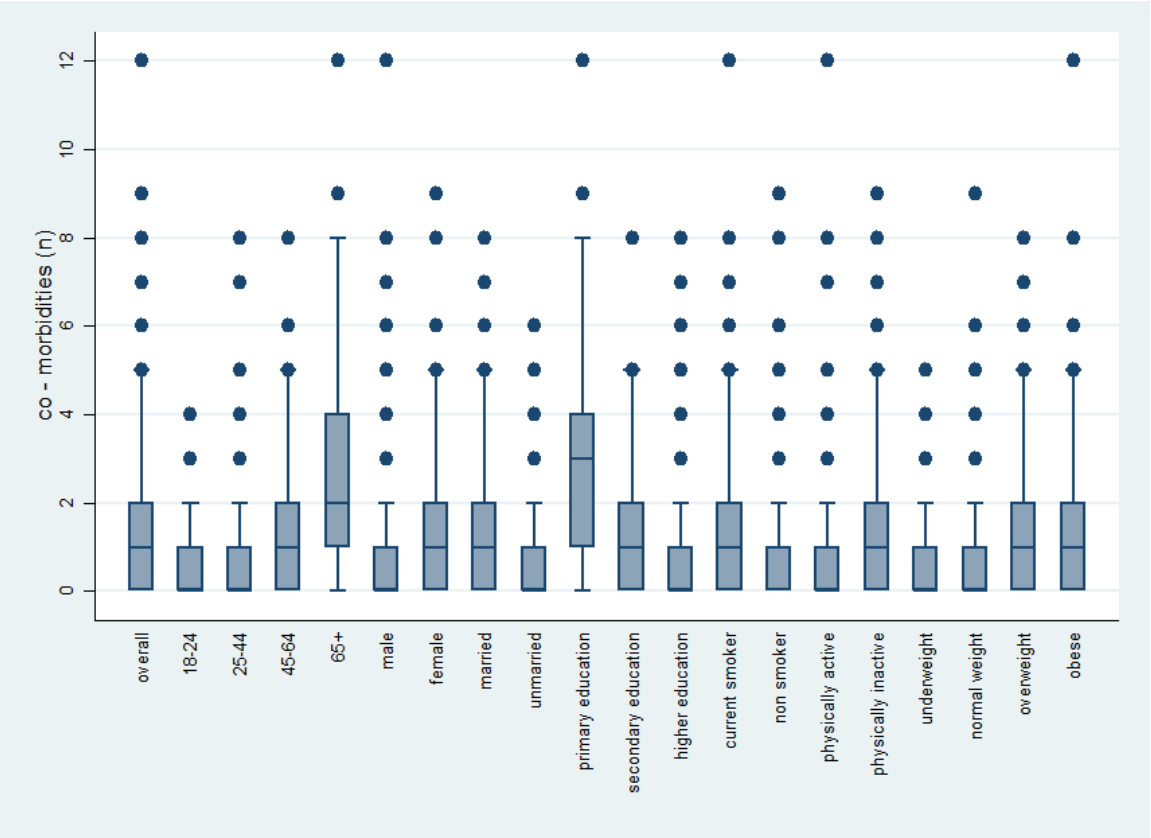


Table 3.5 presents the demographic, socioeconomic, and lifestyle characteristics of the study participants by the level of multimorbidity (0 or 1 morbidities, 2 morbidities, 3 morbidities, and more than 3 morbidities). As mentioned before, the multimorbidity rate increased significantly with age and was higher in women than in men something that was also observed in terms of multimorbidity level. Specifically, the mean age of the participants was 37, 49, 54 and 58 years old for people with 0 or 1 morbidities, 2 morbidities, 3 morbidities, or more than 3 morbidities, respectively ($p < 0.01$). Moreover, although women have a higher prevalence of multimorbidity compared to men, among men, 9.7% have more than 3 morbidities while among women 6.4% have more than 3 morbidities.

Regarding the socio-economic characteristics of the participants, we found that among divorced/widowed participants, 22% of them had 3 or more morbidities while the corresponding percentages among married and unmarried participants were 9% and 4%, respectively ($p<0.01$) (***Figure 3.4***). Similarly, we reported that 27% of the participants

who completed only primary education had 0 or 1 morbidities while among the participants who completed secondary and higher education, 74% and 71% reported as having 0 or 1 morbidities, respectively ($p<0.01$).

Figure 3.4: Marital status (married, unmarried, divorced/widowed) by multimorbidity level (0 or 1 morbidities, 2 morbidities, 3 morbidities and more than 3 morbidities).

Furthermore, we found statistically significant differences in physical activity status among the four groups of multilevel. A larger number of physically inactive participants reported as having 3 or more morbidities compared to physically active (11% vs. 5%) ($p<0.01$). However, we did not find statistically significant differences between smoking status and multimorbidity level. Also, even though we did not find statistically significant association between multimorbidity level and BMI as a continuous measure, we found statistically significant differences between multimorbidity level and BMI categories. Precisely, the smallest percentage (56.6%) of 0 or 1 morbidities was identified among obese people.

Table 3.5: Characteristics of participants by multilevel (0 or 1 morbidities, 2 morbidities, 3 morbidities and more than 3 morbidities).

Characteristics	**Multilevel**				**p-value**
	0 or 1 (N=847)	**2** (N=129)	**3** (N=70)	**>3** (N=94)	
Age (years) (mean ± SD)	36.6 ± 14.2	48.8 ± 17.6	53.7 ± 17.3	58.0 ± 18.1	**<.01**[i]
Age group [N (%)][a]					
18-24	154 (18.2)	7 (5.4)	2 (2.9)	4 (4.3)	**<.01**[h]
25-44	440 (52.0)	47 (36.4)	18 (25.7)	19 (20.2)	
45-64	211 (24.9)	44 (34.1)	30 (42.9)	29 (30.8)	
65+	42 (4.9)	31 (24.1)	20 (28.5)	42 (44.7)	
Sex [N (%)][b]					
Women	461 (54.5)	71 (55.0)	48 (68.6)	62 (66.0)	**0.03**[h]
Men	385 (45.5)	58 (45.0)	22 (31.4)	32 (34.0)	
Geographical area [N (%)][c]					
Nicosia	362 (42.8)	56 (43.4)	31 (44.3)	44 (46.8)	0.14[h]
Limassol	222 (26.3)	36 (27.9)	23 (32.9)	30 (31.9)	
Larnaka	135 (16.0)	18 (14.0)	11 (15.7)	7 (7.4)	
Paphos	91 (10.8)	15 (11.6)	2 (2.9)	5 (5.3)	
Ammochostos	35 (4.1)	4 (3.1)	3 (4.2)	8 (8.5)	
Residency [N (%)][d]					
Urban	636 (75.6)	105 (81.4)	57 (81.4)	66 (71.0)	0.21[h]
Rural	205 (24.4)	24 (18.6)	13 (18.6)	27 (29.0)	
Marital status [N (%)][d]					
Married	422 (50.1)	85 (66.4)	54 (77.1)	55 (59.8)	**<.01**[h]
Unmarried	371 (44.0)	28 (21.9)	6 (8.6)	16 (17.4)	
Divorced / Widowed	50 (5.9)	15 (11.7)	10 (14.3)	21 (22.8)	
Educational level [N (%)][d]					
Primary education	18 (2.1)	12 (9.4)	10 (14.3)	26 (27.7)	**<.01**[h]
Secondary education	251 (29.9)	45 (35.2)	21 (30.0)	21 (22.3)	
Higher education	572 (68.0)	71 (55.4)	39 (55.7)	47 (50.0)	
Salary [N (%)][e]					
Low	188 (22.4)	18 (14.0)	15 (21.7)	20 (21.3)	0.19[h]
Middle	418 (49.8)	73 (56.6)	30 (43.5)	41 (43.6)	
High	233 (27.8)	38 (29.4)	24 (34.8)	33 (35.1)	
Physical activity [N (%)][f]					
No	407 (48.5)	76 (58.9)	43 (62.3)	65 (69.2)	**<.01**[h]
Yes	433 (51.5)	53 (41.1)	26 (37.7)	29 (30.8)	
Current smoker [N (%)][d]					
No	559 (66.6)	76 (58.9)	38 (54.3)	58 (61.7)	0.08[h]

Yes	281 (33.5)	53 (41.1)	32 (45.7)	36 (38.3)	
BMI (kg/m^2) (mean ± SD)	24.5 ± 4.4	26.3 ± 4.7	26.6 ± 5.2	26.3 ± 5.0	0.59[i]
BMI group [N (%)][g]					
Underweight	37 (4.4)	2 (1.6)	1 (1.5)	2 (2.2)	**<.01[h]**
Normal	453 (54.4)	52 (40.6)	24 (35.8)	36 (38.7)	
Overweight	257 (30.9)	42 (32.8)	23 (34.3)	40 (43.0)	
Obese	86 (10.3)	32 (25.0)	19 (28.4)	15 (16.1)	

Bold values represent p < 0.05; Abbreviations: SD, standard deviation ;[a] N=1140; [b]N=1139;[c]N=1138; [d]N=1133; [e]N=1131; [f]N=1132;[g]N=112; [h]Differences between multimorbidity and no-multimorbidity groups of individuals were evaluated by the chi-square test; [i]Differences between multimorbidity and no-multimorbidity groups of individuals were evaluated by the ANOVA test.

3.1.5 Prevalent chronic diseases and combinations of human systems' diseases

The crude prevalence of specific chronic diseases indicated that the most prevalent chronic diseases were hyperlipidemia (17%), followed by hypertension (13%), thyroid diseases (8%), gastric reflux (7%), polycystic ovarian syndrome (6%), and asthma (6%) (***Table 3.6***), with figures increasing with age (*p<0.01*). Among multimorbidity individuals more than half of them had hyperlipidemia (***Figure 3.5***) or hypertension (***Figure 3.6***) while almost a quarter of them reporting being diagnosed with a thyroid disease (***Figure 3.7***).

Table 3.6: Crude prevalence of chronic diseases overall as well as by sex and age group.

Chronic diseases	**Overall** (N=1140)	**Women** (N=643) [N (%)]	**Men** (N=497) [N (%)]	**p-value**
Number of co-morbidities (mean ± SD)	1.07 ± 1.49	1.14 ± 1.48	0.98 ± 1.49	0.07[c]
Hyperlipidemia (E78.5)	198 (17.4)	100 (15.6)	98 (19.8)	0.07[a]
18-24	5 (2.6)	5 (5.0)	0 (0.0)	0.02[b]
25-44	44 (22.2)	18 (18.0)	26 (26.5)	
45-64	87 (43.9)	50 (50.0)	37 (37.8)	
65+	62 (31.3)	27 (27.0)	35 (35.7)	
Hypertension (I10)	147(12.9)	64 (10.0)	83 (16.7)	**<.01**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.69[b]
25-44	15(10.2)	5 (7.8)	10 (12.0)	
45-64	68 (42.3)	31 (48.4)	37 (44.6)	
65+	64 (43.5)	28 (43.8)	36 (43.4)	

Thyroid diseases (E02, E03.8, E03.9, E05.90, E07.9)	96 (8.4)	79 (12.3)	17 (3.4)	**<.01**[a]
18-24	2 (2.0)	2 (2.5)	0 (0.0)	0.14[b]
25-44	38 (39.6)	33 (41.8)	5 (29.4)	
45-64	40 (41.7)	34 (43.0)	6 (35.3)	
65+	16 (16.7)	10 (12.7)	6 (35.3)	
Gastric reflux (K21)	84 (7.4)	50 (7.8)	34 (6.8)	0.54[a]
18-24	3 (3.6)	2 (4.0)	1 (2.9)	0.83[b]
25-44	33 (39.3)	21 (42.0)	12 (35.3)	
45-64	25 (29.8)	13 (26.0)	12 (35.3)	
65+	23 (27.3)	14 (28.0)	9 (26.5)	
Polycystic ovarian syndrome (E28.2)	69 (6.1)	69 (6.1)	-	-
18-24	8 (11.6)	8 (11.6)	-	
25-44	49 (71.0)	49 (71.0)	-	
45-64	10 (14.5)	10 (14.5)	-	
65+	2 (2.9)	2 (2.9)	-	
Asthma (J45)	65 (5.7)	35 (5.5)	30 (6.0)	0.68[a]
18-24	14 (21.5)	8 (22.9)	6 (20.0)	0.82[b]
25-44	29 (44.6)	14 (40.0)	15 (50.0)	
45-64	16 (24.6)	10 (28.6)	6 (20.0)	
65+	6 (9.3)	3 (8.5)	3 (10.0)	
Irritable Bowel syndrome (K58)	55 (4.8)	47 (7.3)	8 (1.6)	**<.01**[a]
18-24	4 (7.3)	3 (6.4)	1 (12.5)	0.64[b]
25-44	23 (41.8)	19 (40.4)	4 (50.0)	
45-64	21 (38.2)	18 (38.3)	3 (37.5)	
65+	7 (12.7)	7 (14.9)	0 (0.0)	
Depression (F32, F33)	39 (3.4)	29 (4.5)	10 (2.0)	**0.02**[a]
18-24	5 (12.8)	4 (13.8)	1 (10.0)	0.32[b]
25-44	14 (35.9)	9 (31.0)	5 (50.0)	
45-64	16 (41.0)	14 (48.3)	2 (20.0)	
65+	4 (10.3)	2 (6.9)	2 (20.0)	
Glaucoma/Cataract (H40, H25)	39 (3.4)	15 (2.3)	24 (4.8)	**0.02**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.13[b]
25-44	3 (7.7)	0 (0.0)	3 (12.5)	
45-64	4 (10.3)	3 (1.7)	1 (4.2)	
65+	32 (82.0)	12 (19.7)	20 (83.3)	
Blindness/Low vision (H54.0)	38 (3.3)	22 (3.4)	16 (3.2)	0.85[a]
18-24	5 (13.2)	3 (13.6)	2 (12.5)	**0.02**[b]
25-44	10 (26.3)	9 (41.0)	1 (6.2)	
45-64	7 (18.4)	5 (22.7)	2 (12.5)	
65+	16 (42.1)	5 (22.7)	11 (68.8)	

Rheumatoid arthritis (MO6.9)	32 (2.8)	22 (68.8)	10 (31.3)	0.15[a]
18-24	1 (3.1)	1 (4.5)	0 (0.0)	0.13[b]
25-44	4 (12.5)	1 (4.5)	3 (30.0)	
45-64	13 (40.6)	11 (50.0)	2 (20.0)	
65+	14 (43.8)	9 (41.0)	5 (50.0)	
Chronic Sinusitis (J32)	29 (2.5)	19 (3.0)	10 (2.0)	0.31
18-24	3 (10.3)	2 (10.5)	1 (10.0)	0.30
25-44	14 (48.3)	8 (42.1)	6 (60.0)	
45-64	11 (37.9)	9 (47.4)	2 (20.0)	
65+	1 (3.5)	0 (0.0)	1 (10.0)	
Inflammatory bowel disease/ chronic enteritis/ ulcerative colitis (K50-K52)	32 (2.8)	21 (3.3)	11 (2.2)	0.28[a]
18-24	1 (3.1)	1 (4.8)	0 (0.0)	0.67[b]
25-44	9 (28.1)	7 (33.3)	2 (18.2)	
45-64	12 (37.5)	7 (33.3)	5 (45.4)	
65+	10 (31.3)	6 (28.6)	4 (36.4)	
Type II diabetes mellitus (E11)	25 (2.2)	13 (2.0)	12 (2.4)	**0.02**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.46[b]
25-44	4 (16.0)	2 (15.4)	2 (16.7)	
45-64	7 (37.5)	5 (38.5)	2 (16.7)	
65+	14 (54.1)	6 (46.1)	8 (66.6)	
Chronic Bronchitis (J41, J42)	25 (2.2)	13 (2.0)	12 (2.4)	0.66
18-24	3 (12.0)	2 (15.4)	1 (8.4)	0.40
25-44	11 (44.0)	7 (53.8)	4 (33.3)	
45-64	6 (24.0)	3 (23.1)	3 (25.0)	
65+	5 (20.0)	1 (7.7)	4 (33.3)	
Type I diabetes mellitus (E10)	24 (2.1)	8 (1.3)	16 (3.2)	0.66[a]
18-24	1 (4.2)	1 (12.5)	0 (0.0)	0.31[b]
25-44	1 (4.2)	0 (0.0)	1 (6.2)	
45-64	9 (37.5)	4 (50.0)	5 (31.3)	
65+	13 (54.1)	3 (37.5)	10 (62.5)	
Heart failure (I50)	16 (1.4)	8 (1.3)	8 (1.6)	0.60[a]
18-24	1 (6.3)	1 (12.5)	0 (0.0)	
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	5 (31.2)	2 (25.0)	3 (37.5)	
65+	10 (62.5)	5 (62.5)	5 (62.5)	
Atrial fibrillation (I48.91)	11 (1.0)	5 (0.8)	6 (1.2)	0.46[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.23[b]
25-44	2 (18.2)	2 (40.0)	0 (0.0)	
45-64	1 (27.3)	1 (20.0)	2 (33.3)	
65+	5 (54.5)	2 (40.0)	4 (66.7)	

Chronic kidney disease (N18.9)	11 (1.0)	7 (1.1)	4 (0.8)	0.63[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.47[b]
25-44	2 (18.2)	2 (28.5)	0 (0.0)	
45-64	5 (45.4)	3 (43.0)	2 (50.0)	
65+	4 (36.4)	2 (28.5)	2 (50.0)	
Breast cancer (C50.9)	11 (1.0)	11 (1.7)	0 (0.0)	-
18-24	0 (0.0)	0 (0.0)	0 (0.0)	
25-44	1 (9.1)	1 (9.1)	0 (0.0)	
45-64	6 (54.5)	6 (54.5)	0 (0.0)	
65+	4 (36.4)	4 (36.4)	0 (0.0)	
Hearing loss/Deafness (H90, H91)	10 (0.9)	5 (0.8)	5 (1.0)	0.68[a]
18-24	1 (10.0)	1 (20.0)	0 (0.0)	0.57[b]
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	2 (20.0)	1 (20.0)	1 (20.0)	
65+	7 (70.0)	3 (60.0)	4 (80.0)	
Erectile dysfunction (N52.9)	9 (0.8)	-	9 (1.8)	-
18-24	0 (0.0)	-	0 (0.0)	
25-44	1 (11.1)	-	1 (11.1)	
45-64	3 (33.3)	-	3 (33.3)	
65+	5 (55.6)	-	5 (55.6)	
Angina (I20.9)	8 (0.7)	3 (0.5)	5 (1.0)	0.28 [a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.10 [b]
25-44	2 (25.0)	2 (66.7)	0 (0.0)	
45-64	1 (12.5)	0 (0.0)	1 (20.0)	
65+	5 (62.5)	1 (33.3)	4 (80.0)	
Coronary heart disease (I25.1)	7 (0.6)	1 (0.2)	6 (1.2)	**0.02**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.35[b]
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	4 (57.1)	1 (100.0)	3 (50.0)	
65+	3 (42.9)	0 (0.0)	3 (50.0)	
Prostate cancer (C61)	7 (0.6)	-	7 (1.4)	-
18-24	0 (0.0)	-	0 (0.0)	
25-44	0 (0.0)	-	0 (0.0)	
45-64	2 (28.6)	-	2 (28.6)	
65+	5 (71.4)	-	5 (71.4)	
Anorexia/Bulimia (F50.0, F50.2)	6 (0.5)	6 (0.9)	0 (0.0)	**0.03**[a]
18-24	2 (33.3)	2 (33.3)	0 (0.0)	-
25-44	1 (16.7)	1 (16.7)	0 (0.0)	
45-64	3 (50.0)	3 (50.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Crohn's disease (K50)	6 (0.5)	4 (0.6)	2 (0.4)	0.61[a]

18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.08[b]
25-44	3 (50.0)	1 (25.0)	2 (100.0)	
45-64	3 (50.0)	3 (75.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Epileptic (G40.909)	5 (0.4)	2 (0.3)	3 (0.6)	0.46[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.36[b]
25-44	4 (80.0)	2 (100.0)	2 (66.7)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	1 (20.0)	0 (0.0)	1 (33.3)	
Chronic Obstructive Pulmonary Disease (K50-52)	4 (0.3)	1 (0.2)	3 (0.6)	0.21
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.14
25-44	1 (25.0)	0 (0.0)	1 (33.3)	
45-64	1 (25.0)	1 (100.0)	0 (0.0)	
65+	2 (50.0)	0 (0.0)	2 (66.7)	
Cervical cancer (C53.9)	2 (0.2)	2 (0.3)	-	-
18-24	0 (0.0)	0 (0.0)	-	
25-44	0 (0.0)	0 (0.0)	-	
45-64	1 (50.0)	1 (50.0)	-	
65+	1 (50.0)	1 (50.0)	-	
Chronic hepatitis (K73)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	2 (100.0)	0 (0.0)	2 (100.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Cirrhosis (K74.60)	2 (0.2)	2 (0.3)	0 (0.0)	0.21[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	1 (50.0)	1 (50.0)	0 (0.0)	
65+	1 (50.0)	1 (50.0)	0 (0.0)	
HIV (B20)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (50.0)	0 (0.0)	1 (50.0)	
45-64	1 (50.0)	0 (0.0)	1 (50.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Dementia/Alzheimer disease (G30.9, F03)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	2 (100.0)	0 (0.0)	2 (100.0)	
Parkinson disease (G20)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]

18-24	0 (0.0)	0 (0.0)	0 (0.0)	
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	2 (100.0)	0 (0.0)	2 (100.0)	
Colon cancer (C18.9)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	1 (100.0)	1 (100.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Melanoma (C43)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	1 (100.0)	1 (100.0)	0 (0.0)	
Lupus (M32.9)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (100.0)	1 (100.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Multiple sclerosis (G35)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (100.0)	1 (100.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Leukemia (C95.9)	1 (0.1)	0 (0.0)	1 (0.2)	0.26[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (100.0)	0 (0.0)	1 (100.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Urinary cancer (C67)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	1 (100.0)	1 (100.0)	0 (0.0)	
Schizophrenia/Bipolar (F20.9, F31.9)	0 (0.0)	0 (0.0)	0 (0.0)	-
18-24	0 (0.0)	0 (0.0)	0 (0.0)	
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Ovarian cancer (C56.9)	0 (0.0)	0 (0.0)	-	-
18-24	0 (0.0)	0 (0.0)	-	

25-44	0 (0.0)	0 (0.0)	-	
45-64	0 (0.0)	0 (0.0)	-	
65+	0 (0.0)	0 (0.0)	-	
Abbreviations: SD, standard deviation; Bold values represent p < 0.05; [a] Differences between men and women were evaluated by the chi-square test; [b] Differences between men and women among the four age groups of the study were evaluated by the chi-square test; [c] Differences between men and women were evaluated by the t- test.				

Figure 3.5: Prevalence of hyperlipidemia among individuals with multimorbidity and without multimorbidity.

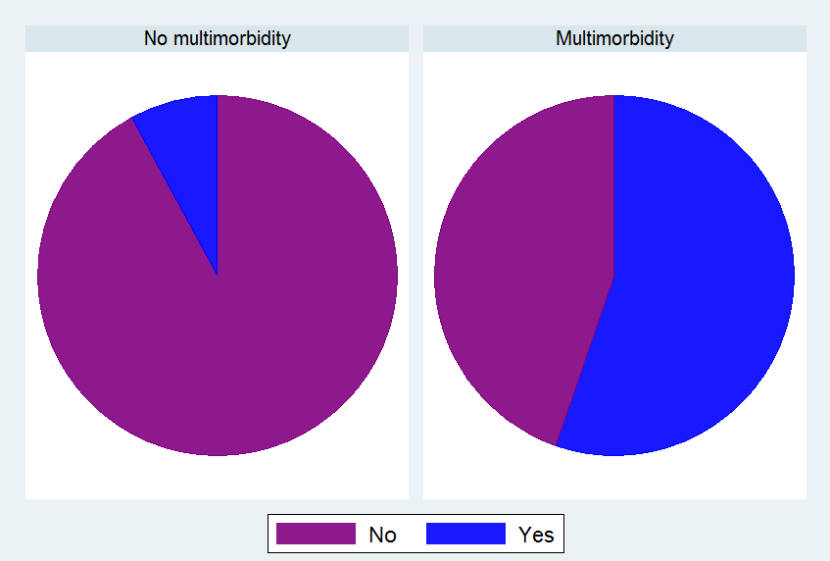


Figure 3.6: Prevalence of hypertension among multimorbidity and no-multimorbidity individuals.

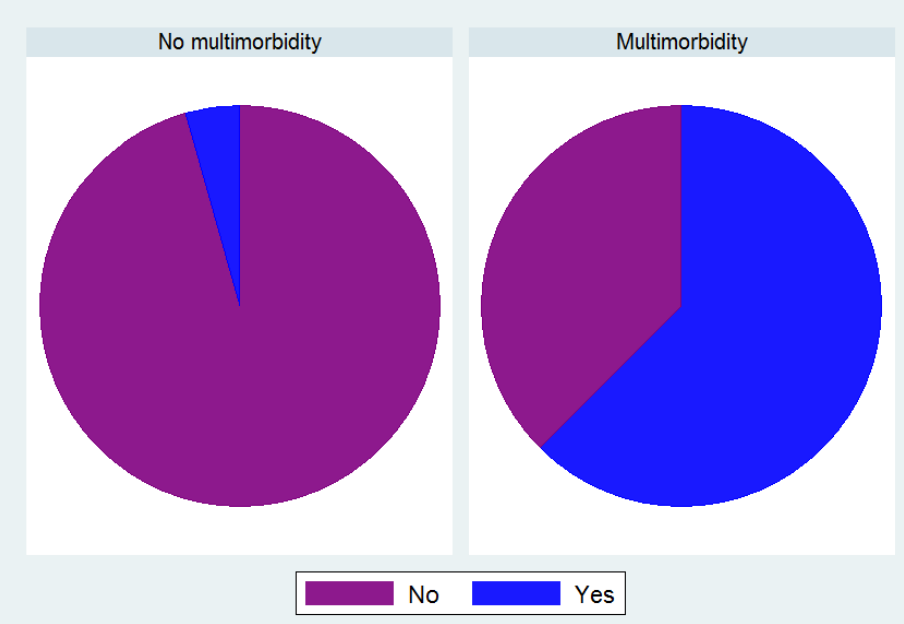
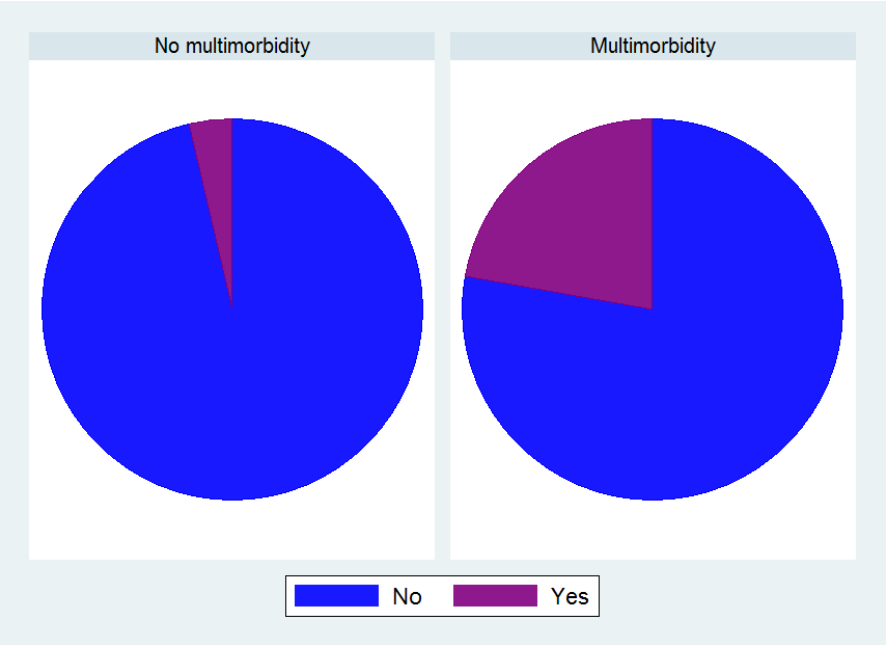


Figure 3.7: Prevalence of thyroid diseases among multimorbidity and no-multimorbidity individuals.



Among men, the most prevalent chronic diseases were hyperlipidemia (20%), hypertension (17%), and gastric reflux (7%), while among women these were hyperlipidemia (16%), thyroid diseases (12%), and hypertension (10%). We found statistically significant differences of hypertension prevalence between sex ($p<0.01$) as well as of thyroid diseases ($p<0.01$), irritable bowel syndrome ($p<0.01$), depression ($p=0.02$), glaucoma/cataract ($p=0.02$), diabetes type I ($p=0.02$), coronary heart disease ($p=0.02$), and anorexia/bulimia ($p=0.03$). More specifically, among women a higher prevalence of thyroid diseases, irritable bowel syndrome, depression, and anorexia/bulimia was reported compared to men. On the other hand, among men we observed a higher prevalence of hypertension, glaucoma/cataract, diabetes type I, and coronary heart disease compared to women (***Table 3.6***). In addition, the most prevalent type of cancer was prostate cancer for men and breast cancer for women.

Table 3.6 also provides the prevalence of different chronic diseases by sex and age groups. We found that among women with hyperlipidemia the largest percentage was reported in individuals aged 45-64 years old (50%) whereas among men the corresponding percentage was 38%. Furthermore, among men with hyperlipidemia, we reported largest number of individuals in age groups 45-64 and 65+ years old (***Table 3.6***).

Table 3.7: Crude prevalence of chronic diseases overall as well as by gender and age group.

Chronic diseases	**Overall** (N=1140)	**Women** (N=643) [N (%)]	**Men** (N=497) [N (%)]	**p-value**
Number of co-morbidities (mean ± SD)	1.07 ± 1.49	1.14 ± 1.48	0.98 ± 1.49	0.07[c]
Hyperlipidemia (E78.5)	198 (17.4)	100 (15.6)	98 (19.8)	0.07[a]
18-24	5 (2.6)	5 (5.0)	0 (0.0)	0.02[b]
25-44	44 (22.2)	18 (18.0)	26 (26.5)	
45-64	87 (43.9)	50 (50.0)	37 (37.8)	
65+	62 (31.3)	27 (27.0)	35 (35.7)	
Hypertension (I10)	147(12.9)	64 (10.0)	83 (16.7)	**<.01**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.69[b]
25-44	15(10.2)	5 (7.8)	10 (12.0)	
45-64	68 (42.3)	31 (48.4)	37 (44.6)	
65+	64 (43.5)	28 (43.8)	36 (43.4)	
Thyroid diseases (E02, E03.8, E03.9, E05.90, E07.9)	96 (8.4)	79 (12.3)	17 (3.4)	**<.01**[a]
18-24	2 (2.0)	2 (2.5)	0 (0.0)	0.14[b]
25-44	38 (39.6)	33 (41.8)	5 (29.4)	
45-64	40 (41.7)	34 (43.0)	6 (35.3)	
65+	16 (16.7)	10 (12.7)	6 (35.3)	
Gastric reflux (K21)	84 (7.4)	50 (7.8)	34 (6.8)	0.54[a]
18-24	3 (3.6)	2 (4.0)	1 (2.9)	0.83[b]
25-44	33 (39.3)	21 (42.0)	12 (35.3)	

45-64	25 (29.8)	13 (26.0)	12 (35.3)	
65+	23 (27.3)	14 (28.0)	9 (26.5)	
Polycystic ovarian syndrome (E28.2)	69 (6.1)	69 (6.1)	-	-
18-24	8 (11.6)	8 (11.6)	-	
25-44	49 (71.0)	49 (71.0)	-	
45-64	10 (14.5)	10 (14.5)	-	
65+	2 (2.9)	2 (2.9)	-	
Asthma (J45)	65 (5.7)	35 (5.5)	30 (6.0)	0.68[a]
18-24	14 (21.5)	8 (22.9)	6 (20.0)	0.82[b]
25-44	29 (44.6)	14 (40.0)	15 (50.0)	
45-64	16 (24.6)	10 (28.6)	6 (20.0)	
65+	6 (9.3)	3 (8.5)	3 (10.0)	
Irritable Bowel syndrome (K58)	55 (4.8)	47 (7.3)	8 (1.6)	**<.01**[a]
18-24	4 (7.3)	3 (6.4)	1 (12.5)	0.64[b]
25-44	23 (41.8)	19 (40.4)	4 (50.0)	
45-64	21 (38.2)	18 (38.3)	3 (37.5)	
65+	7 (12.7)	7 (14.9)	0 (0.0)	
Depression (F32, F33)	39 (3.4)	29 (4.5)	10 (2.0)	**0.02**[a]
18-24	5 (12.8)	4 (13.8)	1 (10.0)	0.32[b]
25-44	14 (35.9)	9 (31.0)	5 (50.0)	
45-64	16 (41.0)	14 (48.3)	2 (20.0)	
65+	4 (10.3)	2 (6.9)	2 (20.0)	
Glaucoma/Cataract (H40, H25)	39 (3.4)	15 (2.3)	24 (4.8)	**0.02**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.13[b]

25-44	3 (7.7)	0 (0.0)	3 (12.5)	
45-64	4 (10.3)	3 (1.7)	1 (4.2)	
65+	32 (82.0)	12 (19.7)	20 (83.3)	
Blindness/Low vision (H54.0)	38 (3.3)	22 (3.4)	16 (3.2)	0.85[a]
18-24	5 (13.2)	3 (13.6)	2 (12.5)	**0.02**[b]
25-44	10 (26.3)	9 (41.0)	1 (6.2)	
45-64	7 (18.4)	5 (22.7)	2 (12.5)	
65+	16 (42.1)	5 (22.7)	11 (68.8)	
Rheumatoid arthritis (MO6.9)	32 (2.8)	22 (68.8)	10 (31.3)	0.15[a]
18-24	1 (3.1)	1 (4.5)	0 (0.0)	0.13[b]
25-44	4 (12.5)	1 (4.5)	3 (30.0)	
45-64	13 (40.6)	11 (50.0)	2 (20.0)	
65+	14 (43.8)	9 (41.0)	5 (50.0)	
Chronic Sinusitis (J32)	29 (2.5)	19 (3.0)	10 (2.0)	0.31
18-24	3 (10.3)	2 (10.5)	1 (10.0)	0.30
25-44	14 (48.3)	8 (42.1)	6 (60.0)	
45-64	11 (37.9)	9 (47.4)	2 (20.0)	
65+	1 (3.5)	0 (0.0)	1 (10.0)	
Inflammatory bowel disease/ chronic enteritis/ ulcerative colitis (K50-K52)	32 (2.8)	21 (3.3)	11 (2.2)	0.28[a]
18-24	1 (3.1)	1 (4.8)	0 (0.0)	0.67[b]
25-44	9 (28.1)	7 (33.3)	2 (18.2)	
45-64	12 (37.5)	7 (33.3)	5 (45.4)	
65+	10 (31.3)	6 (28.6)	4 (36.4)	

Type I diabetes mellitus (E11)	25 (2.2)	13 (2.0)	12 (2.4)	**0.02**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.46[b]
25-44	4 (16.0)	2 (15.4)	2 (16.7)	
45-64	7 (37.5)	5 (38.5)	2 (16.7)	
65+	14 (54.1)	6 (46.1)	8 (66.6)	
Chronic Bronchitis (J41, J42)	25 (2.2)	13 (2.0)	12 (2.4)	0.66
18-24	3 (12.0)	2 (15.4)	1 (8.4)	0.40
25-44	11 (44.0)	7 (53.8)	4 (33.3)	
45-64	6 (24.0)	3 (23.1)	3 (25.0)	
65+	5 (20.0)	1 (7.7)	4 (33.3)	
Type I diabetes mellitus (E10)	24 (2.1)	8 (1.3)	16 (3.2)	0.66[a]
18-24	1 (4.2)	1 (12.5)	0 (0.0)	0.31[b]
25-44	1 (4.2)	0 (0.0)	1 (6.2)	
45-64	9 (37.5)	4 (50.0)	5 (31.3)	
65+	13 (54.1)	3 (37.5)	10 (62.5)	
Heart failure (I50)	16 (1.4)	8 (1.3)	8 (1.6)	0.60[a]
18-24	1 (6.3)	1 (12.5)	0 (0.0)	
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	5 (31.2)	2 (25.0)	3 (37.5)	
65+	10 (62.5)	5 (62.5)	5 (62.5)	
Atrial fibrillation (I48.91)	11 (1.0)	5 (0.8)	6 (1.2)	0.46[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.23[b]
25-44	2 (18.2)	2 (40.0)	0 (0.0)	
45-64	1 (27.3)	1 (20.0)	2 (33.3)	

65+	5 (54.5)	2 (40.0)	4 (66.7)	
Chronic kidney disease (N18.9)	11 (1.0)	7 (1.1)	4 (0.8)	0.63[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.47[b]
25-44	2 (18.2)	2 (28.5)	0 (0.0)	
45-64	5 (45.4)	3 (43.0)	2 (50.0)	
65+	4 (36.4)	2 (28.5)	2 (50.0)	
Breast cancer (C50.9)	11 (1.0)	11 (1.7)	0 (0.0)	-
18-24	0 (0.0)	0 (0.0)	0 (0.0)	
25-44	1 (9.1)	1 (9.1)	0 (0.0)	
45-64	6 (54.5)	6 (54.5)	0 (0.0)	
65+	4 (36.4)	4 (36.4)	0 (0.0)	
Hearing loss/Deafness (H90, H91)	10 (0.9)	5 (0.8)	5 (1.0)	0.68[a]
18-24	1 (10.0)	1 (20.0)	0 (0.0)	0.57[b]
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	2 (20.0)	1 (20.0)	1 (20.0)	
65+	7 (70.0)	3 (60.0)	4 (80.0)	
Erectile dysfunction (N52.9)	9 (0.8)	-	9 (1.8)	-
18-24	0 (0.0)	-	0 (0.0)	
25-44	1 (11.1)	-	1 (11.1)	
45-64	3 (33.3)	-	3 (33.3)	
65+	5 (55.6)	-	5 (55.6)	
Angina (I20.9)	8 (0.7)	3 (0.5)	5 (1.0)	0.28 [a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.10 [b]
25-44	2 (25.0)	2 (66.7)	0 (0.0)	

45-64	1 (12.5)	0 (0.0)	1 (20.0)	
65+	5 (62.5)	1 (33.3)	4 (80.0)	
Coronary heart disease (I25.1)	7 (0.6)	1 (0.2)	6 (1.2)	**0.02**[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.35[b]
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	4 (57.1)	1 (100.0)	3 (50.0)	
65+	3 (42.9)	0 (0.0)	3 (50.0)	
Prostate cancer (C61)	7 (0.6)	-	7 (1.4)	-
18-24	0 (0.0)	-	0 (0.0)	
25-44	0 (0.0)	-	0 (0.0)	
45-64	2 (28.6)	-	2 (28.6)	
65+	5 (71.4)	-	5 (71.4)	
Anorexia/Bulimia (F50.0, F50.2)	6 (0.5)	6 (0.9)	0 (0.0)	**0.03**[a]
18-24	2 (33.3)	2 (33.3)	0 (0.0)	-
25-44	1 (16.7)	1 (16.7)	0 (0.0)	
45-64	3 (50.0)	3 (50.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Crohn's disease (K50)	6 (0.5)	4 (0.6)	2 (0.4)	0.61[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.08[b]
25-44	3 (50.0)	1 (25.0)	2 (100.0)	
45-64	3 (50.0)	3 (75.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Epileptic (G40.909)	5 (0.4)	2 (0.3)	3 (0.6)	0.46[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.36[b]

25-44	4 (80.0)	2 (100.0)	2 (66.7)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	1 (20.0)	0 (0.0)	1 (33.3)	
Chronic Obstructive Pulmonary Disease (K50-52)	4 (0.3)	1 (0.2)	3 (0.6)	0.21
18-24	0 (0.0)	0 (0.0)	0 (0.0)	0.14
25-44	1 (25.0)	0 (0.0)	1 (33.3)	
45-64	1 (25.0)	1 (100.0)	0 (0.0)	
65+	2 (50.0)	0 (0.0)	2 (66.7)	
Cervical cancer (C53.9)	2 (0.2)	2 (0.3)	-	-
18-24	0 (0.0)	0 (0.0)	-	
25-44	0 (0.0)	0 (0.0)	-	
45-64	1 (50.0)	1 (50.0)	-	
65+	1 (50.0)	1 (50.0)	-	
Chronic hepatitis (K73)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	2 (100.0)	0 (0.0)	2 (100.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Cirrhosis (K74.60)	2 (0.2)	2 (0.3)	0 (0.0)	0.21[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	1 (50.0)	1 (50.0)	0 (0.0)	
65+	1 (50.0)	1 (50.0)	0 (0.0)	
HIV (B20)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]

18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (50.0)	0 (0.0)	1 (50.0)	
45-64	1 (50.0)	0 (0.0)	1 (50.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Dementia/Alzheimer disease (G30.9, F03)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	2 (100.0)	0 (0.0)	2 (100.0)	
Parkinson disease (G20)	2 (0.2)	0 (0.0)	2 (0.4)	0.11[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	2 (100.0)	0 (0.0)	2 (100.0)	
Colon cancer (C18.9)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	1 (100.0)	1 (100.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Melanoma (C43)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	1 (100.0)	1 (100.0)	0 (0.0)	

Lupus (M32.9)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (100.0)	1 (100.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Multiple sclerosis (G35)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (100.0)	1 (100.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Leukemia (C95.9)	1 (0.1)	0 (0.0)	1 (0.2)	0.26[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	1 (100.0)	0 (0.0)	1 (100.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	0 (0.0)	0 (0.0)	0 (0.0)	
Urinary cancer (C67)	1 (0.1)	1 (0.2)	0 (0.0)	0.38[a]
18-24	0 (0.0)	0 (0.0)	0 (0.0)	-
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	
65+	1 (100.0)	1 (100.0)	0 (0.0)	
Schizophrenia/Bipolar (F20.9, F31.9)	0 (0.0)	0 (0.0)	0 (0.0)	-
18-24	0 (0.0)	0 (0.0)	0 (0.0)	
25-44	0 (0.0)	0 (0.0)	0 (0.0)	
45-64	0 (0.0)	0 (0.0)	0 (0.0)	

65+	0 (0.0)	0 (0.0)	0 (0.0)	
Ovarian cancer (C56.9)	0 (0.0)	0 (0.0)	-	-
18-24	0 (0.0)	0 (0.0)	-	
25-44	0 (0.0)	0 (0.0)	-	
45-64	0 (0.0)	0 (0.0)	-	
65+	0 (0.0)	0 (0.0)	-	

Abbreviations: SD, standard deviation; Bold values represent $p < 0.05$; [a] Differences between males and females were evaluated by the chi-square test; [b] Differences between males and females among the four age groups of the study were evaluated by the chi-square test; [c] Differences between males and females were evaluated by the t- test.

The most prevalent chronic diseases were diseases of the circulatory system (30%), followed by the endocrine system (21%), digestive-excretory system (15%), nervous system (13%), and respiratory system (11%) (***Table 3.7***). We reported statistically significant differences in circulatory, endocrine, digestive/excretory, immune and reproductive systems between men and women ($p<0.01$). Specifically, we observed a larger percentage of men in diseases of the circulatory and reproductive systems compared to women (40% vs. 23% and 2% vs. 0%). On the other hand, we observed a larger percentage of women in diseases of the endocrine, digestive/excretory and immune systems compared to men (26% vs. 11%, 16% vs. 13% and 5% vs. 2%).

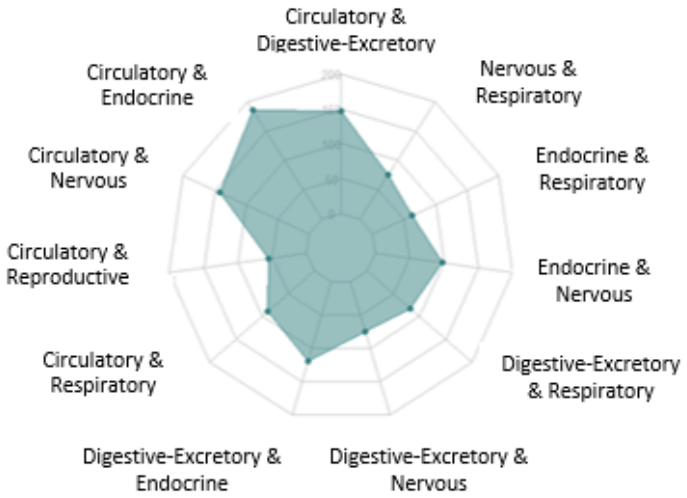
Table 3.8: Crude prevalence of diseases by human systems overall and by sex.

Human systems	**Overall** (N=955)	**Women** [N=583 (%)][a]	**Men** [N=372 (%)][b]	**p-value**
Circulatory	283 (29.6)	133 (22.8)	150 (40.3)	**<0.01**[c]
Endocrine	196 (20.5)	154 (26.4)	42 (11.3)	**<0.01**[c]
Digestive /Excretory	143 (15.0)	95 (16.3)	48 (12.9)	**<0.01**[c]
Nervous	119 (12.5)	71 (12.2)	48 (12.9)	0.45[c]
Respiratory	104 (10.9)	57 (9.8)	47 (12.6)	0.74[c]
Immune	35 (3.7)	28 (4.8)	7 (1.9)	**<0.01**[c]
Skeletal/Muscular	32 (3.3)	22 (3.8)	10 (2.7)	0.15[c]
Neoplasm	23 (2.4)	16 (2.7)	7 (1.9)	0.20[c]
Renal/Urinary	11 (1.2)	7 (1.2)	4 (1.1)	0.63[c]
Reproductive	9 (0.9)	0 (0.0)	9 (2.4)	**<0.01**[c]

Bold values represent $p < 0.05$; [a] N=total number women who were reported with at least one chronic disease of a human system); [b] N=total number men who were reported with at least one chronic disease of a human system); [c] Differences between men and women were evaluated by the chi-square test.

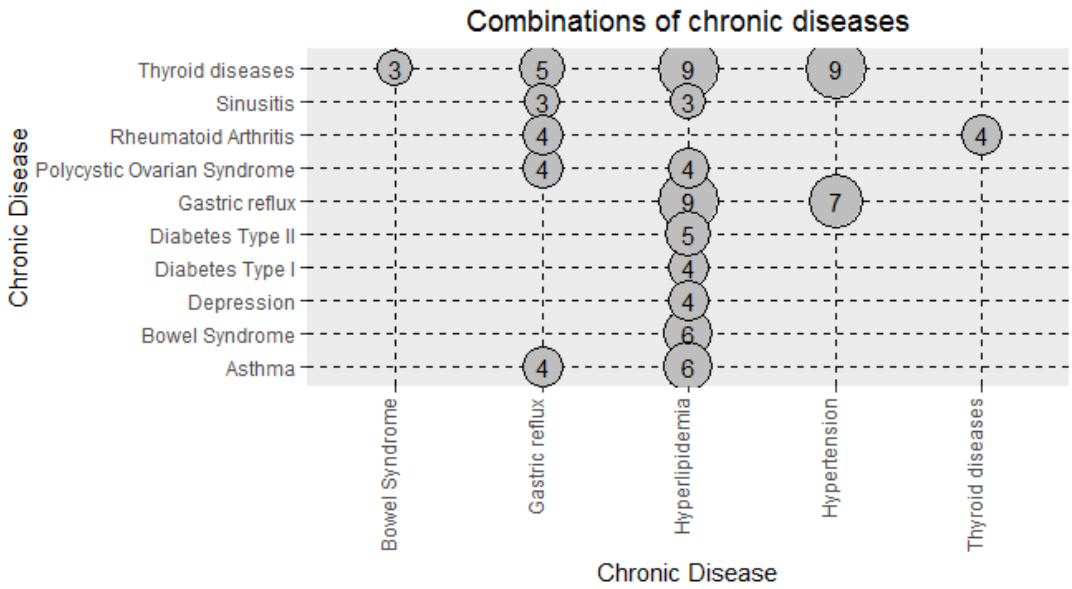
We found all the combinations between the human systems' diseases among people with multimorbidity, in order to identify the diseases of human systems, which are presented more together in multimorbidity individuals. Specifically, we found 36 combinations of human systems' diseases, which are presented in ***Appendix Table 6***. Hence, we found that the most prevalent conditions in this group were diseases of circulatory/endocrine systems, followed by circulatory/digestive-excretory systems, and circulatory/nervous systems. Specifically, the most common combinations among people with multimorbidity were diseases of the circulatory and endocrine systems (25%), followed by circulatory and digestive-excretory systems (20%), circulatory and nervous systems (19%) (***Figure 3.8***).

Figure 3.8: Combinations of human systems' diseases among people with multimorbidity.



Apart from the combinations between the human systems' diseases among people with multimorbidity, we also found the combinations between the specific 47 chronic diseases among people with multimorbidity. The most prevalent combinations of chronic diseases were hyperlipidemia-thyroid diseases (9%), hypertension- thyroid diseases (9%), and hyperlipidemia-gastric reflux (8%) (***Figure 3.9***).

Figure 3.9: Combinations of chronic diseases among people with multimorbidity.



3.1.6 Factors associated with multimorbidity

Multivariable linear regression analysis was performed to evaluate the significance of different factors (age, sex, marital status, educational level, salary categories, physical activity, smoking, and BMI) on the average number of chronic diseases per individual (***Table 3.8***).

We reported a positive association of age, being unmarried, and BMI with the number of chronic diseases present. More specifically, as the age ($p<0.01$) and BMI ($p=0.02$) increases, the number of chronic diseases in an individual increases too. On the other hand, we found an inverse association between being women and physical activity with the number of chronic diseases. Specifically, being a woman ($p<0.01$) and being physically active ($p=0.02$) decreases the number of chronic diseases an individual has.

Table 3.9: Multivariable linear regression analysis of number of morbidities.

Characteristics	**Coefficient**	**95% Confidence Interval**	**p-value**
Age (per 1 year)	0.04	0.03, 0.05	**<0.01**
Sex			
Men	*Ref*		
Women	-0.34	-0.51, -0.17	**<0.01**
Marital status			
Married	*Ref*	*Ref*	*Ref*
Unmarried	0.35	0.14, 0.56	**<0.01**
Divorced/widowed	0.28	-0.01, 0.56	0.06
Educational status (1:primary, 2:medium, 3: higher)	-0.12	-0.28, 0.04	0.16
Salary (1: low, 2: middle, 3: high)	0.09	-0.04, 0.22	0.17
Physically active			
No	*Ref*	*Ref*	
Yes	-0.19	-0.35, -0.03	**0.02**
Current smoker			
No	*Ref*	*Ref*	
Yes	0.04	-0.12, 0.20	0.64
BMI (per 1 kg/m^2)	0.02	0.00, 0.04	**0.02**
Abbreviations: Y, yes; N, no; BMI, Body Mass Index; Bold font indicates statistical significance ($p<0.05$).			

Discriminant classification analysis, with the calculation of the Wilk's lambda and the Fisher's classification function coefficients, was used to explore the patterns of characteristics of people with multimorbidity. A value of the Wilk's lambda close to 1, indicates better discriminating ability. The Wilk's lambda was equal to 0.776 ($p<0.01$), a value close to 1, which indicates that the estimated model has the ability to classify people in the different multimorbidity classes efficiently. Discriminant analysis revealed that in individuals with 2-morbidities increased age, and higher BMI contributes more in their categorization as having 2-comorbidities compared to none or 1-morbidity (***Table 3.9***). Similarly, in individuals with 3-morbidities increased age, current smoking, and higher salary are the dominant factors to characterize those participants, whereas, among individuals with >3-morbidities, men sex, higher salary, and increased BMI seems to characterize them better.

Table 3.10: Hierarchical discriminant analysis.

Characteristics	**2-morbidities** (N=129)	**3-morbidities** (N=70)	**>3-morbidities** (N=94)
Age (per 1 year)	0.98	0.14	-0.29
Sex			
Men	*Ref*	*Ref*	
Women	-0.33	0.22	0.70
Marital status			
Married	-1.98	-0.97	-0.26
Unmarried	0.06	-1.57	-2.95
Educational status (1: primary, 2: medium, 3: higher)	-0.08	-0.40	-1.67
Salary (1: low, 2: moderate, 3: high)	0.05	0.18	0.15
Physically inactive			
No	*Ref*	*Ref*	
Yes	-0.10	-0.20	-0.23
Current smoker			
No	*Ref*	*Ref*	
Yes	0.09	0.32	0.02
BMI (per 1 kg/m^2)	0.16	-0.41	0.48
Abbreviations: Y, yes; N, no; BMI, Body Mass Index; Lambda (the closer to 1, the higher the discriminating ability) = 0.776**,** p-value<0.01			

Multinomial logistic regression was performed to evaluate the significance of different factors (marital status, educational level, salary categories, physical activity, smoking and BMI) on the level of multimorbidity (0 or 1 morbidities, 2 morbidities, 3 morbidities, more than 3 morbidities) after accounting for age and sex. The coefficients of variation within each region were 75%, 73%, 72%, 63%, and 73% for Nicosia, Limassol, Larnaka, Paphos, and Ammochostos, respectively. Moreover, the variability of between regions was only 1%.

The coefficients of the mixed effects multinomial regression model showed that the presence of 2 morbidities in an individual compared to none or 1 morbidity was associated with increased age and BMI. Similarly, the presence of 3 morbidities was associated with being a women, a current smoker, as well as with increased age and BMI. In addition, having 3 or more morbidities was associated with increased age, being women, being unmarried, and having completed a secondary education (***Table 3.10***).

Table 3.11: Multinomial regression of multimorbidity level (base outcome = 0 or 1 morbidities).

Characteristics	**Multimorbidity level**		
	2 morbidities[a]	**3 morbidities**[a]	**>3 morbidities**[a]
Age (per 1 year)	**0.04 (0.03, 0.06)**	**0.06 (0.04, 0.08)**	**0.08 (0.06, 0.10)**
Sex			
Men	*Ref*	*Ref*	*Ref*
Women	-0.41 (-0.86, 0.04)	**-1.24 (-1.90, -0.58)**	**-1.14 (-1.72, -0.55)**
Marital status			
Married	*Ref*	*Ref*	*Ref*
Unmarried	0.15 (-0.44, 0.75)	-0.65 (-1.63, 0.34)	**1.10 (0.33, 1.86)**
Divorced/widowed	0.16 (-0.49, 0.82)	-0.32 (-1.20, 0.56)	0.55 (-0.12, 1.22)
Educational status (1:primary, 2:medium, 3: higher)	-0.02 (-0.42, 0.38)	0.23 (-0.30, 0.76)	-0.18 (-0.64, 0.27)
Salary (1: low, 2: middle, 3: high)	0.09 (-0.24, 0.43)	0.13 (-0.31, 0.57)	0.37 (-0.03, 0.78)
Physically inactive			
No	*Ref*	*Ref*	*Ref*
Yes	-0.17 (-0.58, 0.25)	-0.07 (-0.63, 0.49)	-0.44 (-0.96, 0.08)
Current smoker			
No	*Ref*	*Ref*	*Ref*
Yes	0.24 (-0.18, 0.66)	**0.59 (0.02, 1.16)**	0.23 (-0.29, 0.75)
BMI (per 1 kg/m^2)	**0.05 (0.01, 0.09)**	**0.06 (0.01, 0.12)**	0.04 (-0.02, 0.09)
Abbreviations: Y, yes; N, no; BMI, Body Mass Index; Confidence Interval (CI), Bold values represent $p < 0.05$; [a] β (95% CI)			

4 Chapter 4 – Adherence to Mediterranean Diet and relationship to multimorbidity

4.1.1 Adherence to the Mediterranean Diet

The median Mediterranean Diet score of the participants was 15 (quartiles, q_1=13, q_3=18) with the maximum score being 34 and the minimum 5. The tertiles of adherence to a Mediterranean Diet were defined as follows: low adherence (score <13), moderate adherence (score 13-17), and high adherence (score >17). Specifically, 367 (32.7%) participants were in the low adherence to the Mediterranean Diet tertile, 413 (36.8%) participants were in the moderate adherence to the Mediterranean Diet tertile and 343 (30.5%) participants were in the high adherence to the Mediterranean Diet tertile.

We observed a higher median value of the Mediterranean Diet score in individuals aged 18-24 years old and those aged 65 years old and older compared to those who were 25-64 years old (***Table 4.1***). Furthermore, more women were in the low adherence tertile than the high adherence one (64% vs. 36%) compared to men (27% vs. 35%) ($p<0.01$) and the median value of the Mediterranean Diet score was 16 for men and 15 for women.

Similarly, a higher percentage of rural residents and physically active participants were in the high adherence tertile compared to the urban residents and physically inactive participants, respectively (both $p<0.05$). Among urban residents the smallest percentage of participants was in the high adherence tertile while among rural residents the smallest percentage was in the low adherence tertile and the largest in the high adherence tertile. Similarly, almost 35% of physically active individuals were in high adherence tertile compared to the corresponding tertile in physically inactive people (27%).

Other characteristics, such as geographical area and BMI, were similar among the three tertiles of adherence to the Mediterranean Diet (***Table 4.1***). Although we did not identify any statistically significant differences among the five geographical areas of Cyprus, it is important to note that the largest percentages in the high adherence tertile were observed in Paphos and Ammochostos areas, which are less urban regions.

Table 4.1: Adherence to Mediterranean Diet.

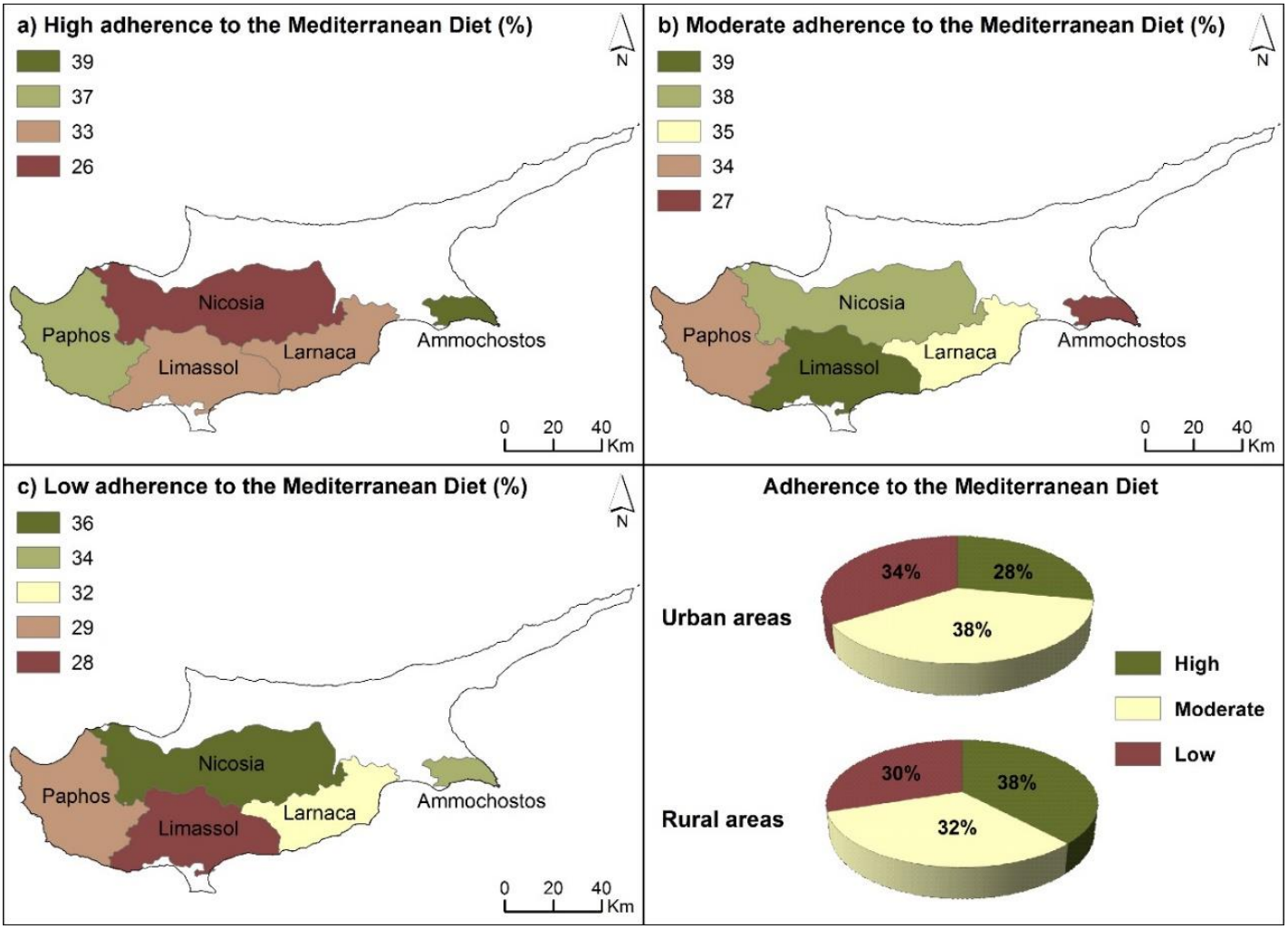
Characteristics	**Mediterranean Diet score**				**p-value**
	Overall[h] (N=1123)	**Low** (N=367)	**Moderate** (N=413)	**High** (N=343)	
Age group [N (%)][a]					
18-24	16 (13, 18)	45 (27.8)	65 (40.1)	52 (32.1)	0.26[i]
25-44	15 (13, 18)	170 (32.9)	184 (35.6)	163 (31.5)	
45-64	15 (12, 18)	115 (37.2)	106 (34.3)	88 (28.5)	
65+	16 (13, 18)	37 (27.4)	58 (43.0)	40 (29.6)	
Sex [N (%)][b]					
Men	16 (13, 19)	132 (26.8)	187 (38.0)	173 (35.2)	**<.01**[i]
Women	15 (12, 18)	235 (37.3)	226 (35.9)	169 (26.8)	
Geographical area [N (%)][c]					
Nicosia	15 (12, 18)	178 (36.4)	184 (37.6)	127 (26.0)	0.10[i]
Limassol	16 (13, 19)	86 (28.4)	118 (38.9)	99 (32.7)	
Larnaka	15 (13, 18)	54 (31.6)	60 (35.1)	57 (33.3)	
Paphos	16 (13, 19)	32 (29.4)	37 (33.9)	40 (36.7)	
Ammochostos	16 (13, 19)	17 (34.7)	13 (26.5)	19 (38.8)	
Residency [N (%)][d]					
Urban	15 (13, 18)	287 (33.8)	323 (38.0)	239 (28.2)	**0.01**[i]
Rural	16 (13, 18)	79 (29.6)	87 (32.6)	101 (37.8)	
Marital status [N (%)][d]					
Married	16 (13, 18)	178 (29.2)	242 (39.7)	189 (31.1)	**<.01**[i]
Unmarried	16 (13, 19)	132 (32.1)	144 (35.0)	135 (32.9)	
Divorced / Widowed	13 (10.5, 16)	54 (56.3)	25 (26.0)	17 (17.7)	
Educational level [N (%)][d]					
Primary education	16 (13, 18)	18 (27.3)	25 (37.9)	23 (34.8)	0.34[i]
Secondary education	15 (12, 18)	122 (36.5)	121 (36.2)	91 (27.3)	
Higher education	15 (13, 18)	224 (31.3)	265 (37.0)	227 (31.7)	
Salary [N (%)][e]					
Low	15 (13, 18)	82 (34.9)	85 (36.2)	68 (28.9)	0.24[i]
Middle	15 (13, 18)	190 (34.4)	191 (34.5)	172 (31.1)	
High	16 (13, 18)	93 (28.5)	135 (41.4)	98 (30.1)	
Physical activity [N (%)][f]					
No	16 (13, 19)	155 (29.1)	192 (36.1)	185 (34.8)	**<.01**[i]
Yes	15 (12, 18)	210 (36.0)	217 (37.2)	156 (26.8)	
Current smoker [N (%)][a]					
No	15 (13, 18)	141 (35.3)	140 (35.1)	118 (29.6)	0.37[i]
Yes	16 (13, 18)	224 (31.2)	271 (37.8)	222 (31.0)	
BMI group [N (%)][g]					

Underweight	16 (13, 19)	14 (34.1)	12 (29.3)	15 (36.6)	0.56[i]
Normal	15 (13, 18)	176 (31.6)	210 (37.8)	170 (30.6)	
Overweight	15 (13, 18)	115 (32.4)	139 (39.2)	101 (28.4)	
Obese	15.5 (12, 18)	56 (36.8)	47 (30.9)	49 (37.3)	
Bold values represent $p < 0.05$; [a] N=1123; [b]N=1122; [c]N=1121; [d]N=1116; [e]N=1114; [f]N=1115; [g]N=1104; [h]Median (IQR); [i]Differences between Mediterranean Diet adherence tertiles were evaluated by the Chi2 test.					

In order to assess the spatial distribution of the adherence to the Mediterranean Diet in the general population in Cyprus, the parameter of spatial heterogeneity was accounted for and the analysis was based on the districts of Cyprus (Nicosia, with total population 332,200; Limassol, 239,400; Larnaca, 144,900; Paphos, 91,300; and Ammochostos, 47,000).

Mapping Mediterranean Diet adherence across Cypriot districts exhibited higher rates of high adherence in Ammochostos and Paphos (39% and 37% respectively), and lower rates in the other districts (***Figure 4.1a***). It is important to mention, as mentioned above, that Ammochostos is primarily a rural area as well as Paphos in its largest part. The lowest adherence to Mediterranean Diet was seen in the capital of Cyprus, Nicosia district (***Figure 4.1a*** *and* ***Figure 4.1c***). Rural areas were characterized by higher adherence to Mediterranean Diet. Specifically, high adherence was 10% higher in rural areas than urban areas (38% vs. 28%), which were characterized primarily with low and moderate adherence (38% and 34%, respectively) (***Figure 4.1d***).

Figure 4.1: Spatial analysis of Mediterranean Diet adherence by region of residence and level of urban city.



When considering factors which may affect the Mediterranean Diet score in the population, including age, sex, geographical area, residency, marital, educational and salary status, physical activity levels, smoking habits, and BMI, we observed that being divorced/widowed compared to being married as well as people who completed a secondary education compared to people having primary education was associated with a lower score ($p<0.05$). On the other hand, being women, being from Limassol or Paphos compared to Nicosia, living in a rural region, and being are physically active were associated with a higher score (***Table 4.2***).

Table 4.2: Multivariate linear regression for the factors associated with the Mediterranean Diet score.

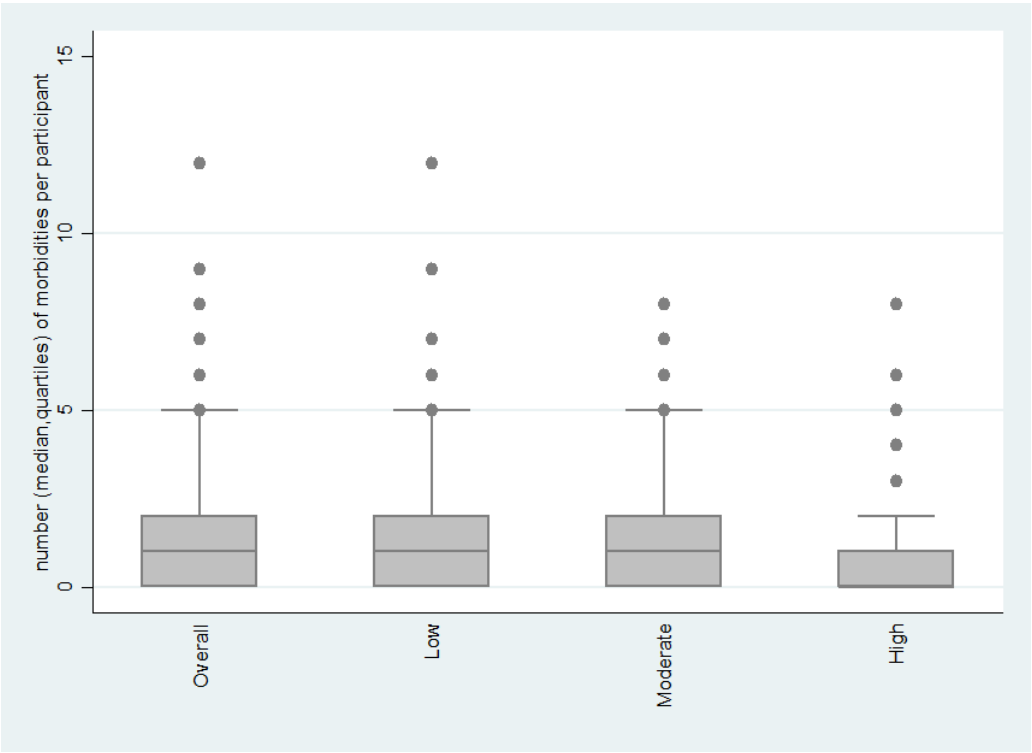
Characteristics	β (95%CI)	Standardized β	p-value
Age group [N (%)][a]			
18-24	*Ref*	*Ref*	
25-44	-0.56 (-1.44, 0.33)	-0.07	0.22
45-64	-0.23 (-1.27, 0.80)	-0.03	0.66
65+	-0.30 (-1.57, 0.96)	-0.02	0.64
Sex [N (%)][b]			
Men	*Ref*	*Ref*	
Women	**0.96 (0.42, 1.50)**	**0.12**	<.01
Geographical area [N (%)][c]			
Nicosia	*Ref*	*Ref*	
Limassol	**0.98 (0.40, 1.56)**	**0.11**	<.01
Larnaka	0.53 (-0.19, 1.25)	0.05	0.15
Paphos	**0.89 (0.05, 1.74)**	**0.07**	0.04
Ammochostos	0.94 (-0.28, 2.16)	0.05	0.13
Residency [N (%)][d]			
Urban	*Ref*	*Ref*	
Rural	**0.71 (0.12, 1.31)**	**0.08**	0.02
Marital status [N (%)][d]			
Married	*Ref*	*Ref*	
Unmarried	-0.25 (-0.91, 0.41)	-0.03	0.45
Divorced / Widowed	**-2.12 (-3.00, -1.24)**	**-0.15**	<.01
Educational level [N (%)][d]			
Primary education	*Ref*	*Ref*	
Secondary education	**-1.58 (-2.83, -0.34)**	**-0.18**	0.01
Higher education	-1.25 (-2.56, 0.05)	-0.15	0.06
Salary [N (%)][e]			
Low	*Ref*	*Ref*	
Middle	0.09 (-0.62, 0.79)	0.01	0.81
High	0.24 (-0.61, 1.08)	0.03	0.59
Physical activity [N (%)][f]			
No	*Ref*	*Ref*	
Yes	**0.74 (0.25, 1.23)**	**0.09**	<.01
Current smoker [N (%)][a]			
No	*Ref*	*Ref*	
Yes	-0.20 (-0.71, 0.32)	-0.02	0.46
BMI group [N (%)][g]			
Underweight	*Ref*	*Ref*	

Normal	0.37 (-0.88, 1.62)	0.02	0.56
Overweight	-0.30 (-0.87. 0.27)	-0.04	0.30
Obese	-0.49 (-1.25, 0.27)	-0.04	0.21
Bold values represent p < 0.05; Abbreviations: Confidence Interval (CI); [a] N=1123; [b]N=1122; [c]N=1121; [d]N=1116; [e]N=1114; [f]N=1115; [g]N=1104			

4.1.2 Association of Mediterranean Diet with multimorbidity

The median number of conditions per participant was 1 (quartiles, q_1=0 and q_3=2) with the maximum number being 12. ***Figure 4.2*** illustrates the distribution of co-morbidities by Mediterranean Diet adherence. Among the three levels of Mediterranean Diet adherence, on average, a higher number of morbidities was reported in the low adherence group whereas the moderate and high adherence groups seem to have a lower number of multi-morbidities. The highest number of morbidities in the low adherence tertile was 12 while the corresponding number in the moderate and high adherence tertiles was 8.

Figure 4.2: Distribution of co-morbidities overall and by Mediterranean Diet tertiles.



We used logistic regression models to examine the association of the adherence to the Mediterranean Diet on the odds of having more than two chronic conditions. The unadjusted analysis showed that the respondents who were in the high adherence group had a lower risk of multimorbidity compared to respondents in the low adherence group (***Table 4.3***, unadjusted OR=0.64, 95% CI: 0.45, 0.90). More specifically, participants in the high MedDietScore tertile presented about 36% lower risk of multimorbidity, compared to those in the low MedDietScore tertile.

The relation remained statistically significant even after adjusting for age, sex, smoking habits, and physical activity (***Table 4.3***, adjusted OR=0.68, 95% CI: 0.46, 0.99) indicating that participants in the high MedDietScore tertile presented about 32% lower risk of multimorbidity compared to those in the low MedDietScore tertile, after adjusting for age, sex, smoking habits, and physical activity.

Although the interaction term between sex and Mediterranean Diet score was not statistically significant, historical data suggests that both morbidities and dietary habits may differ between men and women. Therefore, we stratified the analysis by sex and we found that the association between MedDietScore tertiles and multimorbidity was statistically significant only in women (***Table 4.3***, unadjusted OR=0.57, 95% CI: 0.36, 0.90). The relation remained statistically significant even after adjusting for age (***Table 4.3***, adjusted OR=0.61, 95% CI: 0.38, 0.99). The relation of MedDietScore tertiles and multimorbidity among men was similar to that among women, however, the association was not statistically significant.

Table 4.3: Logistic regression analysis of the association of adherence to Mediterranean Diet and multimorbidity.

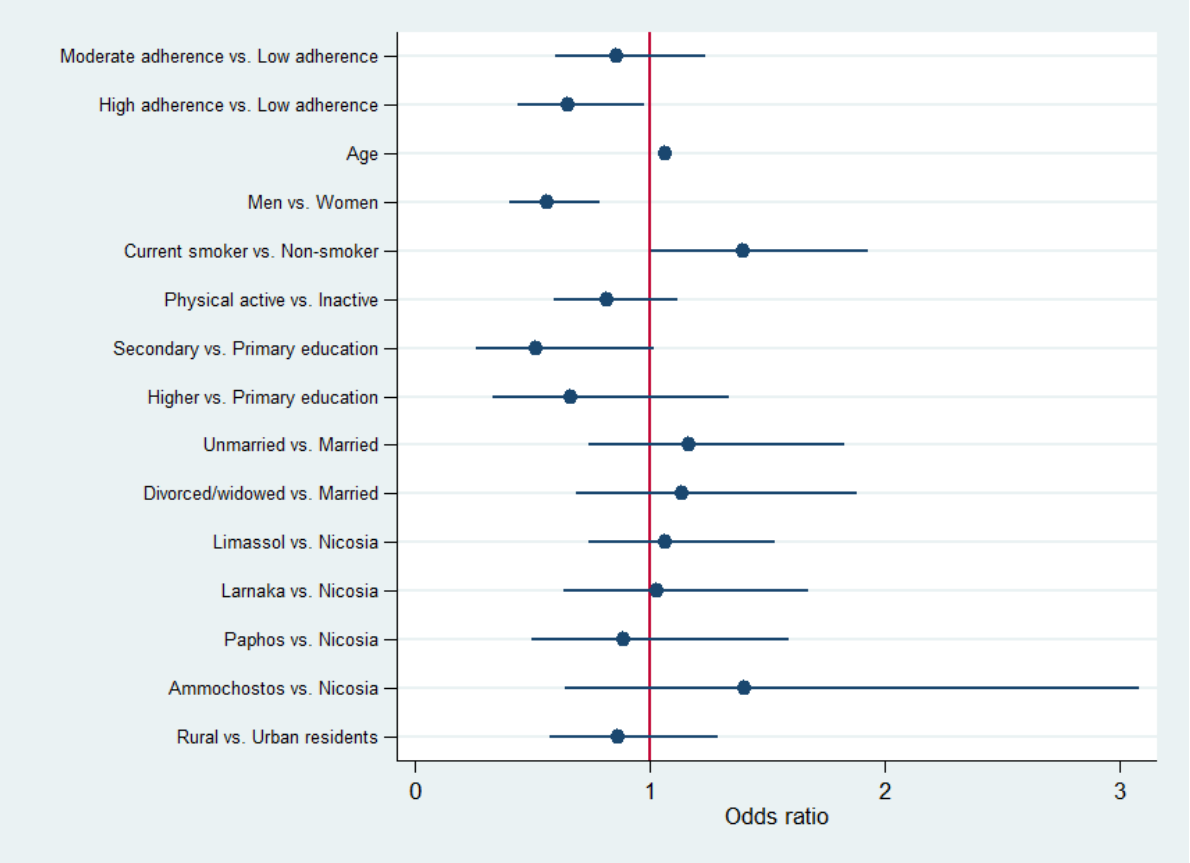
	Total (N = 1123)	**Women** (N = 630)	**Men** (N = 492)
	OR (95%CI)	OR (95%CI)	OR (95%CI)
Model 1: Crude model			
MedDietScore tertiles			
Low	*Ref*	*Ref*	*Ref*
Moderate	0.85 (0.62, 1.16)	0.71 (0.48, 1.07)	1.23 (0.72, 2.08)
High	**0.64 (0.45, 0.90)**	**0.57 (0.36, 0.90)**	0.87 (0.50, 1.52)
Model 2: Model 1 plus age, (sex)			
MedDietScore tertiles			
Low	*Ref*	*Ref*	*Ref*

Moderate	0.85 (0.60, 1.20)	0.74 (0.48, 1.13)	1.05 (0.57, 1.94)
High	**0.65 (0.44, 0.95)**	**0.61 (0.38, 0.99)**	0.71 (0.37, 1.36)
Model 3: Model 2 plus smoking habits, physical activity			
MedDietScore tertiles			
Low	*Ref*	*Ref*	*Ref*
Moderate	0.88 (0.62, 1.25)	0.76 (0.49, 1.18)	1.10 (0.60, 2.04)
High	**0.68 (0.46, 0.99)**	0.63 (0.39, 1.02)	0.77 (0.40, 1.48)
Abbreviations: Confidence Interval (CI); Odds Ratio (OR); ORs and their corresponding 95%CIs were obtained from logistic regression analysis; Bold values represent $p < 0.05$			

Hierarchical multivariable logistic regression models were used to assess the association of multimorbidity and Mediterranean diet adherence adjusting for social and demographic indicators. Firstly, we adjusted for age and sex, then we added lifestyle habits, including smoking habits and physical activity level, and finally socioeconomic and demographic characteristics, including educational and marital status, geographical area, and residency, were added. The final fully adjusted model is presented in ***Figure 4.3***. The results indicated that the adjusted odds of multimorbidity were consistently lower and statistically significant for respondents in the high adherence group compared to the low adherence group.

Other factors such as age, sex and educational status were also statistically significant predictors for the presence of multimorbidity in an individual. Specifically, men had lower adjusted odds of multimorbidity (OR=0.56; 95% CI: 0.41, 0.78) and the risk was 1.06 times higher for every one-year increase in age (OR= 1.05, 95% CI: 1.04, 1.07). We also found that people who completed a secondary education had lower adjusted odds of multimorbidity (OR=0.49; 95% CI: 0.25, 0.96) compared to those who completed only primary education.

Figure 4.3: Logistic regression analysis of the association of adherence to Mediterranean Diet and multimorbidity adjusting for socio, demographic and lifestyle characteristics. Odds ratios (95% confidence intervals, CI).



4.1.3 Mediterranean Diet and specific chronic diseases

As discussed in Section 3.3, the most prevalent chronic diseases in our study were hyperlipidemia, followed by hypertension and thyroid diseases. The median Mediterranean Diet score of the participants who did not have hyperlipidemia was 15 (quartiles, q_1=13, q_3=18) with the maximum score being 34 while the median Mediterranean Diet score of the participants who had hyperlipidemia was 16 (quartiles, q_1=13, q_3=18) with the maximum score being 29. The association between hyperlipidemia and Mediterranean Diet adherence (***Figure 4.4***) was not statistically significant (p=0.99). Furthermore, a larger percentage of men was observed in high adherence tertile compared to women (58% vs 42%) as well as a smaller percentage of men was reported in low adherence tertile compared to women (35% vs. 65%) (p=0.02) (***Table 4.5***).

Figure 4.4: Box plot (quartiles, maximum and minimum values) of Mediterranean Diet score over individuals with and without hyperlipidemia.

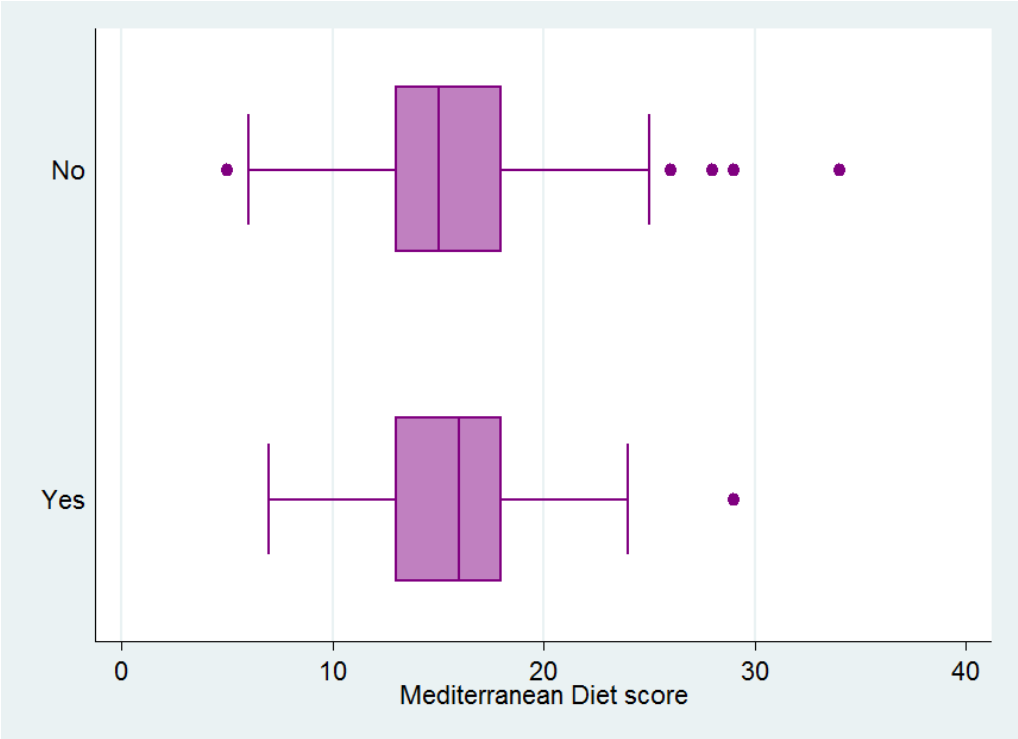


Table 4.4: Mediterranean Diet adherence and specific chronic diseases.

Chronic diseases	**Overall** (N=1123)	**Low** (N=367)	**Moderate** (N=413)	**High** (N=343)	**p-value**
Hyperlipidemia (E78.5)					
	16 (13, 18)	58 (29.9)	79 (40.7)	57 (29.4)	0.44[a]
Women	15 (12, 17)	38 (39.2)	35 (36.1)	24 (24.7)	**0.02**[a]
Men	16 (14, 18)	20 (20.6)	44 (45.4)	33 (34.0)	
Hypertension (I10)					
	15 (13, 18)	46 (31.9)	59 (41.0)	39 (27.1)	0.48[a]
Women	14 (12, 17)	26 (42.6)	23 (37.7)	12 (19.7)	**0.04**[a]
Men	16 (14, 18)	20 (24.1)	36 (43.4)	27 (32.5)	
Thyroid diseases (E02, E03.8, E03.9, E05.90, E07.9)					
	14 (12, 17)	38 (40.4)	34 (36.2)	22 (23.4)	0.17[a]
Women	14 (12, 16)	34 (44.2)	25 (32.5)	18 (23.3)	0.21[a]
Men	15 (14, 17)	4 (23.5)	9 (53.0)	4 (23.5)	
Gastric reflux (K21)					
	16 (12, 18)	25 (30.9)	31 (38.2)	25 (30.9)	0.93[a]
Women	15 (12, 17)	19 (39.6)	18 (37.5)	11 (27.9)	0.07[a]
Men	16 (15, 19)	6 (18.2)	13 (39.4)	14 (42.4)	
Polycystic ovarian syndrome (E28.2)					
	15 (13, 18)	27 (39.1)	23 (33.3)	19 (27.6)	0.50[a]
Women	15 (13, 18)	27 (39.1)	23 (33.3)	19 (27.6)	-
Men	-	-	-	-	

Asthma (J45)					
	18 (18, 18)	28 (44.4)	17 (27.0)	18 (28.6)	0.10[a]
Women	14.5 (12, 18)	16 (47.0)	9 (26.5)	9 (26.5)	0.89[a]
Men	15 (13, 19)	12 (41.4)	8 (27.6)	9 (31.0)	
Irritable Bowel syndrome (K58)					
	15 (11, 18)	23 (42.6)	16 (29.6)	15 (27.8)	0.27[a]
Women	15 (11, 18)	21 (45.6)	13 (28.3)	12 (26.1)	0.55[a]
Men	16 (13, 19.5)	2 (25.0)	3 (37.5)	3 (37.5)	
Depression (F32, F33)					
	14 (12, 16)	17 (43.6)	15 (38.5)	7 (17.9)	0.17[a]
Women	14 (12, 16)	12 (41.4)	11 (37.9)	6 (20.7)	0.74[a]
Men	13.5 (13, 15)	5 (50.0)	4 (40.0)	1 (10.0)	
Glaucoma/Cataract (H40, H25)					
	16 (13, 18)	13 (34.2)	13 (34.2)	12 (31.6)	0.95[a]
Women	15 (12, 18)	6 (42.8)	4 (28.6)	4 (28.6)	0.69[a]
Men	16 (13, 18)	7 (29.2)	9 (37.5)	8 (33.3)	
Blindness/Low vision (H54.0)					
	16 (13, 18)	11 (29.0)	16 (42.0)	11 (29.0)	0.78[a]
Women	15.5 (13, 18)	8 (36.4)	8 (36.4)	6 (27.2)	0.48[a]
Men	16 (14, 18)	3 (18.7)	8 (50.0)	5 (31.3)	
Rheumatoid arthritis (MO6.9)					
	15 (12, 17)	12 (38.7)	13 (41.9)	6 (19.4)	0.39[a]
Women	15 (12, 17)	8 (38.1)	9 (42.9)	4 (19.0)	0.99[a]
Men	14.5 (12, 16)	4 (40.0)	4 (40.0)	2 (20.0)	

Chronic sinusitis (J32)					
	15 (12, 17)	11 (40.8)	12 (44.4)	4 (14.8)	0.20[a]
Women	14 (12, 17)	9 (50.0)	6 (33.3)	3 (16.7)	0.25[a]
Men	16 (15, 16)	2 (22.2)	6 (66.7)	1 (11.1)	
Inflammatory bowel disease/ chronic enteritis/ ulcerative colitis (K50-K52)					
	13 (11, 16)	18 (56.2)	11 (34.4)	3 (9.4)	<0.01[a]
Women	13 (12, 16)	12 (57.1)	8 (38.1)	1 (4.8)	0.44[a]
Men	13 (10, 16)	6 (54.5)	3 (27.3)	2 (18.2)	
Type I diabetes mellitus (E11)					
	17.5 (13, 20)	8 (33.3)	4 (16.7)	12 (50.0)	0.06[a]
Women	17 (11, 20.5)	3 (37.5)	1 (12.5)	4 (50.0)	0.91[a]
Men	17.5 (13, 20)	5 (31.2)	3 (18.8)	8 (50.0)	
Chronic Bronchitis (J41, J42)					
	15 (13, 17)	6 (26.1)	14 (60.9)	3 (13.0)	**0.04[a]**
Women	15.5 (12.5, 17)	4 (33.3)	7 (58.3)	1 (8.4)	0.62[a]
Men	15 (14, 17)	2 (18.2)	7 (63.6)	2 (18.2)	
Type II diabetes mellitus (E10)					
	20 (20, 20)	8 (33.3)	8 (33.3)	8 (33.3)	0.93[a]
Women	14 (11, 18)	6 (50.0)	2 (16.7)	4 (33.3)	0.14[a]
Men	16 (14, 18)	2 (16.7)	6 (50.0)	4 (33.3)	
Heart failure (I50)					
	16 (14, 18)	3 (20.0)	6 (40.0)	6 (40.0)	0.54[a]
Women	16 (12, 19)	2 (28.5)	2 (28.5)	3 (43.0)	0.63[a]
Men	16 (14, 18)	1 (12.5)	4 (50.0)	3 (37.5)	

Atrial fibrillation (I48.91)					
	14 (12, 16)	5 (50.0)	5 (50.0)	0 (0.0)	0.11[a]
Women	13.5 (10.5, 16)	2 (50.0)	2 (50.0)	0 (0.0)	1.0[a]
Men	14 (13, 16)	3 (50.0)	3 (50.0)	0 (0.0)	
Chronic kidney disease (N18.9)					
	15 (13, 16)	3 (30.0)	6 (60.0)	1 (10.0)	0.20[a]
Women	15 (15, 17)	1 (16.6)	4 (66.8)	1 (16.6)	0.27[a]
Men	13.55 (13, 15)	2 (50.0)	2 (50.0)	0 (0.0)	
Breast cancer (C50.9)					
	16 (16, 16)	4 (36.4)	5 (45.4)	2 (18.2)	0.66[a]
Women	16 (16, 16)	4 (36.4)	5 (45.4)	2 (18.2)	-
Men	-	-	-	-	
Hearing loss/Deafness (H90, H91)					
	16.5 (14, 18)	2 (20.0)	4 (40.0)	4 (40.0)	0.66[a]
Women	17 (14, 18)	1 (20.0)	2 (40.0)	2 (40.0)	1.0[a]
Men	16 (16, 18)	1 (20.0)	2 (40.0)	2 (40.0)	
Erectile dysfunction (N52.9)					
	17 (17, 20)	2 (22.2)	3 (33.3)	4 (44.5)	0.64[a]
Women	-	-	-	-	-
Men	17 (17, 20)	2 (22.2)	3 (33.3)	4 (44.5)	
Angina (I20.9)					
	13 (13, 13)	1 (14.3)	3 (42.9)	3 (42.9)	0.56[a]
Women	17.5 (16, 19)	0 (0.0)	1 (50.0)	1 (50.0)	0.79[a]
Men	16 (15, 18)	1 (20.0)	2 (40.0)	2 (40.0)	

Coronary heart disease (I25.1)					
	14 (12, 17)	3 (42.9)	3 (42.9)	1 (14.2)	0.64[a]
Women	12 (12, 12)	1 (100.0)	0 (0.0)	0 (0.0)	
Men	15 (13, 17)	2 (33.3)	3 (50.0)	1 (16.7)	
Prostate cancer (C61)					
	16 (14, 18)	1 (14.3)	4 (57.1)	2 (28.6)	0.47[a]
Women	-	-	-	-	-
Men	16 (14, 18)	1 (14.3)	4 (57.1)	2 (28.6)	
Anorexia/Bulimia (F50.0, F50.2)					
	14.5 (12, 17)	3 (50.0)	2 (33.3)	1 (16.7)	0.62[a]
Women	14.5 (12, 17)	3 (50.0)	2 (33.3)	1 (16.7)	-
Men	-	-	-	-	
Crohn's disease (K50)					
	13 (11, 14)	4 (66.6)	1 (16.7)	1 (16.7)	0.20[a]
Women	13 (12, 13.5)	3 (75.0)	1 (25.0)	0 (0.0)	
Men	14.5 (10, 19)	1 (50.0)	0 (0.0)	1 (50.0)	
Epileptic (G40.909)					
	16 (16, 16)	2 (50.0)	1 (25.0)	1 (25.0)	0.76[a]
Women	12 (12, 12)	1 (100.0)	0 (0.0)	0 (0.0)	0.51[a]
Men	16 (16, 16)	1 (33.3)	1 (33.3)	1 (33.3)	
Chronic Obstructive Pulmonary Disease (K50-52)					
	14.5 (12, 17)	2 (50.0)	1 (25.0)	1 (25.0)	0.76[a]
Women	11 (11, 11)	1 (100.0)	0 (0.0)	0 (0.0)	0.51[a]
Men	16 (13, 18)	1 (33.3)	1 (33.3)	1 (33.3)	

Cervical cancer (C53.9)					
	14.5 (12, 17)	1 (50.0)	1 (50.0)	0 (0.0)	0.64[a]
Women	14.5 (12, 17)	1 (50.0)	1 (50.0)	0 (0.0)	-
Men	-	-	-	-	
Chronic hepatitis (K73)					
	16 (15, 17)	0 (0.0)	2 (100.0)	0 (0.0)	0.18[a]
Women	-	-	-	-	-
Men	16 (15, 17)	0 (0.0)	2 (100.0)	0 (0.0)	
Cirrhosis (K74.60)					
	17 (12, 22)	1 (50.0)	0 (0.0)	1 (50.0)	0.56[a]
Women	17 (12, 22)	1 (50.0)	0 (0.0)	1 (50.0)	-
Men	-	-	-	-	
Cirrhosis (K74.60)					
	16 (15, 17)	0 (0.0)	2 (100.0)	0 (0.0)	0.18[a]
Women	-	-	-	-	-
Men	16 (15, 17)	0 (0.0)	2 (100.0)	0 (0.0)	
Dementia/Alzheimer disease (G30.9, F03)					
	19 (19, 19)	0 (0.0)	2 (100.0)	0 (0.0)	0.18[a]
Women	-	-	-	-	-
Men	19 (19, 19)	0 (0.0)	2 (100.0)	0 (0.0)	
Parkinson disease (G20)					
	13.5 (10, 17)	1 (50.0)	1 (50.0)	0 (0.0)	0.64[a]
Women	-	-	-	-	-
Men	13.5 (10, 17)	1 (50.0)	1 (50.0)	0 (0.0)	

Colon cancer (C18.9)					
	10 (10, 10)	1 (100.0)	0 (0.0)	0 (0.0)	0.36[a]
Women	-	-	-	-	-
Men	10 (10, 10)	1 (100.0)	0 (0.0)	0 (0.0)	
Melanoma (C43)					
	13 (13, 13)	1 (100.0)	0 (0.0)	0 (0.0)	0.36[a]
Women	13 (13, 13)	1 (100.0)	0 (0.0)	0 (0.0)	-
Men	-	-	-	-	
Lupus (M32.9)					
	12 (12, 12)	1 (100.0)	0 (0.0)	0 (0.0)	
Women	12 (12, 12)	1 (100.0)	0 (0.0)	0 (0.0)	-
Men	-	-	-	-	
Multiple sclerosis (G35)					
	26 (26, 26)	0 (0.0)	0 (0.0)	1 (100.0)	0.32[a]
Women	26 (26, 26)	0 (0.0)	0 (0.0)	1 (100.0)	-
Men	-	-	-	-	
Leukemia (C95.9)					
	19 (19, 19)	0 (0.0)	0 (0.0)	1 (100.0)	0.32[a]
Women	-	-	-	-	-
Men	19 (19, 19)	0 (0.0)	0 (0.0)	1 (100.0)	
Urinary cancer (C67)					
	17 (17, 17)	0 (0.0)	1 (100.0)	0 (0.0)	0.42[a]
Women	17 (17, 17)	0 (0.0)	1 (100.0)	0 (0.0)	-
Men	-	-	-	-	

Schizophrenia/Bipolar (F20.9, F31.9)					
	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Women	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
Men	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Ovarian cancer (C56.9)					
	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
Women	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
Men	-	-	-	-	
Bold values represent $p < 0.05$; [a] Differences between men and women were evaluated by the chi-square test.					

The results were similar for the other two prevalent chronic diseases. Specifically, participants with and without hypertension had a median Mediterranean Diet score of 15 (quartiles, q_1=13, q_3=18) (p=0.91) (***Figure 4.5***). Among individuals with hypertension, the higher value of Mediterranean Diet score was identified among men compared to the corresponding score among women (16 vs. 14) (p=0.04). Specifically, 69% of the participants who classified in high adherence tertile were men and 31% were women.

The largest difference between the median Mediterranean Diet scores was identified in people with thyroid and no thyroid diseases (***Figure 4.6***), with people with thyroid diseases having a median Mediterranean Diet score of 14 (quartiles, q_1=12, q_3=17.5) with a maximum score of 24 while people without thyroid diseases had a median Mediterranean Diet score of 16 with a maximum score of 34 (quartiles, q_1=13, q_3=18) ($p < 0.05$).

Figure 4.5: Box plot (quartiles, maximum and minimum values) of Mediterranean Diet score over individuals with and without hypertension.

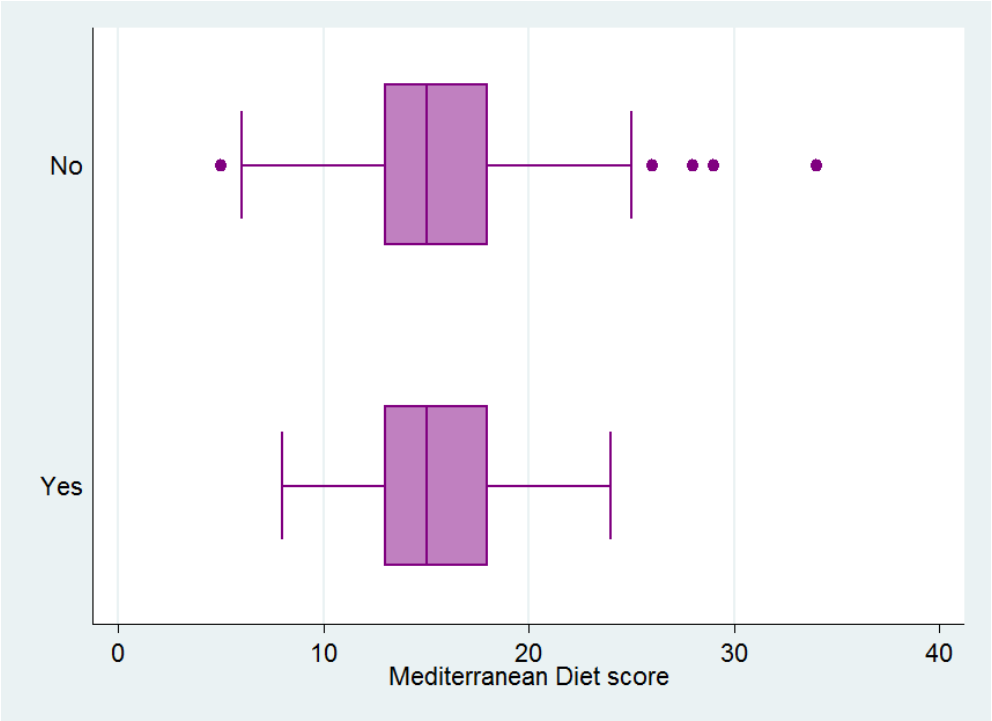
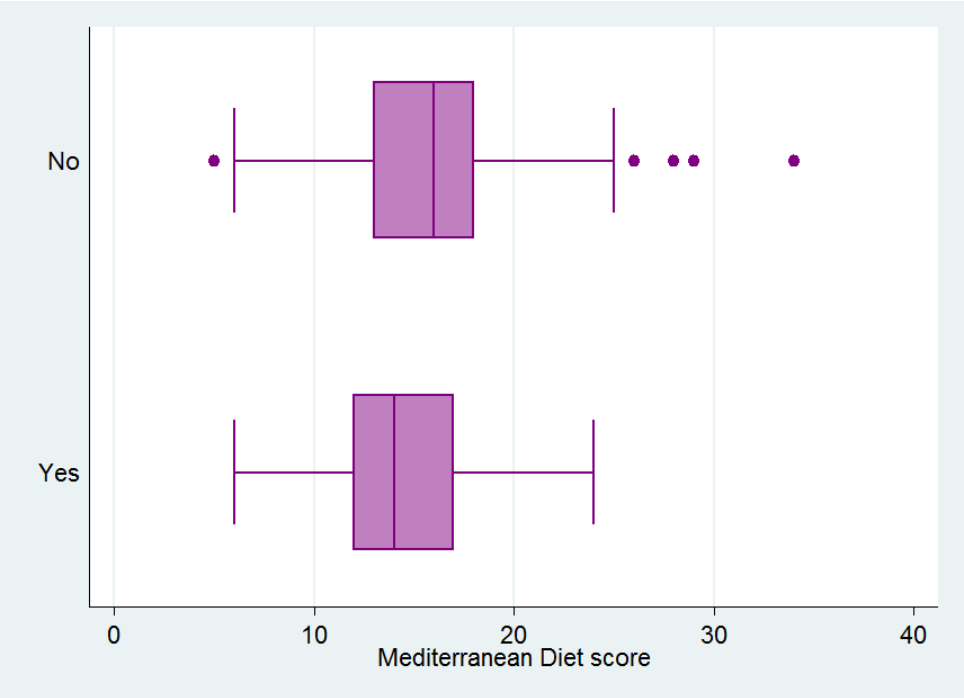


Figure 4.6: Box plot (quartiles, maximum and minimum values) of Mediterranean Diet score over individuals with and without thyroid diseases.



Although, we did not find any other statistically significant associations among the adherence of Mediterranean Diet and the other chronic diseases considered (***Table 4.4***), it is worth mentioning that higher Mediterranean Diet score values were observed among men in the majority of the chronic diseases (i.e. Gastric reflux, Asthma, Irritable Bowel syndrome, Glaucoma/Cataract, Blindness/Low vision, Type I diabetes mellitus, Type II diabetes mellitus, Atrial fibrillation, Coronary Heart Disease, Crohn's disease, Epilepsy) compared to women.

Finally, ***Table 4.5*** provides results on the adherence to Mediterranean Diet of the Cypriot population among people with or without chronic diseases, grouped by human systems. Although we did not find any statistical significant associations between any human system and the adherence to Mediterranean Diet, it is important to mention that individuals with a disease of the circulatory or digestive/excretory or immune or neoplasm or reproductive system have a higher median value of the Mediterranean Diet score compared to those without a disease in the corresponding system. For example, in individuals who reported having a disease of the digestive/excretory or reproductive systems, the median Mediterranean Diet score was 18 and 17, respectively, whereas the corresponding medians among people without a disease were 16 and 15, respectively.

Table 4.5: Mediterranean Diet adherence by the human systems.

Human systems	**Overall** (N=1123)	**Low** (N=367)	**Moderate** (N=413)	**High** (N=343)	**p-value**
Circulatory					
No	15 (13, 18)	283 (77.1)	299 (72.4)	263 (76.7)	0.24[a]
Yes	16 (13, 18)	84 (22.9)	114 (27.6)	80 (23.3)	
Endocrine					
No	16 (13, 18)	295 (80.4)	347 (84.0)	287 (83.7)	0.35[a]
Yes	15 (13, 18)	72 (19.6)	66 (16.0)	56 (16.3)	
Digestive /Excretory					
No	16 (13, 18)	314 (85.6)	364 (88.1)	305 (89.2)	0.32[a]
Yes	18 (18, 18)	53 (14.4)	49 (11.9)	37 (10.8)	
Nervous					
No	16 (13, 18)	322 (87.7)	367 (89.1)	315 (92.1)	0.15[a]
Yes	15 (13, 17)	45 (12.3)	45 (10.9)	7 (7.9)	
Respiratory					
No	16 (13, 18)	327 (89.1)	374 (90.6)	320 (93.6)	0.11[a]
Yes	15 (12, 17)	10 (10.9)	39 (9.4)	22 (6.4)	
Immune					
No	15 (13, 18)	355 (96.7)	402 (97.3)	332 (96.8)	0.86[a]
Yes	15 (13, 19)	12 (3.3)	11 (2.7)	11 (3.2)	
Skeletal/Muscular					
No	15 (13, 18)	355 (96.7)	400 (96.9)	337 (98.2)	0.39[a]
Yes	15 (12, 17)	12 (3.3)	13 (3.1)	6 (1.8)	
Neoplasm					
No	15 (13, 18)	359 (97.8)	401 (97.3)	339 (98.8)	0.34[a]
Yes	16 (13, 17)	8 (2.2)	11 (2.7)	4 (1.2)	
Renal/Urinary					
No	15 (13, 18)	364 (99.2)	407 (98.6)	342 (99.7)	0.24[a]
Yes	15 (13, 16)	2 (0.8)	1 (1.4)	1 (0.3)	
Reproductive					
No	15 (13, 18)	365 (99.5)	409 (99.3)	339 (98.8)	0.64[a]
Yes	17 (17, 20)	2 (0.5)	3 (0.7)	4 (1.2)	

Bold values represent $p < 0.05$; [a] Differences between men and women were evaluated by the chi-square test.

5 Chapter 5 – Quality of sleep and multimorbidity

5.1 Quality of sleep

The median Pittsburgh Sleep Quality score of the participants was 5 (quartiles, q_1=3, q_3=7) with the highest score being 17 out of a maximum possible score of 21 and with higher values indicating a worse quality of sleep. The tertiles of the quality of sleep were defined as follows: good quality of sleep (score <4), moderate quality of sleep (score 4-6), and poor quality of sleep (score >6) with 541 (47.4%), 273 (24.0) and 326 (28.6) participants included in them.

We found a statistically significant difference among the quality of sleep tertiles between men and women with women having a poorer quality of sleep compared to men (***Table 5.1***). Specifically, we observed a higher median value of quality of sleep score in women compared to men, something that indicates a worse quality of sleep (p=0.03). Similarly, a higher median value of quality of sleep score was reported in the residents of Pafos area compared to the residents of the four remaining geographical areas of Cyprus (p<0.01). Furthemore, among individuals who were categorized in the poor quality of sleep tertile, 10% were divorced/widowed while the corresponding percentages in good and moderate quality of sleep tertiles were 9% and 7%, respectively (p=0.03). Other characteristics, such as age, residency, educational and salary status, exercise, smoking, and BMI were similar among the three tertiles of quality of sleep. However, we found a worse quality of sleep in individuals aged 65 years old and older, in people who completed a primary or a secondary education, in physically inactive participants, and in overweight/obese individuals (***Table 5.1***).

Table 5.1: Baseline characteristics by quality of sleep tertiles.

Characteristics	**Quality of sleep score**				**p-value**
	Overall[h] (N=1140)	**Good** (N=541)	**Moderate** (N=273)	**Poor** (N=326)	
Quality of sleep score	5 (3, 7)	3 (2, 4)	5 (5, 6)	9 (7, 10)	**<.01**[i]
Age group [N (%)][a]					
18-24	5 (3, 7)	76 (45.5)	49 (29.3)	42 (25.2)	0.17[i]
25-44	5 (3, 7)	247 (47.1)	135 (25.8)	142 (27.1)	
45-64	5 (3, 7)	155 (49.4)	62 (19.7)	97 (30.9)	
65+	5 (3, 8)	63 (46.7)	27 (20.0)	45 (33.3)	
Sex [N (%)][b]					
Men	4 (3, 6)	251 (50.5)	124 (25.0)	122 (24.5)	**0.03**[i]
Women	5 (3, 7)	289 (45.0)	149 (23.2)	204 (31.8)	
Geographical area [N (%)][c]					
Nicosia	5 (3, 7)	239 (48.5)	124 (25.1)	130 (26.4)	**<.01**[i]
Limassol	5 (3, 7)	151 (48.6)	72 (23.1)	88 (28.3)	
Larnaka	5 (3, 7)	83 (48.5)	43 (25.2)	45 (26.6)	
Paphos	6 (4, 8)	42 (37.2)	19 (16.8)	52 (46.0)	
Ammochostos	5 (2, 6)	24 (48.0)	15 (30.0)	11 (22.0)	
Residency [N (%)][d]					
Urban	5 (3, 7)	408 (47.2)	202 (23.4)	254 (29.4)	0.54[i]
Rural	5 (3, 7)	128 (47.6)	80 (26.0)	71 (26.4)	
Marital status [N (%)][d]					
Married	5 (3, 7)	307 (49.8)	130 (21.1)	179 (29.1)	**0.03**[i]
Unmarried	5 (3, 7)	185 (43.9)	123 (29.2)	113 (26.9)	
Divorced / Widowed	5 (3, 8)	47 (49.0)	18 (18.7)	31 (32.3)	
Educational level [N (%)][d]					
Primary education	5 (3, 8)	30 (45.5)	13 (19.7)	23 (34.8)	0.79[i]
Secondary education	5 (3, 7)	163 (48.2)	82 (24.3)	93 (27.5)	
Higher education	4 (1, 6)	343 (47.0)	177 (24.3)	209 (28.7)	
Salary [N (%)][e]					
Low	5 (3, 7)	104 (43.1)	64 (26.6)	73 (30.3)	0.19[i]
Middle	5 (3, 7)	259 (46.1)	140 (24.9)	163 (29.0)	
High	4 (3, 7)	173 (52.7)	68 (20.7)	87 (26.4)	
Physical activity [N (%)][f]					
No	5 (3, 7)	275 (50.8)	125 (23.1)	141 (26.1)	0.08[i]
Yes	4 (3, 7)	262 (44.3)	147 (24.9)	182 (30.8)	
Current smoker [N (%)][d]					
No	5 (3, 7)	178 (44.3)	97 (24.1)	127 (31.6)	0.18[i]
Yes	5 (3, 7)	360 (49.3)	175 (23.9)	196 (26.8)	
BMI group [N (%)][g]					

Underweight	5 (3, 7)	18 (42.9)	13 (31.0)	11 (26.1)	0.15[i]
Normal	5 (3, 7)	277 (49.0)	142 (25.1)	146 (25.9)	
Overweight	5 (3, 8)	164 (45.3)	75 (20.7)	123 (34.0)	
Obese	5 (3, 7)	75 (49.3)	38 (25.0)	39 (25.7)	

Bold values represent $p < 0.05$; [a] N=1140; [b]N=1139; [c]N=1138; [d]N=1133; [e]N=1131; [f]N=1132; [g]N=1121; [h]Median (IQR); [i]Differences between quality of sleep tertiles were evaluated by the ANOVA test.

5.1.1 Associations of quality of sleep and multimorbidity

Figure 5.1 indicates the distribution of multi-morbidities by quality of sleep. The median number of morbidities among the participants who classified in the poor quality of sleep tertile was 1 (quartiles, q_1=1 and q_3=2) while the median number of morbidities among the participants who classified in the good and moderate quality of sleep tertiles was 0 (quartiles, q_1=0 and q_3=1) and 1 (quartiles, q_1=0 and q_3=1) respectively.

People who were in the poor quality of sleep group, vs. the good quality of sleep tertile, had a higher risk of having 2, 3, or more than 3 morbidities compared to having no morbidities with RR of 1.84, 2.31 and 3.36, respectively. Similar results were obtained in women, while in men a statistically significant association of poor quality of sleep was found only for having 3 or more morbidities (***Table 5.2***).

Figure 5.1: Distribution of multi-morbidities overall and by quality of sleep tertiles.

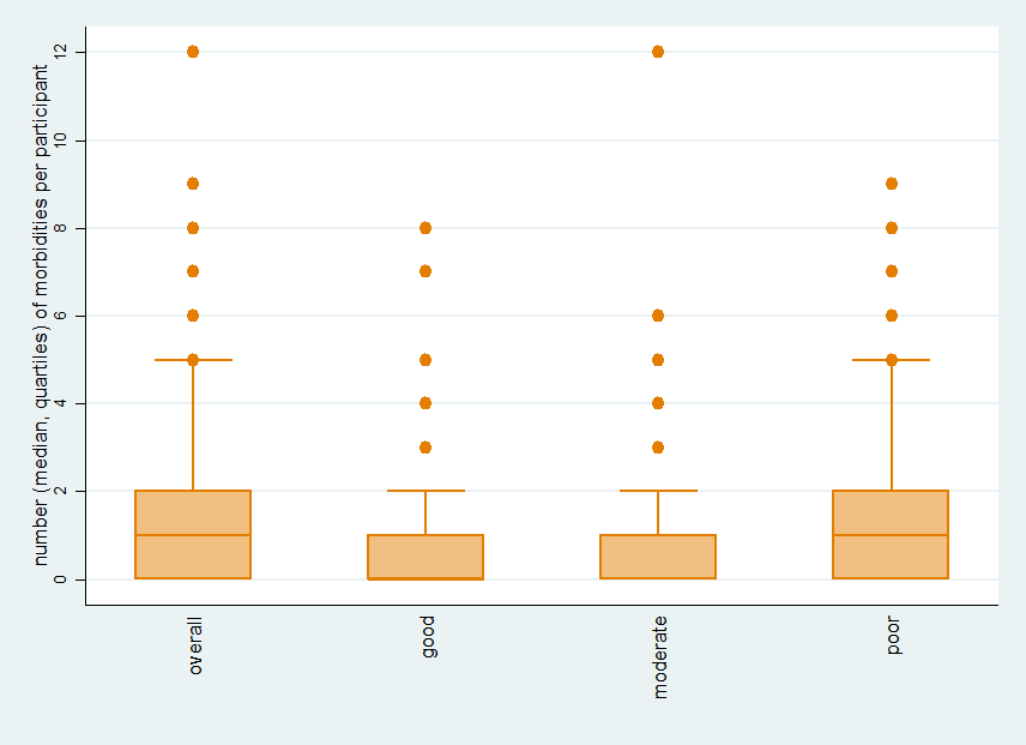


Table 5.2: Multinomial logistic regression of quality of sleep on multimorbidity level (base outcome = 0 or 1 morbidities) after accounting for the age and sex distribution, and separately by sex after accounting for the age.

	Multimorbidity level		
	2	**3**	**>3**
Total (N=1140)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	1.23 (0.74, 2.05)	1.64 (0.83, 3.21)	**2.29 (1.23, 4.29)**
Poor	**1.84 (1.18, 2.86)**	**2.31 (1.29, 4.16)**	**3.36 (1.94, 5.83)**
Women (N = 642)			
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	1.05 (0.52, 2.13)	1.43 (0.62, 3.31)	**2.27 (1.07, 4.81)**
Poor	**1.98 (1.11, 3.50)**	**2.49 (1.24, 5.00)**	**2.85 (1.45, 5.62)**
Men (N = 497)			
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	1.56 (0.75, 3.27)	2.52 (0.80, 7.97)	2.44 (0.77, 7.67)
Poor	1.69 (0.83, 3.43)	2.11 (0.68, 6.55)	**4.98 (1.92, 12.91)**
Bold values represent p < 0.05; Abbreviations: Confidence Interval (CI); Relative Risk (RR)			

We used logistic regression models to examine the association of the quality of sleep with the odds of having more than two chronic conditions. The unadjusted model suggested that participants who were in the poor quality of sleep group had a higher risk of multimorbidity compared to participants in the good quality of sleep group (***Table 5.3***, unadjusted OR=2.19, 95% CI: 1.61, 2.99).

The model was then adjusted for possible confounders, including age, sex, smoking, and physical activity status. When adjusted only for age and sex (*model 2,* ***Table 5.3)*** being in the moderate group had an adjusted OR equal to 1.57 (95% CI: 1.07, 2.32) when compared to the good quality of sleep, and when further adjusted for smoking habits and physical activity (*model 3,* ***Table 5.3)*** the adjusted OR=1.54 (95% CI: 1.04, 2.27). Being in the low quality of sleep was also significantly associated with multimorbidity in the adjusted models (***Table 5.3***, adjusted OR=2.21, 95% CI: 1.56, 3.14). Specifically, individuals who were in the poor quality of sleep group had a 2.21 times higher odds of multimorbidity compared to respondents in the good quality of sleep group, even after adjusting for potential confounders.

The interaction term between sex and quality of sleep score was statistically significant for both sex and poor quality of sleep tertile ($p<0.05$) so we stratified the analysis by sex. We found that the association between poor quality of sleep and multimorbidity was statistically significant in both sexes ($p < 0.05$), with women having a higher risk of multimorbidity compared to men. Specifically, the risk of multimorbidity was 2.41 and 1.79 times higher for women and men, respectively, in those participants who were classified in the poor quality of sleep tertile compared to those who were classified in the good quality of sleep tertile (***Table 5.3)***.

Table 5.3: Logistic regression analysis evaluating the association of level of quality of sleep with multimorbidity, overall and by sex.

	Total (N = 1140)	**Women** (N = 642)	**Men** (N = 497)
	OR (95%CI)	OR (95%CI)	OR (95%CI)
Model 1: Crude model			
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	1.25 (0.88, 1.77)	1.37 (0.87, 2.17)	1.09 (0.64, 1.86)
Poor	**2.19 (1.61, 2.99)**	**2.41 (1.62, 3.59)**	**1.79 (1.09, 2.95)**
Model 2: Model1 plus age, (sex)			
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	**1.57 (1.07, 2.32)**	1.47 (0.90, 2.40)	1.88 (1.00, 3.55)
Poor	**2.30 (1.62, 3.25)**	**2.35 (1.53, 3.61)**	**2.29 (1.26, 4.14)**
Model 3: Model 2 plus smoking habits, physical activity			
Good	*Ref*	*Ref*	*Ref*
Moderate	**1.54 (1.04, 2.27)**	1.47 (0.90, 2.41)	1.76 (0.93, 3.34)
Poor	**2.21 (1.56, 3.14)**	**2.29 (1.49, 3.53)**	**2.18 (1.19, 3.98)**
Abbreviations: Confidence Interval (CI); Odds Ratio (OR); ORs and their corresponding 95%CIs were obtained from logistic regression analysis; Bold values represent $p < 0.05$.			

The association of sleep quality and multimorbidity remained statistically significant even after adjusting for demographics and socioeconomic factors (i.e. age, gender, educational, marital and salary status, geographical area, and residency) (***Table 5.4***). Specifically, participants who were in the poor quality of sleep tertile had 2.24 times higher odds of having multimorbidity compared to participants in the good quality of sleep tertile after adjusting for the other variables (95% CI: 1.57, 3.20). Furthermore, individuals with a moderate quality of sleep had a higher risk of having more than two

morbidities compared to those categorized in the good quality of sleep tertile (adjusted OR=1.56, 95% CI: 1.05, 2.31).

After the addition of lifestyle habits in the model (***Table 5.4***), including smoking and physical activity, the adjusted odds of multimorbidity were consistently higher and statistically significant for respondents in the poor (adjusted OR=2.21, 95% CI: 1.5, 3.16) and moderate quality of sleep tertiles compared to the good quality of sleep group (adjusted OR=1.55, 95% CI: 1.04, 2.30).

Table 5.4: Odds ratios and 95% confidence intervals of quality of sleep tertiles in relation to multimorbidity adjusting for a. education status, b. marital status, and c. salary status.

Models	**Model 1: Crude model**	**Model 2: Crude model adjusted for demographic and socioeconomic characteristics**	**Model 3: Model 2 adjusted for lifestyle characteristics**
Quality of sleep tertiles	OR (95%CI)	OR (95%CI)	OR (95%CI)
2nd vs 1st	1.26 (0.89, 1.78)	**1.56 (1.05, 2.31)**	**1.55 (1.04, 2.30)**
3rd vs 1st	**1.17 (1.60, 2.96)**	**2.24 (1.57, 3.20)**	**2.21 (1.55, 3.16)**
Age, per 1 year	-	**1.06 (1.05, 1.08)**	**1.06 (1.05, 1.08)**
Men sex	-	**0.57 (0.41, 0.79)**	0.54 (0.38, 0.77)
Educational status			
Primary education	-	*Ref*	*Ref*
Secondary education	-	**0.47 (0.23, 0.94)**	0.51 (0.25, 1.03)
Higher education	-	0.53 (0.25, 1.13)	0.57 (0.27, 1.23)
Marital status			
Married	-	*Ref*	*Ref*
Unmarried	-	1.14 (0.73, 1.79)	1.16 (0.73, 1.83)
Divorced/Widow	-	1.19 (0.72, 1.98)	1.16 (0.70, 1.94)
Salary group			
Low	-	*Ref*	*Ref*
Moderate	-	**1.65 (1.04, 2.62)**	**1.61 (1.01, 2.56)**
High	-	1.51 (0.88, 2.59)	1.53 (0.90, 2.63)
Geographical area			
Nicosia	-	*Ref*	*Ref*
Limassol	-	1.03 (0.71, 1.48)	1.04 (0.72, 1.50)
Larnaka	-	0.99 (0.61, 1.61)	1.03 (0.63, 1.69)
Paphos	-	0.78 (0.44, 1.39)	0.76 (0.42, 1.36)
Ammochostos	-	1.48 (0.67, 3.27)	1.48 (0.67, 3.27)
Residency, rural/urban	-	0.81 (0.54, 1.21)	0.81 (0.54, 1.22)
Current smoking, yes/no	-	-	1.29 (0.54, 1.22)
Physical activity, yes/no	-	-	0.83 (0.60, 1.14)

5.1.2 Associations of quality of sleep and specific chronic diseases

We also found statistically significant differences between quality of sleep and the presence of hyperlipidemia, hypertension, gastric reflux, asthma, glaucoma/cataract, rheumatoid arthritis, type I diabetes mellitus, and hearing loss/deafness (all $p<0.05$) (***Table 5.5***). Specifically, among individuals in the poor quality of sleep tertile 22% had hyperlipidemia, 17% had hypertension, 10% had gastric reflux, 6% had asthma, 5% had rheumatoid arthritis, 3% had type I diabetes mellitus, and 2% had hearing loss/deafness while the corresponding percentages in the good quality of sleep tertile were 14%, 11%, 5%, 4%, 2%, 2%, 2% and 1%, respectively.

Table 5.5: Quality of sleep in each chronic disease reported in the study, overall and by sex.

Chronic disease	**Overall**	**Good**	**Moderate**	**Poor**	**p-value**
Hyperlipidemia (E78.5)					
	5 (3, 8)	77 (38.9)	49 (24.7)	72 (36.4)	**0.01**[a]
Women	6 (4, 8)	33 (33.0)	26 (26.0)	41 (41.0)	0.21[a]
Men	5 (3, 7)	44 (44.9)	23 (23.5)	31 (31.6)	
Hypertension (I10)					
	5 (3, 8)	59 (40.1)	32 (21.8)	56 (38.1)	**0.02**[a]
Women	6 (4, 9)	19 (29.7)	17 (26.6)	28 (43.7)	0.07[a]
Men	5 (3, 8)	40 (48.2)	15 (18.1)	28 (33.7)	
Thyroid diseases (E02, E03.8, E03.9, E05.90, E07.9)					
	5 (3, 8)	41 (42.7)	18 (18.8)	37 (38.5)	0.07[a]
Women	5 (3, 10)	30 (38.0)	16 (20.2)	33 (41.8)	0.13[a]
Men	4 (2, 6)	11 (64.7)	2 (11.8)	4 (23.5)	
Gastric reflux (K21)					
	5.5 (4, 7)	29 (34.5)	24 (28.6)	31 (36.9)	**0.04**[a]
Women	5 (3, 7)	17 (34.0)	14 (28.0)	19 (38.0)	0.97[a]
Men	6 (4, 7)	12 (35.3)	10 (29.4)	12 (35.3)	
Polycystic ovarian syndrome (E28.2)					
	6 (3, 9)	24 (34.8)	18 (26.1)	27 (39.1)	-
Women	6 (3, 9)	24 (34.8)	18 (26.1)	27 (39.1)	-
Men	-	-	-	-	
Asthma (J45)					
	6 (3, 7)	21 (32.3)	24 (36.9)	20 (30.8)	**0.02**[a]

Women	5 (3, 7)	14 (40.0)	12 (34.3)	9 (25.7)	0.34[a]
Men	6 (5, 7)	7 (23.3)	12 (40.0)	11 (36.7)	
Irritable Bowel syndrome (K58)					
	5 (4, 7)	19 (34.5)	16 (29.1)	20 (36.4)	0.14[a]
Women	6 (4, 8)	15 (31.9)	14 (29.8)	18 (38.3)	0.60[a]
Men	4.5 (3, 6.5)	4 (50.0)	2 (25.0)	2 (25.0)	
Depression (F32, F33)					
	6 (4, 8)	12 (30.8)	12 (30.8)	15 (38.4)	0.10[a]
Women	6 (4, 8)	9 (31.0)	9 (31.0)	11 (38.0)	0.93[a]
Men	6 (2, 7)	3 (30.0)	3 (30.0)	4 (40.0)	
Glaucoma/Cataract (H40, H25)					
	6 (4, 9)	13 (33.3)	8 (20.5)	18 (46.2)	**0.04**[a]
Women	7 (4, 12)	4 (26.7)	1 (6.7)	10 (66.6)	0.09[a]
Men	5 (3, 7.5)	9 (37.5)	7 (29.2)	8 (33.3)	
Blindness/Low vision (H54.0)					
	5.5 (3, 9)	15 (39.5)	6 (15.8)	17 (44.7)	0.07[a]
Women	5.5 (4, 9)	8 (36.4)	4 (18.2)	10 (45.4)	0.85[a]
Men	5.3 (3. 9)	7 (43.7)	2 (12.6)	7 (43.7)	
Rheumatoid arthritis (MO6.9)					
	7 (3.5, 11)	9 (28.1)	6 (18.8)	17 (53.1)	**<0.01**[a]
Women	8.5 (4, 12)	6 (27.3)	4 (18.2)	12 (54.5)	0.97[a]
Men	6.5 (3, 7)	3 (30.0)	2 (20.0)	5 (50.0)	
Chronic sinusitis (J32)					
	5 (4, 7)	9 (31.0)	11 (38.0)	9 (31.0)	0.12[a]

Women	5 (3, 8)	6 (31.6)	7 (36.8)	6 (31.6)	0.99[a]
Men	6 (4, 7)	3 (30.0)	4 (40.0)	3 (30.0)	
Inflammatory bowel disease/ chronic enteritis/ ulcerative colitis (K50-K52)					
	6 (3, 8)	13 (40.6)	7 (21.9)	12 (37.5)	0.52[a]
Women	6 (3, 8)	8 (38.1)	4 (19.0)	9 (42.9)	0.68[a]
Men	6 (3, 8)	5 (45.4)	3 (27.3)	3 (27.3)	
Type I diabetes mellitus (E11)					
	5 (3, 10)	12 (50.0)	1 (4.2)	11 (45.8)	**0.04**[a]
Women	10 (7.5, 12.5)	1 (12.5)	1 (12.5)	6 (75.0)	**0.02**[a]
Men	3.5 (2, 7.5)	11 (68.7)	0 (0.0)	5 (31.3)	
Chronic Bronchitis (J41, J42)					
	5 (3, 7)	12 (48.0)	5 (20.0)	8 (32.0)	0.87[a]
Women	5 (3, 7)	6 (46.1)	2 (15.4)	5 (38.5)	
Men	4 (2, 6.5)	6 (50.0)	3 (25.0)	3 (25.0)	
Type II diabetes mellitus (E10)					
	5 (3, 6)	12 (48.0)	7 (28.0)	6 (24.0)	0.83[a]
Women	5 (3, 7)	6 (46.1)	3 (23.1)	4 (30.8)	0.68[a]
Men	4.5 (2.5, 6)	6 (50.0)	4 (33.3)	2 (16.7)	
Heart failure (I50)					
	7.5 (3.5, 11)	5 (31.2)	2 (17.5)	9 (56.3)	0.05[a]
Women	9 (5.5, 12.5)	2 (25.0)	0 (0.0)	6 (75.0)	
Men	5 (3.5, 8.5)	3 (37.5)	2 (25.0)	2 (37.5)	
Atrial fibrillation (I48.91)					
	7 (5, 11)	2 (18.2)	3 (27.3)	6 (54.5)	0.10[a]

Women	11 (5, 13)	1 (20.0)	1 (20.0)	3 (60.0)	0.88[a]
Men	6.5 (6, 8)	1 (16.7)	2 (33.3)	3 (50.0)	
Chronic kidney disease (N18.9)					
	6 (4, 7)	4 (36.4)	4 (36.4)	3 (27.2)	0.60[a]
Women	5 (4, 7)	3 (42.8)	2 (28.6)	2 (28.6)	0.76[a]
Men	6 (5, 7)	1 (25.0)	2 (50.0)	1 (25.0)	
Breast cancer (C50.9)					
	5 (5, 5)	4 (36.3)	3 (27.4)	4 (36.3)	0.75[a]
Women	5 (5, 5)	4 (36.3)	3 (27.4)	4 (36.3)	-
Men	-	-	-	-	
Hearing loss/Deafness (H90, H91)					
	7 (3, 8)	4 (40.0)	0 (0.0)	6 (60.0)	**0.05**[a]
Women	7 (4, 7)	2 (40.0)	0 (0.0)	3 (60.0)	1.0[a]
Men	7 (3, 8)	2 (40.0)	0 (0.0)	3 (60.0)	
Erectile dysfunction (N52.9)					
	4 (4, 9)	5 (55.6)	1 (11.1)	3 (33.3)	0.67[a]
Women	-	-	-	-	-
Men	4 (4, 9)	5 (55.6)	1 (11.1)	3 (33.3)	
Angina (I20.9)					
	8 (4.5, 10)	2 (25.0)	2 (25.0)	4 (50.0)	0.34[a]
Women	6 (3, 11)	1 (33.3)	1 (33.3)	1 (33.3)	0.77[a]
Men	10 (6, 10)	1 (20.0)	1 (20.0)	3 (60.0)	
Coronary heart disease (I25.1)					
	7 (4, 9)	2 (28.6)	1 (14.3)	4 (57.1)	0.24[a]

Women	8 (8, 8)	0 (0.0)	0 (0.0)	1 (100.0)	0.65[a]
Men	6.5 (4, 9)	2 (33.3)	1 (16.7)	3 (50.0)	
Prostate cancer (C61)					
	8 (2, 10)	3 (42.9)	0 (0.0)	4 (57.1)	0.16[a]
Women	-	-	-	-	-
Men	8 (2, 10)	3 (42.9)	0 (0.0)	4 (57.1)	
Anorexia/Bulimia (F50.0, F50.2)					
	6.5 (3, 10)	3 (50.0)	0 (0.0)	3 (50.0)	0.30[a]
Women	6.5 (3, 10)	3 (50.0)	0 (0.0)	3 (50.0)	-
Men	-	-	-	-	
Crohn's disease (K50)					
	6 (5, 7)	1 (16.7)	3 (50.0)	2 (33.3)	0.23[a]
Women	6.5 (5.5, 7.5)	0 (0.0)	2 (50.0)	2 (50.0)	0.22[a]
Men	5 (4, 6)	1 (50.0)	1 (50.0)	0 (0.0)	
Epileptic (G40.909)					
	6 (4, 7)	2 (40.0)	1 (20.0)	2 (20.0)	0.85[a]
Women	6.5 (6, 7)	0 (0.0)	1 (50.0)	1 (50.0)	0.23[a]
Men	4 (3. 7)	2 (66.7)	0 (0.0)	1 (33.3)	
Chronic Obstructive Pulmonary Disease (K50-52)					
	4.5 (2, 7)	2 (50.0)	1 (25.0)	1 (25.0)	0.87[a]
Women	3 (3, 3)	1 (100.0)	0 (0.0)	0 (0.0)	0.72[a]
Men	6 (1, 8)	1 (33.3)	1 (33.3)	1 (33.3)	
Cervical cancer (C53.9)					
	2 (2, 2)	2 (100.0)	0 (0.0)	0 (0.0)	0.33[a]

Women	2 (2, 2)	2 (100.0)	-	-	-
Men	-	-	-	-	
Chronic hepatitis (K73)					
	7 (4, 10)	1 (50.0)	0 (0.0)	1 (50.0)	0.67[a]
Women	-	-	-	-	-
Men	7 (4, 10)	1 (50.0)	0 (0.0)	1 (50.0)	
Cirrhosis (K74.60)					
	6.5 (5, 8)	0 (0.0)	1 (50.0)	1 (50.0)	
Women	6.5 (5, 8)	0 (0.0)	1 (50.0)	1 (50.0)	-
Men	-	-	-	-	
HIV (B20)					
	6 (2, 10)	1 (50.0)	0 (0.0)	1 (50.0)	0.67[a]
Women	-	-	-	-	-
Men	6 (2, 10)	1 (50.0)	0 (0.0)	1 (50.0)	
Dementia/Alzheimer disease (G30.9, F03)					
	10.5 (9, 12)	0 (0.0)	0 (0.0)	2 (100.0)	0.08[a]
Women	-	-	-	-	-
Men	10.5 (9, 12)	-	-	2 (100.0)	
Parkinson disease (G20)					
	8 (7, 9)	0 (0.0)	0 (0.0)	2 (100.0)	0.08
Women	-	-	-	-	-
Men	8 (7, 9)	-	-	2 (100.0)	
Colon cancer (C18.9)					
	3 (3, 3)	1 (100.0)	0 (0.0)	0 (0.0)	0.58[a]

Women	-	-	-	-	-
Men	3 (3, 3)	1 (100.0)	-	-	
Melanoma (C43)					
	16 (16, 16)	0 (0.0)	0 (0.0)	1 (100.0)	0.29[a]
Women	16 (16, 16)	-	-	1 (100.0)	-
Men	-	-	-	-	
Lupus (M32.9)					
	7 (7, 7)	0 (0.0)	0 (0.0)	1 (100.0)	-
Women	7 (7, 7)	-	-	1 (100.0)	-
Men	-	-	-	-	
Multiple sclerosis (G35)					
	9 (9, 9)	0 (0.0)	0 (0.0)	1 (100.0)	0.29[a]
Women	9 (9, 9)	-	-	1 (100.0)	-
Men	-	-	-	-	
Leukemia (C95.9)					
	7 (7, 7)	0 (0.0)	0 (0.0)	1 (100.0)	0.29[a]
Women	-	-	-	-	-
Men	7 (7, 7)	-	-	1 (100.0)	
Urinary cancer (C67)					
	15 (15, 15)	0 (0.0)	0 (0.0)	1 (100.0)	0.29[a]
Women	15 (15, 15)	-	-	1 (100.0)	-
Men	-	-	-	-	
Schizophrenia/Bipolar (F20.9, F31.9)					
	-	0 (0.0)	0 (0.0)	0 (0.0)	-

Women	-	-	-	-	-
Men	-	-	-	-	
Ovarian cancer (C56.9)					
	-	0 (0.0)	0 (0.0)	0 (0.0)	-
Women	-	-	-	-	-
Men	-	-	-	-	
Bold values represent $p < 0.05$; [a] Differences were evaluated by the chi-square test					

Furthermore, the median quality of sleep score of the participants who did not have hyperlipidemia was 5 (quartiles, q_1=3, q_3=7) with the maximum score being 17 while the median quality of sleep score of the participants who had hyperlipidemia was 5 (quartiles, q_1=3, q_3=8) with the maximum score being 16 (p=0.03) (***Figure 5.2***). The median quality of sleep score of the participants who did not have hyperlipidemia was 5 and of those with hyperlipidemia 5 (p=0.03); the corresponding values for individuals with and without hypertension were 5 and 5, respectively (p=0.04) (***Figure 5.3***) and for those with and without thyroid diseases the median scores were 5 and 5 (p=0.14) (***Figure 5.4***).

Although, we did not identify any other statistically significant associations, it is important to note that higher scores for quality of sleep, which indicate a worse quality of sleep, were reported in individuals with melanoma, urinary cancer, dementia/ Alzheimer disease, heart failure, and angina.

Figure 5.2: Box plot of quality of sleep score for individuals with and without thyroid diseases.

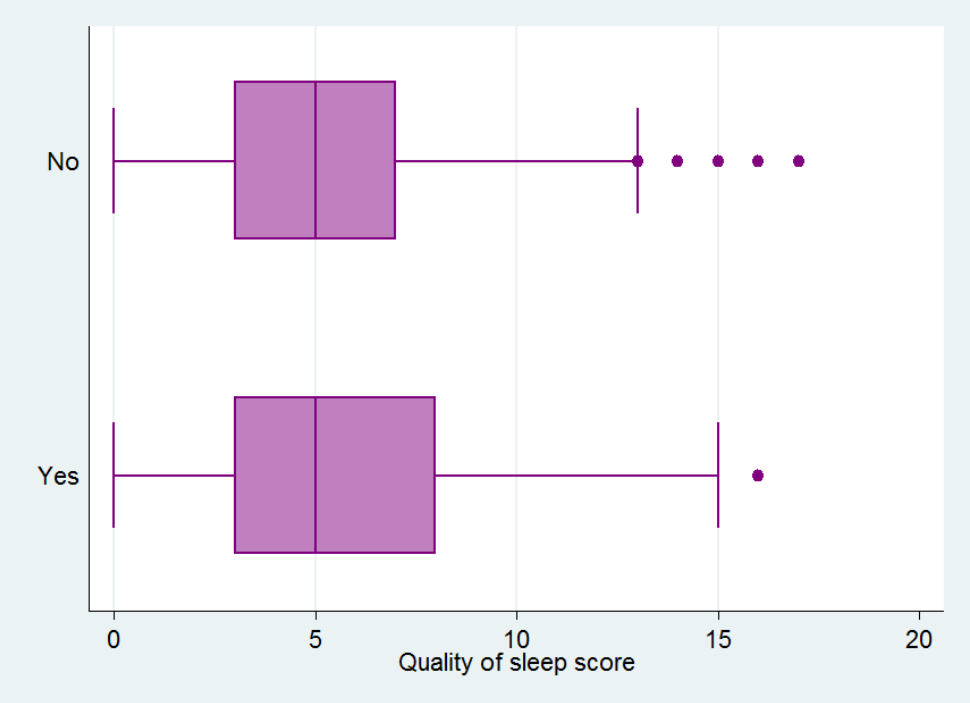


Figure 5.3: Box plot of quality of sleep score for individuals with and without hypertension.

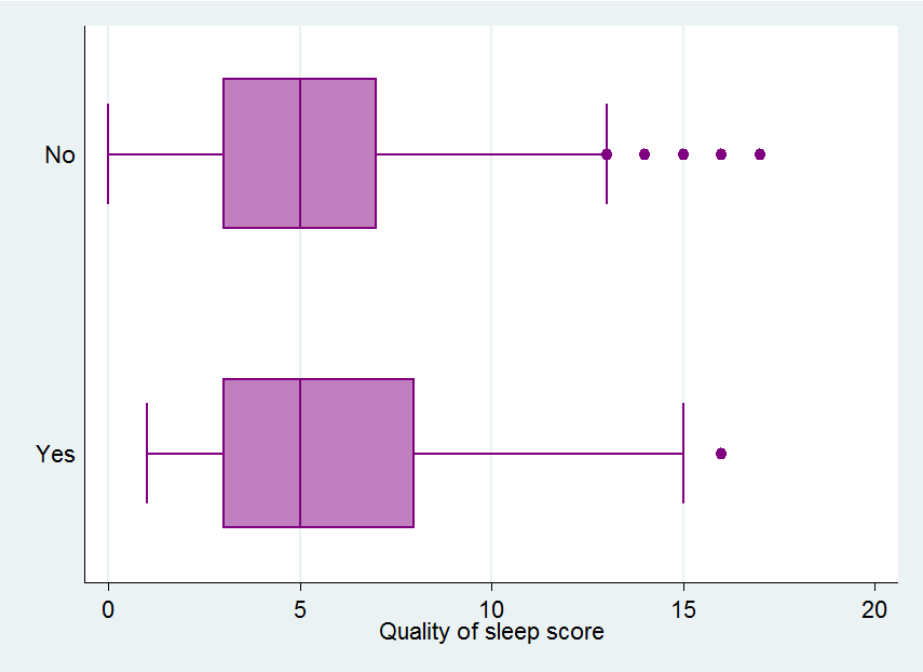
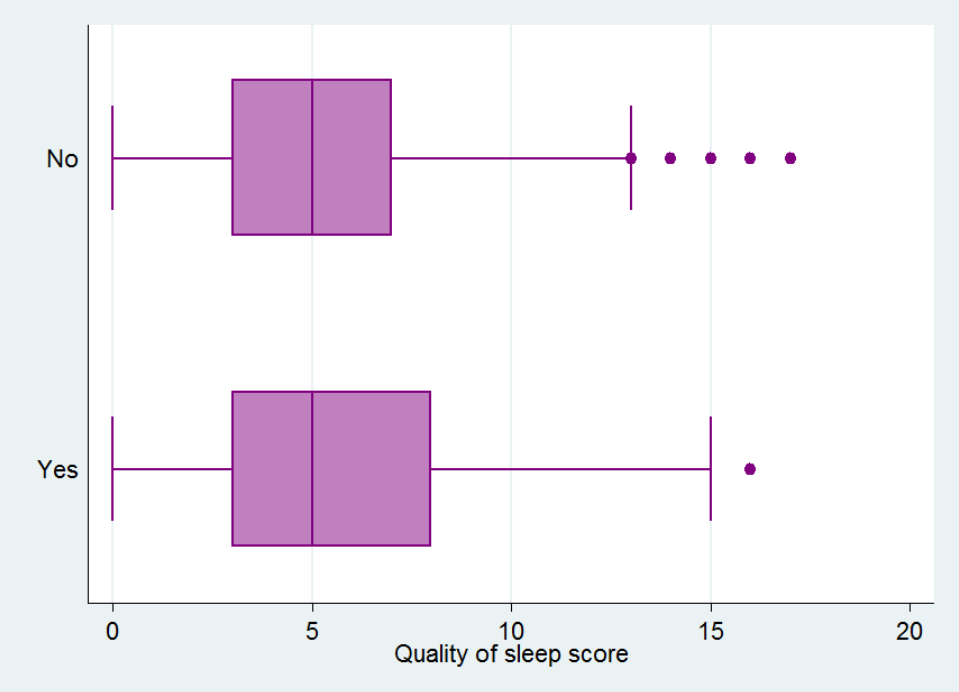


Figure 5.4: Box plot of quality of sleep score for individuals with and without thyroid diseases.



We also found statistically significant associations between quality of sleep and the majority of the human systems (***Table 5.6***). Firstly, we found a statistically significant difference between individuals with at least one disease of the circulatory system and those who did not have any disease of the circulatory system ($p<0.01$). A larger percentage of the individuals with at least one disease of the circulatory system was identified in the poor quality of sleep tertile compared to the corresponding percentage in the good quality of sleep tertile (31% vs. 21%). Similarly, we found larger percentages in the poor quality of sleep tertile compared to the good quality of sleep tertile, in all the other systems. Participants, with at least one disease of the immune system have a larger median value of quality of sleep score compared to those with no disease of the immune system (7 vs. 5). The results indicates that the participants with at least one disease of the immune system have a poorer quality of sleep compared to those with no disease of the immune system. Moreover, participants, with at least one disease of the skeletal/ muscular system have a larger median value of quality of sleep score compared to those with no disease of the skeletal/ muscular system (7 vs. 5). Hence, participants with at least one disease of the skeletal/ muscular system have a poorer quality of sleep compared to those with no disease of the skeletal/muscular system.

Table 5.6: Quality of sleep in each human system reported in the study.

Human systems	**Overall** (N=1140)	**Good** (N=541)	**Moderate** (N=273)	**Poor** (N=326)	**p-value**
Circulatory					
No	5 (3, 7)	426 (78.7)	205 (75.1)	226 (69.3)	**<0.01**[a]
Yes	5 (3, 8)	115 (21.3)	68 (24.9)	100 (30.7)	
Endocrine					
No	5 (3, 7)	460 (85.0)	231 (84.6)	253 (77.6)	**0.01**[a]
Yes	5 (3, 8)	81 (15.0)	42 (15.4)	73 (22.4)	
Digestive /Excretory					
No	5 (3, 7)	491 (90.8)	237 (86.8)	268 (82.5)	**<0.01**[a]
Yes	6 (4, 8)	50 (9.2)	36 (13.2)	57 (17.5)	
Nervous					
No	5 (3, 7)	497 (92.0)	245 (90.1)	277 (85.0)	**<0.01**[a]
Yes	6 (3, 8)	43 (8.0)	27 (9.9)	49 (15.0)	
Respiratory					
No	5 (3, 7)	501 (92.8)	239 (87.6)	295 (90.5)	**0.05**[a]
Yes	5 (3, 7)	39 (7.2)	34 (12.4)	31 (9.5)	
Immune					
No	5 (3, 7)	531 (98.3)	266 (97.4)	307 (94.2)	**<0.01**[a]
Yes	7 (4, 10)	9 (1.7)	7 (2.6)	19 (5.8)	

Skeletal/Muscular					
No	5 (3, 7)	532 (98.3)	267 (97.8)	309 (94.8)	**<0.01**[a]
Yes	7 (3.5, 11)	9 (1.7)	6 (2.2)	17 (5.2)	
Neoplasm					
No	5 (3, 7)	531 (98.2)	269 (98.9)	316 (96.9)	0.22[a]
Yes	5 (5, 5)	10 (1.8)	3 (1.1)	10 (3.1)	
Renal/Urinary					
No	5 (3, 7)	537 (99.3)	269 (98.5)	323 (99.1)	0.60[a]
Yes	6 (4, 7)	4 (0.7)	4 (1.5)	3 (0.9)	
Reproductive					
No	5 (3, 7)	536 (99.1)	271 (99.6)	323 (99.1)	0.67[a]
Yes	4 (4, 9)	5 (0.9)	1 (0.4)	3 (0.9)	
Bold values represent $p < 0.05$; [a] Differences between men and women were evaluated by the chi-square test.					

5.1.3 Association of quality of sleep, Mediterranean Diet and multimorbidity

First, we examined the association between the Mediterranean Diet adherence and quality of sleep using regression analysis. We observed that as the quality of sleep score increases, indicating poorer sleep, the Mediterranean Diet score decreases (p=0.03). When we considered Mediterranean Diet adherence and quality of sleep as categorical variables by using the chi-square test, the results were not statistically significant. Nevertheless, the majority of the participants who had poor quality of sleep also had a low or moderate adherence to the Mediterranean Diet (***Table 5.7***). On the other hand, most of the individuals with a good quality of sleep had a moderate or a high adherence to the Mediterranean Diet.

Table 5.7: Quality of sleep and Mediterranean Diet adherence.

	Mediterranean Diet adherence			
Quality of sleep	Low	Moderate	High	**Total**
Good	162 (29.9)	200 (37.0)	179 (33.1)	541
Moderate	99 (36.3)	95 (34.8)	79 (28.9)	273
Poor	118 (36.2)	118 (36.2)	90 (27.6)	326
Total	379	413	348	1140

We performed a logistic regression analysis to examine the association of the Mediterranean Diet adherence and quality of sleep with the odds of having more than chronic conditions by including both of them simultaneously in the model. The interaction term between quality of sleep and Mediterranean Diet adherence was assessed first and it

was found not to be statistically significant. The model with only main effects (***Table 5.8***) suggested that participants who were in the poor quality of sleep tertile had a higher risk of multimorbidity compared to the participants in the good quality of sleep tertile, over and above the effect of the Mediterranean Diet adherence (unadjusted OR=2.16, 95% CI: 1.59, 2.94).

The model was then adjusted for possible confounders (***Table 5.8***), including age, sex, smoking, and physical activity status. When adjusted only for age and sex (Model 2) being in the poor quality of sleep group had a higher risk of multimorbidity compared to the good quality of sleep group with an OR equal to 2.26 (95% CI: 1.60, 3.20). We further observed a statistically significant association between the moderate quality of sleep and multimorbidity compared to the good quality of sleep group (adjusted OR=1.55, 95% CI: 1.05, 2.28).

When we further adjusted for smoking habits and physical activity level (*Model 3*, ***Table 5.8***) the relationship between moderate and poor quality of sleep with multimorbidity compared to the good quality of sleep remained statistically significant. More specifically, individuals who were in the poor quality of sleep group had about 2 times higher risk of multimorbidity compared to the individuals in the good quality of sleep group (adjusted OR=2.19, 95% CI: 1.54, 3.11).

Table 5.8: Logistic regression analysis evaluating the association of level of quality of sleep and Mediterranean Diet adherence with multimorbidity.

	Total (N = 1140)	**Women** (N = 642)	**Men** (N = 497)
	OR (95%CI)	OR (95%CI)	OR (95%CI)
Model 1: Crude model			
Mediterranean Diet adherence			
Low	*Ref*	*Ref*	*Ref*
Moderate	0.91 (0.66, 1.25)	0.78 (0.52, 1.17)	1.27 (0.75, 2.15)
High	0.74 (0.53, 1.05)	0.71 (0.45, 1.11)	0.92 (0.53, 1.61)
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	1.23 (0.87, 1.75)	1.35 (0.85, 2.14)	1.07 (0.63, 1.83)
Poor	**2.16 (1.59, 2.94)**	**2.35 (1.58, 3.51)**	**1.79 (1.09, 2.94)**
Model 2: Model 1 plus age, (sex)			
Mediterranean Diet adherence			

Low	*Ref*	*Ref*	*Ref*
Moderate	0.90 (0.63, 1.28)	0.80 (0.51, 1.23)	1.06 (0.57, 1.97)
High	0.76 (0.52, 1.11)	0.75 (0.47, 1.22)	0.76 (0.40, 1.46)
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	**1.55 (1.05, 2.28)**	1.43 (0.87, 2.35)	1.83 (0.97, 3.47)
Poor	**2.26 (1.60, 3.20)**	**2.29 (1.49, 3.52)**	**2.29 (1.26, 4.15)**
Model 3: Model 2 plus smoking habits, physical activity			
Mediterranean Diet adherence			
Low	*Ref*	*Ref*	*Ref*
Moderate	0.92 (0.65, 1.32)	0.81 (0.52, 1.27)	1.10 (0.59, 2.04)
High	0.78 (0.53, 1.15)	0.76 (0.47, 1.24)	0.81 (0.42, 1.56)
Quality of sleep tertiles			
Good	*Ref*	*Ref*	*Ref*
Moderate	**1.52 (1.03, 2.25)**	1.44 (0.88, 2.37)	1.73 (0.91, 3.29)
Poor	**2.19 (1.54, 3.11)**	**2.24 (1.45, 2.46)**	**2.18 (1.19, 4.00)**
Abbreviations: Confidence Interval (CI); Odds Ratio (OR); ORs and their corresponding 95%CIs were obtained from logistic regression analysis; Bold values represent $p < 0.05$			

We also stratified the analysis by sex (***Table 5.8***). We found that the association between poor quality of sleep with the odds of having more than two chronic conditions was statistically significant in both sexes ($p < 0.05$), with the association being stronger among women (unadjusted OR=2.35, 95% CI: 1.58, 3.51) than among men (unadjusted OR=1.79, 95% CI: 1.09, 2.94). The relationship remained statistically significant in both sexes even after adjusting for age, smoking habits, and physical activity level.

6 Chapter 6 - Discussion/ Interpretation

This is the first large-scale study investigating multimorbidity in Cyprus using a representative sample of the general adult population and considering 47 different chronic conditions. The study found that the overall age and sex standardized prevalence of multimorbidity was 28.6% with the multimorbidity rate increasing significantly with age. The prevalence of multimorbidity was higher in women than in men, in overweight/ obese people, among divorced/ widowed individuals, in those who completed only primary school, among current smokers and in people who were physically inactive. Moreover, the study found that, overall, the most prevalent chronic diseases were diseases of the circulatory system, which was the case among participants with multimorbidity too, followed by the endocrine system, and the digestive-excretory system. The most prevalent chronic conditions were hyperlipidemia, followed by hypertension, thyroid diseases, and gastric reflux.

In addition, our population-based study of the general adult Cypriot population provided, to the best of our knowledge, the first piece of evidence of the relationship between multimorbidity with adherence to the Mediterranean Diet as well as with quality of sleep. The results suggest that higher adherence to the Mediterranean Diet is associated with lower odds of multimorbidity. Adopting a dietary pattern, which is close to the Mediterranean Diet is beneficial and would help in reducing the risk of multimorbidity. Similarly, the results indicate that good quality of sleep is associated with lower odds of multimorbidity. Having good sleep is beneficial and would help in reducing the risk of multimorbidity. These are important public health results and support the evidence available for the positive impact of a traditional Mediterranean diet and of good quality of sleep.

The overall age and sex standardized prevalence of multimorbidity was 28.6%. This is comparable to other studies with a cross-sectional design and similar definition of multimorbidity carried out in Scotland [17], Australia [13], Serbia [129], and Brazil [24]. The prevalence in Cyprus seems to be lower than the corresponding figures reported for Canada [130], Switzerland [131], and Indonesia [132], but higher than South Asia [16], China [18], and Iran [133]. Moreover, about half of the study participants did not report suffering from any

of the chronic diseases considered, something that is similar to results given for Finland [29] and Italy [134].

We found that the prevalence of multimorbidity was higher in individuals aged 65 years old, followed by those aged 45-64 years old, those 25-44 years old and those 18-24 years old. The observation that the prevalence of multimorbidity increases with age is consistent with reports from other studies around the world [13,18,31]. Specifically, one epidemiological study in Australia [13] estimated the prevalence of multimorbidity in a sample of patients attending general practice and found that prevalence increased with age with 83.2% of patients aged 75 years old or older having multimorbidity. In addition, in an investigation of the prevalence of multimorbidity in the general population of China [18], it has been found that the prevalence of multimorbidity increased with age and specifically by 1.36 times per five years increase, while in Sweden [31], it has been reported that increased age was associated with more than 50% increased risk of multimorbidity. Given the aging population of Cyprus and the fact that multimorbidity increases with age, the prevalence of multimorbidity is expected to rise even higher in the future. Specifically, WHO indicates that in many countries the life expectancy has exceeded 75 years old and given that life expectancy in Cyprus is among the highest in Europe, the number of years living with disabilities due to several chronic conditions will also rise.

Moreover, multimorbidity is inversely related with the number of health centers in each region. Therefore, as the number of health centers in a region increases the multimorbidity prevalence decreases. This finding should motivate the public health authorities of Cyprus in setting priorities in the organization of primary and secondary health care, especially in light of the new general health system currently being implemented. Specifically, in connection to the free access for everyone to the new general health system in Cyprus, it is important for every resident to have access to primary and secondary healthcare near his/ her place of residence. The development of health centers at a reasonable distance in every area of Cyprus, whether urban or rural, in which care will be provided for all health fields is crucial since multimorbidity is also positively correlated with the number of physicians per region. As the number of physicians per region is adequate and there are physicians available from all specialties, citizens will be secured that they will have the appropriate treatment.

Our study suggests that multimorbidity is common not only among the elderly but also among people of younger ages. We reported that 57% of the participants with multimorbidity are in fact younger than 65 years old and, specifically, 8% were 18-24 years old, 16% were 25-44 years old, and 33% were 45-64 years old. Other cross-sectional studies which investigated the prevalence of multimorbidity using medical records or self-reported questionnaires also reported similar findings [22]. We further observed that the prevalence of multimorbidity was higher in women than in men which has also been described in other studies [18,45,132]. An epidemiological study in Iran [45] assessed multimorbidity and its associated risk factors and it has been reported that the odds of multimorbidity was 2.11 fold higher in women compared to men. Similarly, in China [18] it has been reported that women have 1.70 times higher risk of multimorbidity compared to men while a study in Indonesia [132] reported that women had higher prevalence of multimorbidity than men, with the corresponding percentages being 41.5% and 29.5% in women and men, respectively. Given the relatively high prevalence of endocrine disorders, and that in our population a higher percentage of women than men were physically inactive, and had completed primary school only, which was also associated with the presence of multimorbidity, may in part explain the higher prevalence of multimorbidity in women.

We observed significant bivariate associations between socio-demographic characteristics, lifestyle factors, such as marital status, educational level, exercise, smoking, and BMI, and the prevalence of multimorbidity, however, there was no association with geographical area, residency, or salary. We reported that almost half (48%) of the individuals with multimorbidity were divorced or widowed while 73% had completed only primary school. The higher prevalence of multimorbidity in people with lower education concurs with previous results published elsewhere [16,18,22,31] with all previous studies reporting that multimorbidity was less common in the most educated individuals. Lifestyle factors (i.e. physical activity and smoking) were independently associated with multimorbidity, with 63% and 41% of the individuals reported as having multimorbidity being physically inactive and being current smokers, respectively. It was previously observed that lifestyle factors were associated with the prevalence of multimorbidity in other epidemiological studies too [16,18,44]. Given that the major risk factors of chronic conditions include tobacco use and physical inactivity [135,136] it may be

useful to assess the associations of these with multimorbidity and try to address them with relevant public health inverventions. Apart from this, the study reported that 72% of the individuals with multimorbidity were overweight or obese (>25 kg/m^2) which is consistent with another epidemiological study for South Asian adults [16].

Moreover, discriminant analysis was performed to create the profile of multimorbid individuals. The analysis suggested that in individuals with two morbidities increased age, and higher BMI are more dominant factors compared to individuals with none or 1-morbidity category. Hence, it seems that an individual with two morbidities is more commonly at an increased age with a BMI more than 25 kg/m^2. Furthermore, in individuals with three morbidities increased age, current smoking, and higher salary are the dominant factors to characterize those participants while among individuals with >3 morbidities, being a man, having higher salary, and having increased BMI seem to better characterize them. Hence, an individual who has three morbidities is an individual at an increased age, who is a current smoker with a yearly average salary more than 19,500 euros, while an individual with more than 3 morbidities seems to be a man, with a BMI more than 25 kg/m^2, and a yearly average salary more than 19,500 euros. The higher salary as a dominant factor was an unexpected finding, though it was also reported in another epidemiological study in China [18]. There are some possible explanations for that finding. First, the majority of the participants who had a higher salary was more than 45 years old. In addition, people with a lower income may have lower rates of diagnosed conditions because of less visits to the doctor especially since a general public healthcare system was not in place during the period of the study and it has only been recently put in effect. Having the profile of a multimorbid individual is a concise and balanced view of the population's health, which may inform local agencies, such as the Ministry of Health, to assess policies and practices.

We defined multimorbidity as "two or more" morbidities which is the definition most commonly used, however, especially when highly prevalent conditions (e.g., hypertension, hyperlipidemia) are present in the population, using a higher cut-off to define multimorbidity may be preferred. Hence, we estimated the prevalence of study participants having 2, 3, 4, 5 and more than 5 morbidities; this showed that the majority of multimorbid individuals have two morbidities while the cumulative frequency no longer increases after the cut-off of 5 morbidities. Specifically, we identified that among

the study participants, 11.8% had 2 morbidities, 6.6% had 3 morbidities, 5.3% had 4 morbidities, and 0.03% had 5 morbidities. Given that 74.3% had 0 or 1 morbidities, the cumulative frequency until the cut-off of 5 morbidities was 98% and until the largest number of morbidities reported (which was 12), it does not increase sharply.

The main chronic diseases, as reported in the literature, are cardiovascular diseases, chronic kidney diseases, osteoarthritis, endocrine and metabolic diseases, and mental disorders. Our results are in agreement with this, suggesting that the majority of chronic diseases involve the cardiovascular and endocrine system. We identified that hyperlipidemia is prevalent in our study population, similar to studies in China, Brazil, Switzerland, and Indonesia [24,33,132,137], though those studies used dyslipidemia and hypercholesterolemia as their definitions. Hypertension is also quite prevalent in the Cypriot population which is consistent with reports from other cross-sectional studies [15,20,21,132].

We reported that the most prevalent combinations of chronic diseases were hyperlipidemia/ thyroid diseases and hyperlipidemia/ gastric reflux. On the one hand, thyroid dysfunction can have an important effect on lipid profile [138] and it has been shown that the thyroid hormones have an effect on cholesterol synthesis and metabolism and, more specifically, hypothyroidism has been associated with increased levels of triglycerides and cholesterol [139]. On the other hand, a diet high in fat and calories, which is associated with obesity, usually co-exists with gastroesophageal reflux disease and with high cholesterol levels. However, there is no scientific evidence of a direct cause and effect relationship between gastroesophageal reflux disease and hyperlipidemia, so further research is needed to investigate this relationship.

Our study suggests that the Cypriot population is moving away from the traditional Mediterranean Diet something that is consistent with other studies which investigated the adherence to Mediterranean Diet in other Mediterranean countries [50,58] and with an earlier review [140] for two related Greek-speaking Mediterranean populations, namely the Greek and Cypriot populations. Moreover, as reported from an epidemiological study which investigated the worldwide variation of adherence to the Mediterranean Diet during the periods 1961-1965 and 2000-2003 [141], most of the countries seem to be moving away from the traditional Mediterranean Diet pattern.

Specifically, European countries in the Mediterranean, especially Greece, but other countries in the region as well, presented a decrease in the Mediterranean Diet score.

It is true that there is the perception that older people follow the traditional dietary patterns, including Mediterranean Diet [142,143] more than younger people, something though that was not confirmed in our study. In 2005, a study in Cyprus [101] reported that the Mediterranean Diet score in the elderly was higher and that more than 9 out of 10 of the participants in that age group reported that they followed that pattern for at least 30-40 years of their life. It seems that in 2020 none of the study age groups follows the traditional Mediterranean Diet to a large extent, since all age groups had a total score lower than 17, which is considered low adherence to Mediterranean Diet.

We have observed differences in the adherence to the Mediterranean Diet between men and women, and specifically, we found that men's adherence to the Mediterranean Diet was higher than women's which is in agreement with other studies [58,144] but different than the ATTICA study in Greece [145]. Given that the Mediterranean Diet decreases the risk of cardiovascular disease, coronary heart disease, and stroke [54,55] and that in our sample more men than women reported having at least one cardiovascular disease (30% vs. 20%) this may play a role for the higher men's adherence to Mediterranean Diet. More specifically, the ATTICA study in Greece [55] reported that the 5-year incidence of cardiovascular diseases was higher in men compared to women and that the abstinence from the traditional healthy Mediterranean Diet pattern seems to predict cardiovascular diseases events within a 5-year time interval. So, it is possible that men with at least one cardiovascular disease, who are more compared to women, follow a healthy dietary pattern similarly to Mediterranean Diet for their protection of the adverse consequences of cardiovascular diseases including mortality[146].

Although we did not identify statistically significant differences of the adherence to Mediterranean Diet among the five geographical areas of Cyprus, we found statistically significant differences between the residents of urban and rural regions, with people who lived in rural areas having better adherence. Nowadays, diets are changing due to many reasons including urbanization [147] and an increase in consumption of animal foods, sugar, salt, fats, oils, refined grains, and processed foods [147]. People living in cities tend to consume more calories, many of them from carbohydrates, sugary snacks, and processed foods [148], which are widely available in urban areas.

Furthermore, we found that divorced/ widowed people did not adhere to good dietary habits as well as married and unmarried people, a finding which agrees with other epidemiological studies [149–151]. Specifically, it has been reported that divorced/ widowed people did not eat as well as unmarried people [150] and that single people including unmarried, divorced, separated and widowed individuals were less likely to consume high fruit and vegetables [151]. We did not find any statistically significant differences among educational status and salary categories with Mediterranean Diet adherence. Furthermore, people who were physically active and not current smokers had a higher Mediterranean Diet score while obese and overweight people's adherence to Mediterranean Diet was lower than people who classified as normal weight.

The possible health benefits of the Mediterranean Diet have been documented before for a series of cardiovascular outcomes, e.g., coronary heart disease, and stroke [54,152]. It has also been suggested that the Mediterranean Diet has a positive effect on components of metabolic syndrome like waist circumference, high-density lipoprotein cholesterol, triglycerides, systolic and diastolic blood pressure, and glucose [142]. Moreover, a diet which includes a high consumption of fruits and vegetables, whole grains, and fish [48] and a low consumption of animal fat lowers the risk of obesity and cardiovascular diseases, e.g. hypertension and hypercholesterolemia, [49] as well as neoplastic diseases [50]. In Cyprus, it has been reported that adherence to a Mediterranean Diet among elderly people was associated with reduced odds of having hypercholesterolemia, hypertension, diabetes, and obesity [101].

Our results suggest that the Mediterranean Diet was associated with lower risk of multimorbidity. Specifically, having a high adherence to the Mediterranean Diet presents about 36% lower risk of multimorbidity than having a low adherence to the Mediterranean Diet. To the best of our knowledge, this is the first evidence of the association of multimorbidity and Mediterranean Diet. However, there is evidence about the association of Mediterranean Diet and medical multimorbidity and depressive symptoms among elderly participants [66]. The study found that the Mediterranean Diet may contribute to the protection of the development of depressive symptoms in elderly people with multimorbidity. In addition, a cross sectional study in the adult population of Netherlands assessed the association of multimorbidity, which was defined within the cardio-metabolic disease domains, with dietary habits [153]. The results showed that individuals

who were classified in the highest quintile of meat, alcohol, potato, and snack consumption had a higher likelihood of having higher morbidity (as calculated from the study) compared to individuals in the lowest quantile. On the other hand, individuals who were classified in the highest quintile of vegetable, fish, fruit pattern, bread and sweets pattern had a lower likelihood of having higher morbidity scores (as calculated from the study) compared to individuals in the lowest quantile. Furthermore, a diet which is characterized by a high consumption of fruits, legumes, cereals and vegetables, a low consumption of red meat and processed meats, and a moderate consumption of red wine, has been reported to have advantageous effects for lipid metabolism, blood pressure, mortality due to cardiovascular diseases, and obesity [65]. Therefore, it seems that dietary habits, such as a healthy dietary pattern similar to the Mediterranean diet, contribute to the prevention of a number of conditions, which would contribute to the development of multimorbidity.

Mediterranean Diet, defined as the traditional dietary pattern found in Mediterranean countries with production of olives, such as Greece, Southern Italy and Spain [67], meets many criteria of a healthy diet [68]. It is true that, the mechanism by which Mediterranean Diet may be protective against multimorbidity is largely unknown. However, we could hypothesize that Mediterranean Diet may be protective because of the possible anti-oncogenic actions of the oleic acid in olive oil [64], the many other antioxidants in plant foods [154], and the advantageous effects of the diet on blood lipids [64]. Given that Mediterranean Diet is a healthy diet and the fact that a healthy diet is preventive of several non-communicable diseases and conditions [47], our results could add important pieces of evidence towards meeting some criteria of causality and severity tests.

Our study also found that even though the majority of the Cypriot population has a good quality of sleep in general, almost one third of the study population was classified as having a poor quality of sleep. We observed differences in the quality of sleep between men and women, among the residents of the five geographical areas of Cyprus, and among marital status categories. Specifically, women reported a poorer sleep quality compared to men, and this is consistent with other epidemiological studies [155,156]. This finding possibly implicates the state that women have more interruptions of sleep during several stages of life and the role for sex steroids [156]. It has been reported that poor quality

of sleep is associated with lower testosterone concentration in men while estrogens and progesterone levels influence sleep [157].

On the other hand, we did not observe any differences among the four age groups of the study population, among educational and salary status, between the residents of urban and rural regions, and among smoking status and BMI groups. Even though, various epidemiological studies identified a high prevalence of sleep disturbances [81] and a low sleep quality [158] among older adults, in our study, we did not report poorer quality of sleep in people >65 years old compared to people aged <65. Specifically, it has been found that there is a positive correlation between age and sleep quality scores of the elderly people and as age increases the score of the quality of sleep decreases [158]. In our study, the largest quality of sleep score (17), which indicates a worse sleep quality, was reported in people aged 18-44 years old while the corresponding score for individuals aged 65 years old was 16. More specifically, 43% and 31% of the individuals aged 65 years old and older were in the good quality of sleep tertile and poor quality of sleep tertile, respectively. Previous studies suggest that quality of life [158] and exercise [159] could help improve the quality of sleep in elderly people. Given that in our study participants have a high mean score of the quality of life assessment (EQ-5D) and almost 30% of them exercise regularly, these factors may play a role as to why we did not report a poor quality of sleep in participants aged 65+.

We further found that respondents who were classified in the poor quality of sleep group had a higher risk of multimorbidity compared to people who were in the good quality of sleep. Our finding agrees with other epidemiological studies [81,88,98,100,160] which investigated the relationship between multimorbidity and specific sleep disorders, such as insomnia, or variations in sleep-related behavior or sleep disturbances. In addition, having a poor quality of sleep increases the number of chronic diseases in an individual which is consistent with another study which investigates the sleep duration and multimorbidity in Luxembourg [88].

However, it is not clear if poor quality of sleep is a consequence of the presence of several chronic diseases in an individual or whether it leads to an increase of the number of chronic diseases in an individual. It has been reported that lack of sleep affects the endocrine pathways [161] and it could be associated with several chronic diseases including cardio metabolic and neurodegenerative diseases [85,86]. In our study the most

common combinations among people with multimorbidity were diseases of the circulatory and endocrine systems[162] while most of the people with multimorbidity who have an endocrine or circulatory disorder reported having poor quality of sleep. This finding is in agreement with the available literature about the effects of bad sleep behaviors on several chronic diseases.

7 Summary and Recommendations

7.1 Concluding remarks

This dissertation focused on the assessment of the prevalence of multimorbidity in Cyprus and its association with Mediterranean Diet and quality of sleep in a sample of Cypriot adults. Our results suggest that multimorbidity is relatively common in the adult Cypriot population, not only among the elderly but also in younger ages. The most prevalent chronic diseases among people with multimorbidity were hyperlipidemia, followed by hypertension, gastric reflux, and thyroid diseases, while the most common combinations of diseases were of the circulatory and endocrine systems. The findings also suggest that the profile of the multimorbid individual is that of a person at an older age, with a higher BMI, who is a current smoker, and has a higher salary.

The goal of this study was the investigation of multimorbidity focusing not just on an index condition but on the presence of two or more chronic diseases. Chronic diseases is the leading cause of morbidity worldwide with many of these conditions being related to aging. Hence, health systems in Cyprus, and elsewhere, must focus on the combination of chronic conditions that may present in an individual simultaneously. Multimorbidity is common in the Cypriot population, which is the case in other countries as well, hence, it is important to address the issue as effectively as possible. Knowledge about multimorbidity has important implications for prevention, diagnosis, treatment, and prognosis strategies.

Another objective of the dissertation was to explore the association of adherence to the Mediterranean Diet and of quality of sleep with multimorbidity. The findings suggest that the Cypriot population is moving away from the traditional Mediterranean Diet, with men and residents of rural regions being more adherent to that dietary pattern compared to women and residents of urban regions, respectively. In terms of quality of sleep, it seems that the Cypriot population has good quality of sleep, in general, even though almost one third of the population has poor quality of sleep. A closer look at sex and marital status of Cypriot citizens showed that women and married people had a poorer quality of sleep compared to men and unmarried individuals, respectively. The study provides the first evidence of an association between Mediterranean Diet or quality of

sleep and multimorbidity. The results suggest that low adherence to the Mediterranean Diet and poor quality of sleep were associated with higher odds of multimorbidity.

The Mediterranean Diet is considered a healthy diet and it may be preventive of the development of multimorbidity. Even though the mechanism by which the Mediterranean Diet may be protective against multimorbidity is largely unknown, we could hypothesize that it may be because of the possible anti-oncogenic action of the oleic acid in olive oil, the many other anti-oxidants in plant foods and the advantageous effects of the diet on blood lipids. At the same time, good quality of sleep is necessary for good health and well-being as well as for reducing the risk of the development of multimorbidity, as this dissertation reports.

7.2 Limitations and strengths

There are some limitations in our study that should be considered when interpreting the findings. First, the cross-sectional design used means that only associations between the variables of interest could be examined but not causal relationships. Furthermore, the severity of the disease is not taken into account, and all chronic diseases included in the study were provided directly by the participants based on diagnosis by a physician and were given equal weight in the calculation of multi-morbidity, something, however, that is commonly used in studies of multimorbidity. The face-to-face interviews for the medical history assessment could be subjected to social desirability bias though this was mitigated by having trained field workers performing the interviews. In addition, institutionalized individuals were excluded from our sample, although, a high prevalence of chronic diseases and multimorbidity has been identified in this group of people. This may have underestimated the prevalence of multimorbidity in the total population, but it strengthens our results among free-living people.

Notwithstanding these limitations, the study has several strengths as this is a large population-based study using a representative sample of both men and women from all ages (18+) and geographical areas of Cyprus. Other strengths include the collection of detailed data using a validated questionnaire. The majority of the different parts of the questionnaire have been already validated (PSQI, FFQ, PSS-14, and EQ-5D) and the questionnaire was also pilot tested using a sample of 10% of the total sample of the study. Furthermore, detailed data was collected, including information about demographic and

socioeconomic characteristics of the participants, on the presence of 47 chronic conditions, on the participants' dietary habits, including the consumption of 11 food groups (non-refined cereals, fruits, vegetables, legume, potatoes, fish, meat and meat products, poultry, full fat dairy products, olive oil and alcohol intake), on the quality of sleep, on the level of stress, and on the quality of life of the participants, as well as information about other lifestyle habits (i.e. smoking, exercise etc.). Our results could be utilized by the Ministry of Health in order to plan appropriate strategies to reduce the prevalence of multimorbidity and to improve the impact of Mediterranean Diet and good quality of sleep.

7.3 Impact

The results of this dissertation work highlighted the burden of multimorbidity in Cyprus, filling in a gap in knowledge regarding the issue. Individuals with multimorbidity have a need of poly-pharmacy, however, the guidelines worldwide focus on singe chronic conditions and in most cases fail to consider together the different chronic conditions that may be present in an individual simultaneously. The estimation of the prevalence of multimorbidity in the study indicates that almost one third of the general adult Cypriot population has more than two chronic conditions and that multimorbidity is relatively high even in younger people. Given the relatively high prevalence, physicians should be aware of the disease combinations and provide the best care possible. By improving the understanding of clinicians but also of patients of how to manage multiple chronic conditions could help reduce for example potential adverse effects of combinations of medications and allow for a better quality of life. As of 2020 the General Healthcare System has been implemented in Cyprus and based on it all Cypriots can have access to primary and secondary care services, either free or with a small cost, and at the same time each physician of a public or a private hospital or of a health center can, potentially, have access to the medical history of a patient. This would be a good opportunity for the health system to provide continuity in the management of individuals with multimorbidity. For instance, combinations of diseases of circulatory and respiratory systems can have a strong synergistic negative effect [163] and combinations of diseases of skeletal/ muscular system with vascular or gastrointestinal problems may lead to an increase of mortality, especially in older patients [164]. Hence, it is important for a physician to account for the

chronic conditions of each patient carefully and have a comprehensive and more complete understanding of the patient's condition. By doing so, some of the adverse effects such as disabilities, hospital admission, the length of stay and readmission, polypharmacy and mortality could be avoided [32,44].

In addition, the results of the study could be helpful in reducing the risk of multimorbidity. The results indicate that adopting a Mediterranean style diet as well as a good quality of sleep are protective against multimorbidity. Mediterranean Diet is the most extensively studied dietary pattern and it has been found that it is protective against cardiovascular disease, coronary heart disease, and stroke [54,55,60–62], the risk of metabolic syndrome [63], as well as mortality [64]. Our results add evidence of the protective role of Mediterranean diet on multimorbidity providing some of the first evidence of the relationship between adherence to the Mediterranean Diet and multimorbidity in Cyprus. Mediterranean Diet is characterized by a high intake of olive oil, fruit, nuts, vegetables, and cereals, a moderate intake of fish and poultry, a low intake of dairy products, red meat, processed meats, and sweets, and wine in moderation consumed with meals [53]. In particular, several foods of this dietary pattern are common in Cyprus. For instance, the production of olive oil has a significant place in the population and it is the main source of dietary fat, which is usually accompanied by the consumption of large portions of vegetables, either in the form of cooked foods or salads. Also, the production of fresh fruits and vegetables is important in Cyprus and the whole population has access to fresh fruits and vegetables. Furthermore, Cyprus has several farms which produce dairy products, and of course meat, but also since Cyprus is a Mediterranean region fishing is an essential part of life. However, although Cyprus has the majority of the typical foods of the Mediterranean diet, our results suggest that the Cypriot diet is moving away from the traditional Mediterranean Diet and there has been a change in dietary habits towards a more western diet. Hence, there is a need for the development of support programs that will educate people on the benefits of the Mediterranean Diet. Programs that focus on addressing and preventing multimorbidity, promoting the knowledge of the benefits of the Mediterranean Diet should be introduced and should target people from all ages in different setting, including schools, universities, and nursing homes.

It is important, to follow those dietary habits from a young age, so educating young people about the benefits of the Mediterranean diet, is also essential. Programs in schools

with students aged <12 years old (primary school) could be introduced by using experiential activities. Through those activities, children will learn about the value of food, the different food groups, and the need to consume food from all groups, as recommended. In addition, parents could receive appropriate flyers with the pyramid of the Mediterranean Diet and its beneficial effects as well as a suggested diet based on the Mediterranean Diet to follow and adopt, to the extent possible and feasible. In regards to the students of middle schools, high schools, and universities where students could understand better the benefits of the Mediterranean Diet on multimorbidity, a dietary plan based on the Mediterranean Diet could be provided. For instance, a dietary plan may be proposed, after taking into account each student's medical history, which students could follow with the necessary guidance for a set time and after that be able to maintain for the rest of their lives.

Moreover, our results support that adopting a good quality of sleep is beneficial and would help in reducing the risk of multimorbidity. This was the first evidence of the relationship between quality of sleep and multimorbidity in Cyprus. Although the Cypriot population has a good quality of sleep in general, almost one third of the population has a poor quality of sleep. Therefore, any health education program introduced in the population should also outline the positive effects of good sleep. For example, such programs could inform people, and especially young people, of the recommended duration of sleep and the importance of following those recommendations (8.5-9.5 hours for adolescents and 7-9 hours for adults [70,71]). In addition, the program could present the evidence that quality of sleep is affected by sleep disorders, such as insomnia, sleep-disordered breathing, circadian rhythm disorders [75], and obstructive sleep apnoea and also explain the symptoms of those sleep disturbances. Hence, people may recognize those symptoms and address the problem. By tackling those disturbances which affect quality of sleep [75], sleep quality could be improved, and the risk of multimorbidity reduced.

Concluding, the knowledge of the prevalence of multimorbidity in Cyprus and its association with Mediterranean Diet and Quality of sleep add evidence to the existing scientific knowledge. The health system in Cyprus but elsewhere too, should focus on the needs of patients with more than two chronic conditions in order to offer the right treatment overall and avoid any adverse consequences of multimorbidity. In addition, professional, government, and public health decision makers should take into account the

beneficial effects of the Mediterranean Diet and quality of sleep on the development of multimorbidity by educating, informing, and encouraging citizens to have a healthy dietary pattern and improve their sleeping habits.

7.4 Future work

The study examined the association of Mediterranean Diet and quality of sleep with multimorbidity, with both of them reducing the risk of multimorbidity. Future research should replicate these results and add further evidence towards causal effects and magnitude of associations.

In addition, given the large amount of information, which was collected, other associations could also be investigated. For example, one of the next goals would be to examine the association of psychological factors, such as stress, and quality of life with multimorbidity. Furthermore, another goal of the study is to explore multimorbidity in women and examine its association with some women characteristics (such as age of menstruation, age of menopause, parity, and use of contraceptive pills).

Another direction for future research would be to repeat similar investigations among other populations. For example, to the best of our knowledge, there is no study in Greece on multimorbidity and its association with potential risk factors. Greek individuals may be more adherent to the Mediterranean Diet and it would be interesting to see how this may affect the association with multimorbidity.

Furthermore, the study could be repeated in the next few years in order to examine any changes in the prevalence of multimorbidity, cardiometabolic multimorbidity, adherence of the Cypriot population to the Mediterranean Diet, and quality of sleep.

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APPENDIX

Appendix Table 1: Division of rural and urban areas from the Cyprus Agricultural Payments Organization.

Nicosia			
Urban	**Rural**	**Rural**	**Rural**
Nicosia Municipality	Kato Deftera	Astromeritis	Panw Pirgos
Agios Dometios	Pano Deftera	Deneia	Katw Pirgos
Egkomi	Anageia	Mammari	Pachiammos
Strovolos	Psimolofou	Lazania	Frodisia
Aglantzia	Ergates	Gourri	Pigenia
Lakatameia	Episkopeio	Farmakas	Mosfili
Latsia	Pera Oreinis	Kampi	Alevga
Geri	Agioi Trimithias	Atliki	Galata
Anthoupoli	Paliometoxo	Palaichori Morfou	Kakopetria
Dali	Kokkinotrimithia	Palaichori Oreinis	Kalopanagiwtis
Pera Chorio-Nisou	Akaki	Askas	Moutoulas
Agia Barbara	Sia	Fterikoudi	Pedoulas
Alampra	Mathiatis	Platanistasa	Gerakies
Lympia	Lythrodontas	Alwna	Milikouri
	Margi	Alithinou	Alampra
	Kotsiatis	Libadia Pitsillias	
	Analiontas	Polistipos	
	Kataliontas	Lagoudera	
	Agios Sozomenos	Saranti	
	Potamia	Agia Marina Ksiliatou	
	Kapedes	Ksiliatos	
	Kampia	Agios Gewrgios Kaukalou	
	Politico	Agia Eirini	
	Fikardou	Kannavia	
	Arediou	Spilia	
	Agios Ioannis Malountas	Vizakia	
	Malounta	Nikitari	
	Klirou	Panw Koutrafas	
	Kalo Chorio Oreinis	Katw Koutrafas	
	Menoiko	Skouriotissa	

	Agios Epifaneios Oreinis	Katidata	
	Menoiko	Linou	
	Agioi Iliofotes	Flasou	
	Kato Moni	Agios Epifaneios Soleas	
	Orounta	Korakou	
	Peristerona	Eurixou	
	Potami	Tembria	
	Kaliana	Agios Theodoros Soleas	
	Sina Oros	Platani	
Limassol			
Limassol Municipality	Lemythou	Agios Mamas	Mandria
Mesa geitoneia	Prodromos	Kapileio	Katw Platres
Agios Athanasios	Paliomilos	Gerovasa	Panw Platres
Germasogeia	Treis Elies	Dwra	Pera Pedi
Katw Polemidia	Pentakwmo	Malia	Maniatis
Panw Polemidia	Armenochori	Apesia	Pelendri
Ipsonas	Foinikaria	Korfi	Kyperounta
Moutagiagka	Fasoula	Limnatis	Agros
Agios Tichonas	Polydeia	Panw Kivides	Panw Amiantos
Pareklissia	Alassa	Katw Kivides	Katw Amiantos
Monagrouli	Souni-Zakakia	Sotira	Kouka
Moni	Kantou	Agios Amvrosios	Trimiklini
Pirgos	Episkopi	Paramali	Silikou
	Erimi	Pachna	Agios Gewrgios
	Kolossi	Prastio Avdimou	
	Pissouri	Avdimou	
	Asgata	Anwgira	
	Akrounta	Agios Thomas	
	Mathikoloni	Plataniskia	
	Spitali	Alektora	
	Paramitha	Basa Kellakiou	
	Eftagwneia	Sanido	
	Sikopetra	Akapnou	
	Arakapas	Klonari	
	Kalo Chorio	Kellaki	
	Dierwna	Prastio Kellakiou	
	Agios Theodoros	Vikla	

	Agios Ioannis	Lania	
	Agios Pavlos	Loros	
	Agios Constantinos	Monagri	
	Zwopigi	Potamiou	
	Louvaras	Kissousa	
	Gerasa	Bouni	
	Apsiou	Lofou	
	Chandria	Agios Therapon	
	Agridia	Arsos	
	Dimes	Basa Koilaniou	
	Patamitissa	Omodos	
	Katw Milos	Koilani	
Larnaka			
Larnaka Municipality	Avdelerro	Klavdia	
Aradippou	Kelia	Alethriko	
Livadeia	Boroklini	Agglisides	
Dromolaxia	Ksilofagou	Aplania	
Meneou	Kiti	Menogeia	
Oroklini	Tersefanou	Kofinou	
Pila	Kivisili	Skarinou	
Part of Kalo Chorio	Mazotos	Xoirokitia	
	Anafotida	Tochni	
	Alaminos	Kalavassos	
	Agios Theodoros	Mari	
	Maroni	Lelikipos	
	Psematismenos	Odou	
	Zigi	Melini	
	Troulloi	Agioi Vavatsinias	
	Koxi	Vavatsinia	
	Agia Anna	Ora	
	Psevdas	Lageia	
	Mosfiloti	Vavla	
	Pirgoi	Katw Dris	
	Kornos	Parsata	
Paphos			
Paphos municipality	Kouklia	Steni	Agia Marina Kelokedarwn
Geroskipou	Anarita	Agios Isidoros	Pentalia
Konia	Mandria	Persterona	Galataria
Agia Marinouda	Part of Timi	Pelathousa	Koilinia

Koloni	Armou	Kinousa	Bretsia
Axeleia	Marathouna	Neo Chorio	Falia
Chloraka	Tsada	Agios Nikolaos	Pitargou
Lema	Akoursos	Agios Ioannis	Lemona
Empa	Argaka	Arminou	Kourdaka
Tremithousa	Gialia	Mesana	Choulou
Mesa Chorio	Agia Marina	Flousa Kelokedarwn	Drimou
Mesogi	Nea Dimmata	Pratori	Thrinia
Tala	Pwmos	Salamiou	Lasa
Kissonerga	Foinikas	Kedares	Milia
Part of Timis	Nata	Kelokedara	Psathi
Agia Barbara	Choletria	Kidasi	Psiti
Marathounta	Amargeti	Traxipedoula	Anadiou
Koili	Eledio	Stavrokonnou	Kritou Marottou
Pegeia Municipality	Aksilou	Agios Georgios	Agios Dimitrianos
	Episkopi	Prastio Paphou	Kannaviou
	Kallepeia	Mousere	Astrogia
	Letympou	Maronas	Mamountali
	Stroumpi	Ammonia	Lapithoi
	Polemi	Fasoula	Lisos
	Kathikas	Panw Archimandrita	Meladeia
	Theletra	Souskiou	Malandra
	Giolou	Nikokleia	Zacharia
	Kios	Flousa	Sarama
	Tremithousa	Miliou	Loukrounou
	Evretou	Panw Akroudaleia	Kritou Tera
	Simou	Katw Akroudaleia	Tera
	Choli	Skoulli	Goudi
	Karamoulides	Chrisochou	Panw Arodes
	Katw Arodes	Fasli	Panw Panagia
	Ineia	Andrilikou	Statos-Agios Fotios
	Drouseia		
Ammochostos			
Only rural.			

Appendix Table 2: Positive and negative questions of PSS-14 questionnaire.

Negative questions
In the last month, how often have you felt anxious for something that happened unexpectedly?
In the last month, how often have you felt unable to control the important things in your life?
In the last month, how often have you felt nervous or stressed?
In the last month, how often have you found that you could not cope with all the things that you had to?
In the last month, how often have you been angered because of things that happened were outside of your control?
In the last month, how often have you found yourself thinking about things that you have to accomplish?
In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?
Positive questions
In the last month, how often have you dealt successfully with day to day problems and annoyances?
In the last month, how often have you that you were effectively coping with important changes that were occurring in your life?
In the last month, how often have you felt confident about your ability to handle your personal problems?
In the last month, how often have you that things were going your way?
In the last month, how often have you been able to control imitations in your life?
In the last month, how often have you felt that you were on top of things?
In the last month, how often have you been able to control the way you spend your time?

Appendix Table 3: Hospitals and health centers in Cyprus in the five controlled geographical areas of Cyprus.

Hospitals	**Geographical area**				
Public hospitals					
Hospitals	**Nicosia**	**Limassol**	**Larnaka**	**Paphos**	**Ammochostos**
	General hospital of Nicosia	General hospital of Limassol	General hospital of Larnaka	General hospital of Paphos	General hospital of Ammochostos
	Hospital of Archbishop Makarios III	Hospital of Kyperounta		Hospital of Polis Chrysochous	
Health centers	Akaki	Agros	Athienou	Drousia	
	Dali	Avdimou	Kofinou	Panagia	
	Evrichou	Laneia	Lefkara	Pirgos Tillirias	
	Kampos	Omodos	Ormideia	Salamiou	
	Klirou	Platres	Tersefanou	Fiti	
	Palaichori				
	Pedoulas				
Private hospitals	Polyclinic Agiou Maria & Ioannis	Limassol Clinic	Simos Kyriakidis Surgery Clinic	Iasis private hospital	Napa Olympic Private Hospital
	Ophthalmology Clinic of Nicosia	Pantheon Ophthalmological Center	Eugenios Clinic	Evangelismos Hospital	Leto Private Hospital
	Cyprus Institute of Neurology and Genetics	Ophthalmology Clinic Elias N. Elias	Timios Stavros Clinic	Polyclinic Blue Cross Ltd	Polyclinic Santa Marina
	American Medical Center	Agioi Anargyroi Clinic	Timios Stavros Hospital	Royal Artemis Clinic Ltd	
	Evangelistria Medical Center	Marios Liasidis Clinic - The Life-Giving Source	Agios Raphael Private Hospital	City Medical Center	
	Apollonio Private Hospital	Chrystovalantou Clinic Ltd	G. Leontiadis Clinic -	Kinyra Clinic	

			Agios Georgios LTD		
	Mother & Child Medical Center	Asklipios Medical Center			
	Hippocrates Private Hospital	Polyclinic Health			
	Aretaio Hospital	Curie Clinic			
	"Arodafnousa" Palliative Care Nursing Center	Private Hospital of the Apostles Peter and Paul			
	European Clinic	Economou Medical Center			
	Bank of Cyprus Oncology Center	Galinos Medical Center			
	Clinical Ledra				

Appendix Table 4: Terms of the number of hospitals, health centers, physicians' offices and practicing physicians in in the five controlled geographical areas of Cyprus.

Geographical area	Standardized prevalence of multimorbidity	Mean number of diseases	Public hospitals	Rural hospitals & Health centers	Private hospitals & Clinics	Doctors (General Healthcare System of Cyprus)
Nicosia	0.2772	1.1	2	7	12	1282
Limassol	0.2493	1.2	2	5	12	809
Larnaka	0.3046	0.82	1	5	6	434
Paphos	0.3245	0.82	2	6	6	341
Ammochostos	0.3532	1.2	1	0	3	173

Appendix Table 5: Calculation of age and sex standardized prevalence of multilevel (2, 3, 4, 5).

Categories	Multimorbidity individuals	Study population	Rate	Population of Cyprus
2 morbidities				
18-24 years old women	6	93	0.06	43036
18-24 years old men	1	74	0.01	45364
25-44 years old women	29	306	0.09	140612
25-44 years old men	18	218	0.08	124926
45-64 years old women	25	182	0.14	105760
45-64 years old men	19	132	0.14	100404
65+ years old women	11	61	0.18	60078
65+ years old men	20	73	0.27	51689
3 morbidities				
18-24 years old women	2	93	0.02	43036
18-24 years old men	0	74	0	45364
25-44 years old women	15	306	0.05	140612
25-44 years old men	3	218	0.01	124926
45-64 years old women	22	182	0.12	105760
45-64 years old men	8	132	0.06	100404
65+ years old women	9	61	0.15	60078
65+ years old men	11	73	0.15	51689
4 morbidities				
18-24 years old women	4	93	0.04	43036
18-24 years old men	0	74	0	45364
25-44 years old women	14	306	0.05	140612
25-44 years old men	1	218	1/218	124926
45-64 years old women	11	182	0.06	105760
45-64 years old men	4	132	0.03	100404
65+ years old women	12	61	0.20	60078
65+ years old men	7	73	0.10	51689
5 morbidities				
18-24 years old women	0	93	0	43036
18-24 years old men	0	74	0	45364
25-44 years old women	2	306	2/306	140612
25-44 years old men	0	218	0	124926
45-64 years old women	5	182	0.03	105760
45-64 years old men	5	132	0.04	100404
65+ years old women	7	61	0.11	60078
65+ years old men	6	73	0.08	51689

Age and sex standardized prevalence (2 morbidities) =

$$\frac{0.06\times 43036+0.01\times 45364+0.09\times 140612+0.08\times 124926+0.14\times 105760+0.14\times 100404+0.18\times 60078+0.27\times 51689}{43036+45364+140612+124926+105760+100404+60078+51689}$$

$$=\frac{7931799}{671869}=0.118=11.8\%$$

Age and sex standardized prevalence (3 morbidities) =

$$\frac{0.02\times 43036+0\times 45364+0.05\times 140612+0.01\times 124926+0.12\times 105760+0.06\times 100404+0.15\times 60078+0.15\times 51689}{43036+45364+140612+124926+105760+100404+60078+51689}$$

$$=\frac{4462107}{671869}=0.066=6.6\%$$

Age and sex standardized prevalence (4 morbidities) =

$$\frac{0.04\times 43036+0\times 45364+0.05\times 140612+\frac{1}{218}\times 124926+0.06\times 105760+0.03\times 100404+0.20\times 60078+0.10\times 51689}{43036+45364+140612+124926+105760+100404+60078+51689}$$

$$=\frac{358673}{671869}=0.053=5.3\%$$

Age and sex standardized prevalence (5 morbidities) =

$$\frac{0\times 43036+0\times 45364+\frac{2}{306}\times 140612+0\times 124926+0.03\times 105760+0.04\times 100404+0.11\times 60078+0.08\times 51689}{43036+45364+140612+124926+105760+100404+60078+51689}$$

$$=\frac{1885169}{671869}=0.0003=0.03\%$$

Appendix Table 6: The combinations of human systems' diseases among people with multimorbidity.

Combinations of human systems	Frequency in multimorbidity individuals (N=293)
Circulatory - Endocrine	74
Circulatory - Digestive /Excretory	59
Circulatory - Nervous	57
Digestive /Excretory - Endocrine	48
Endocrine - Nervous	39
Circulatory - Respiratory	36
Digestive /Excretory - Respiratory	33
Digestive /Excretory - Nervous	30
Nervous - Respiratory	30
Endocrine - Respiratory	25
Circulatory - Reproductive	22
Circulatory - Skeletal/Muscular	18
Digestive /Excretory - Skeletal/Muscular	17
Endocrine - Skeletal/Muscular	16
Nervous - Skeletal/Muscular	15
Nervous - Reproductive	12
Circulatory - Immune	12
Endocrine - Immune	12
Digestive /Excretory - Immune	11
Immune - Nervous	10
Nervous - Renal/Urinary	9
Circulatory - Renal/Urinary	9
Endocrine - Renal/Urinary	8
Endocrine - Reproductive	8
Immune - Respiratory	7
Respiratory - Skeletal/Muscular	7
Digestive /Excretory - Renal/Urinary	6
Digestive /Excretory - Reproductive	6
Immune - Reproductive	5
Renal/Urinary - Respiratory	5
Renal/Urinary - Skeletal/Muscular	4
Reproductive - Respiratory	4
Renal/Urinary - Reproductive	3
Immune - Skeletal/Muscular	3
Immune - Renal/Urinary	2
Reproductive - Skeletal/Muscular	2

Questionnaire used in the analysis

ΑΝΑΠΤΥΞΗ ΥΠΟΔΟΜΗΣ ΓΙΑ ΕΠΙΔΗΜΙΟΛΟΓΙΚΗ ΕΡΕΥΝΑ

Δείκτης Πολλαπλής Νοσηρότητας του Πληθυσμού της Κύπρου

Διεθνές Ινστιτούτο για την Περιβαλλοντική και Δημόσια Υγεία

Τεχνολογικό Πανεπιστήμιο Κύπρου

Ο στόχος της παρούσας μελέτης είναι να καλύψει το κενό που υπάρχει σχετικά με την Πολλαπλή Νοσηρότητα(ο αριθμός των χρόνιων παθήσεων σε ένα άτομο) στην Κύπρο καθώς και να διερευνήσει τη σχέση μεταξύ Πολλαπλής Νοσηρότητας και Μεσογειακής Διατροφής και Ποιότητας Ύπνου. Αυτή τη στιγμή, δεν υπάρχουν σχετικές πληροφορίες για το πρόβλημα της Πολλαπλής Νοσηρότητας στην Κύπρο και συνεπώς ούτε για την σχέση της με πιθανούς παράγοντες κινδύνου.

Η αποτύπωση της Πολλαπλής Νοσηρότητας σε ένα δεδομένο πληθυσμό έχει πολλά σημαντικά οφέλη στον τομέα της Δημόσιας Υγείας αφού μπορεί να βοηθήσει στην ετοιμασία στρατηγικών πρόληψης, διάγνωσης, θεραπείας και πρόγνωσης. Η κατάλληλη διαχείριση των χρόνιων παθήσεων αποτελεί βασική πρόκληση για τα συστήματα υγείας παγκοσμίως.

Έγκριση Διεξαγωγής Επιδημιολογικής Έρευνας

από Εθνική Επιτροπή Βιοηθικής Κύπρου

ΑΝΑΠΤΥΞΗ ΥΠΟΔΟΜΗΣ ΓΙΑ ΕΠΙΔΗΜΙΟΛΟΓΙΚΗ ΕΡΕΥΝΑ

Για τον Δείκτη Πολλαπλής Νοσηρότητας του Πληθυσμού της Κύπρου

<u>Ερωτηματολόγιο</u>

Οι απαντήσεις που θα δώσετε θα κρατηθούν <u>ανώνυμες</u>

και θα χρησιμοποιηθούν, όπως σας έχει εξηγηθεί, <u>μόνο για τους σκοπούς της έρευνας.</u>

ΠΡΟΣΩΠΙΚΕΣ ΠΛΗΡΟΦΟΡΙΕΣ

1) Ηλικία
2) Βάρος (κιλά):
3) Ύψος (μέτρα):
4) Φύλο:
    a. Άντρας
    b. Γυναίκα
5) Οικογενειακή κατάσταση:
    a. Άγαμος/η
    b. Αρραβωνιασμένος/η
    c. Παντρεμένος/η
    d. Σε διάσταση
    e. Διαζευγμένος/η
    f. Χήρος/α
6) Έχεις παιδιά;
    a. Ναι. Προσδιορίστε αριθμό:
    b. Όχι
7) Σε ποια επαρχία κατοικείς;
    a. Λευκωσία
    b. Λεμεσό
    c. Λάρνακα
    d. Πάφο
    e. Αμμόχωστο

f. Αλλού. Που;

8) Σε τι περιοχή διαμένεις;
   a. Αστική
   b. Αγροτική
9) Ποιο είναι το υψηλότερο επίπεδο εκπαίδευσης που έχεις ολοκληρώσει μέχρι τώρα;
   a. Δημοτικό
   b. Γυμνάσιο
   c. Λύκειο/ Τεχνική Σχολή
   d. Κολλέγιο
   e. ΑΞΙΚ
   f. Πανεπιστήμιο/Μεταπτυχιακό
   g. Διδακτορικό
10) Ποια είναι η παρούσα εργασιακή σου κατάσταση;
   a. Ιδιωτικός υπάλληλος
   b. Αγρότης
   c. Δημόσιος Υπάλληλος
   d. Φοιτητής
   e. Άνεργος
   f. Συνταξιούχος
   g. Ελεύθερος Επαγγελματίας
   h. Νοικοκυρά
   i. Άλλο: _____
11) Το μηνιαίο σου εισόδημα είναι (ευρώ):
   a. Δεν έχω εισόδημα
   b. Λιγότερο από 500
   c. 501-1000
   d. 1001-1500
   e. 1501-2000
   f. Περισσότερο από 2001

ΙΑΤΡΙΚΟ ΙΣΤΟΡΙΚΟ

12) Έχεις διαγνωστεί ποτέ από **ΓΙΑΤΡΟ** με κάποια από τις παρακάτω χρόνιες παθήσεις; Σε κάθε περίπτωση, επιλέξτε το τετράγωνο που αντιπροσωπεύει τη χρόνια πάθηση που έχετε διαγνωστεί.

ΧΡΟΝΙΕΣ ΠΑΘΗΣΕΙΣ	**ΝΑΙ**	**ΟΧΙ**
Ψηλή αρτηριακή πίεση		
Χοληστερόλη		
Καρδιακή ανεπάρκεια		
Στεφανιαία νόσος		
Κολπική μαρμαρυγή		
Στηθάγχη		
Διαβήτης Τύπου Ι		
Διαβήτης Τύπου ΙΙ		
Διαταραχές του θυροειδή (υπερθυρεοειδισμός, υποθυρεοειδισμός, όζοι)		
Χρόνια ηπατίτιδα		
Κύρωση του ήπατος		
Φλεγμονώδης νόσος του εντέρου/ Χρόνια εντερίτιδα/έλκος κολίτιδας		
Σύνδρομο ευερέθιστου εντέρου		
Νόσος του Κρον		
Γαστροοισοφαγική παλινδρόμηση		
Αναιμία		
HIV/AIDS ή άλλα αφροδίσια νοσήματα		
Ρευματοειδής Αρθρίτιδα		
Λύκος		
Άνοια/ Αλτσαχαιμερ		
Σκλήρυνση κατά πλάκας		
Πάρκινσον		
Επιληψία		
Χρόνια βρογχίτιδα		
Άσθμα		
Χρόνια αποφρακτική πνευμονοπάθεια		
Χρόνια ιγμορίτιδα		
Χρόνια πάθηση στα νεφρά		
Τυφλότητα ή χαμηλή όραση		
Γλαύκωμα/Καταρράκτης		
Κώφωση ή σοβαρή απώλεια ακοής		
Στυτική δυσλειτουργία		
Σύνδρομο πολυκυστικών ωοθηκών		
Κατάθλιψη		
Ανορεξία/Βουλιμία		
Σχιζοφρένια/Διπολική διαταραχή		

Καρκίνος της Ουροδόχου Κύστης		
Καρκίνος του Μαστού		
Καρκίνος του Τράχηλου της Μήτρας		
Καρκίνος του Παχέος Εντέρου		
Λευχαιμία		
Καρκίνος του Πνεύμονα		
Μελάνωμα		
Καρκίνος των Ωοθηκών		
Καρκίνος του Προστάτη		
Άλλος καρκίνος. Προσδιορίστε:		
Άλλη πάθηση. Προσδιορίστε:		

Εάν είσαι **ΑΝΤΡΑΣ** προχωρά στην ερώτηση 17

13) Είστε έγκυος;
    a. Ναι
    b. Όχι
14) Σε τι ηλικία σας ήρθε η πρώτη έμμηνος ρύση (περίοδος);
15) Έχετε πάρει αντισυλληπτικά χάπια κατά τη διάρκεια της ζωής σας;
    a. Ναι. Για πόσα χρόνια;
    b. Όχι
16) Σε τι ηλικία σας ήρθε η εμμηνόπαυση;
    a. Δεν μου έχει έρθει ακόμα
    b. Μικρότερη από 40 χρονών
    c. 40-45
    d. 46-50
    e. 51-55
    f. 56-60

Μεγαλύτερη από 60 χρονών

ΔΙΑΤΡΟΦΙΚΕΣ ΣΥΝΗΘΕΙΕΣ

17) Σημείωσε πόσο συχνά κατανάλωσες τα παρακάτω τρόφιμα τον **ΤΕΛΕΥΤΑΙΟ ΜΗΝΑ.**

Προσοχή, θα πρέπει να απαντήσεις έχοντας ως **μερίδα αναφοράς την ποσότητα που αναγράφεται** στις παρενθέσεις. (Συντομευσεις: *φ* = φορές, *γρ*. = γραμμάρια, *τμχ*. = τεμάχιο, *φλ*. = φλιτζάνι τσαγιού = 240 ml)						
Γαλακτοκομικά	**Ποτέ/ Σπάνια**	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥ 2 φ/ ημέρα**
Γάλα/ γιαούρτι πλήρες (1 ποτήρι/ 1 κεσεδάκι)						
Γάλα/ γιαούρτι χαμηλό σε λιπαρά (1 ποτήρι/ 1 κεσεδάκι)						
Τυρί κίτρινο, τυρί σε κρέμα (30 γρ)						
Τυρί φέτα, ανθότυρο (30 γρ)						
Τυρί άπαχο ή χαμηλό σε λιπαρά (light, κότατζ) (30 γρ)						
Χαλούμι (30 γρ)						
Δημητριακά & όσπρια κλπ	**Ποτέ/ Σπάνια**	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥ 2 φ/ ημέρα**
Αυγό (βραστό, τηγανιτό, ομελέτα) (1 τμχ)						
Ψωμί άσπρο (1 φέτα 30γρ ή φέτα τοστ), φρυγανιά (2 τμχ)						
Ψωμί ολικής αλέσεως (1 φέτα 30γρ ή φέτα τοστ), φρυγανιά (2 τμχ)						
Κουλούρι Θες/κης, πίτα (σουβλάκι), ψωμάκια μπέργκερ (1 τμχ)						
Κριτσίνια (2 λεπτά), παξιμάδια (1 μέτριο), κουλούρια (2 μέτρια)						
Δημητριακά πρωινού (½ φλ), μπάρες δημητριακών (1 τμχ)						
Ρύζι λευκό (1 φλ)						
Ρύζι καστανό (1 φλ)						
Μακαρόνια, κριθαράκι, χυλοπίτες, άλλα ζυμαρικά (1 φλ)						
Ζυμαρικά ολικής αλέσεως (1 φλ)						
Πατάτες βραστές, φούρνου, πουρές (1 μέτρια/ ½ φλ)						
Πατάτες τηγανιτές (½ μερίδα εστιατορίου)						
Όσπρια (π.χ. φακές, φασόλια, ρεβίθια) (1 πιάτο)						
Σπανακόρυζο/ λαχανόρυζο (1 πιάτο), γεμιστά (2 μέτρια)						
Μακαρόνια του φούρνου, μουσακάς, παπουτσάκια (1 μερίδα = 150 γρ)						
Αρακάς, φασολάκια, μπάμιες, αγκινάρες (1 πιάτο)						
Κρεατικά	**Ποτέ/ Σπάνια**	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥ 2 φ/ ημέρα**
Μοσχάρι (μπριζόλα, κομμάτι) (150 γρ)						
Μπιφτέκι (2 τμχ), κεφτεδάκια (4 τμχ), κιμάς (1 κουτάλα)						
Σεφταλίες (2 τμχ)						
Κοτόπουλο/ γαλοπούλα (όλα τα είδη) (150 γρ)						
Χοιρινό (μπριζόλα, κομμάτι, σουβλάκι) (150 γρ)						
Αρνί, κατσίκι, κυνήγι, παϊδάκια (150 γρ)						
Αλλαντικά (1 φέτα)						

Λουκάνικα (1 μέτριο), Παστουρμάς (1 μέτριο) μπέικον (2 φέτες)						
Αλλαντικά/ κρεατοσκευάσματα άπαχα ή light (όπως παραπάνω)						
Ψάρια	**Ποτέ/ Σπάνια**	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥2 φ/ ημέρα**
Ψάρια μικρά (150 γρ)						
Ψάρια μεγάλα (150 γρ)						
Θαλασσινά (χταπόδι, καλαμάρι, γαρίδες) (150 γρ)						
Λαχανικά & Φρούτα	**Ποτέ/ Σπάνια**	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥2 φ/ ημέρα**
Τομάτα, αγγούρι, καρότο, πιπεριά (1 φλ. ωμά)						
Μαρούλι, λάχανο, σπανάκι, ρόκα (1 φλ. ωμά)						
Μπρόκολο, κουνουπίδι, κολοκυθάκια, (½ φλ. βραστά)						
Χόρτα, πράσο, σπανάκι, σέλινο (½ φλ. βραστά)						
Πορτοκάλι (1 μέτριο)						
Μήλο, αχλάδι (1 μέτριο)						
Άλλα χειμερινά φρούτα (1 ολόκληρο ή ½ φλ)						
Μπανάνα (1 μέτρια)						
Άλλα καλοκαιρινά φρούτα (1 ολόκληρο ή ½ φλ)						
Χυμός φρούτων (1 ποτήρι)						
Αποξηραμένα φρούτα (¼ φλ.)						
Ξηροί καρποί, σπόροι (1 φλιτζανάκι καφέ)						
Πίτες σπιτικές (π.χ. τυρόπιτα, σπανακόπιτα) (1 κομμάτι)						
Πίτες έτοιμες (1 κομμάτι)						
Τοστ, σάντουιτς (1 ολόκληρο)						
Γλυκά	**Ποτέ/ Σπάνια**	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥ 2 φ/ ημέρα**
Γλυκά ταψιού (1 τμχ)						
Γλυκά κουταλιού, κομπόστα, ζελέ (1 μερίδα)						
Πάστες, τάρτα (1 τμχ)						
Κρουασάν (1), γκοφρέτες (1 μέτρια), κέικ (1 φέτα), μπισκότα (3-4)						
Σοκολάτα (όλα τα είδη) (1 μέτρια ~ 60 γρ)						
Παγωτό, μιλκ σέικ, κρέμα, ρυζόγαλο (1 τμχ)						
Πατατάκια, γαριδάκια, ποπ κορν (1 σακουλάκι ~70 γρ)						
Μέλι, μαρμελάδα, ζάχαρη (π.χ. σε ψωμί, καφέ) (1 κουτ. γλυκού)						
Ποτά & αφεψήματα						
Κρασί (1 ποτήρι = 125 ml)						
Μπύρα (1 ποτήρι = 240 ml)						
Άλλο είδος αλκοόλ (1 ποτό)						
Αναψυκτικά (1 κουτί ~ 330 ml)						
Αναψυκτικά light (1 κουτί ~ 330 ml)						
Καφές (1 φλ. ή ποτήρι)						
Τσάι, άλλα αφεψήματα (1 φλ)						

Διάφορα	**Ποτέ/ Σπάνια**	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥ 2 φ/ ημέρα**
Ελιές (10 μικρές/ 5 μεγάλες)						
Μαγιόνεζα, σως (1 κουτ. σούπας)						
Μαγιονέζα/ σως λάιτ (1 κουτ. σούπας)						
	Ποτέ/ Σπάνια	**1-3 φ/ μήνα**	**1-2 φ/ εβδομ.**	**3-6 φ/ εβδομ.**	**1 φ/ ημέρα**	**≥ 2 φ/ ημέρα**
Πόσες φορές χρησιμοποιείς ελαιόλαδο (οπουδήποτε);						
Πόσες φορές χρησιμοποιείς σπορέλαιο (οπουδήποτε);						
Πόσες φορές χρησιμοποιείς μαργαρίνη (οπουδήποτε);						
Πόσες φορές χρησιμοποιείς βούτυρο (οπουδήποτε);						
Πόσο τρως από το ορατό λίπος και την πέτσα στο κρέας;	όλο	περισσότερο		μέρος		καθόλου
Πόσο συχνά παραγγέλνεις από έξω ή τρως εκτός σπιτιού;						
Πόσο συχνά καταναλώνεις πρωινό;						-
Πόσα γεύματα έχεις συνολικά την ημέρα μαζί με τα σνακ;			1-3		4-5	> 6
Πόσα από αυτά είναι κυρίως γεύματα (πρωινό, μεσ/νό, βρ/νό);			1		2	3
Καταναλώνεις βιολογικά προϊόντα ή προϊόντα σόγιας;			Ναι		Όχι	

18) Παίρνετε συμπληρώματα διατροφής;

a. Βιταμίνες.
    i. Ναι.
    ii. Όχι
b. Πρωτεΐνες.
    i. Ναι.
    ii. Όχι
c. Κρεατίνη.
    i. Ναι.
    ii. Όχι
d. Άλλο. Προσδιορίστε:

ΠΟΙΟΤΗΤΑ ΥΠΝΟΥ

19) Τον τελευταίο μήνα, τι ώρα πήγαινες συνήθως για ύπνο το βράδυ;
20) Τον τελευταίο μήνα, πόση ώρα (πόσα λεπτά) περνούσε συνήθως κάθε βράδυ μέχρι να σε πάρει ο ύπνος;
21) Τον τελευταίο μήνα, τι ώρα σηκωνόσουν συνήθως το πρωί;
22) Τον τελευταίο μήνα, πόσες ώρες κοιμήθηκες **πραγματικά** κάθε νύχτα (Οι ώρες αυτές μπορεί να διαφέρουν από τις ώρες που ήσουν ξαπλωμένος/η);
23) Τον τελευταίο μήνα, πόσο συχνά δυσκολεύτηκες να κοιμηθείς τη νύχτα επειδή:
    a. Χρειάστηκαν πάνω από 30 λεπτά για να σε πάρει ο ύπνος.
        i. Ποτέ τον τελευταίο μήνα
        ii. Λιγότερο από 1 φορά την εβδομάδα
        iii. 1-2 φορές την εβδομάδα
        iv. 3 ή περισσότερες φορές την εβδομάδα
    b. Ξυπνούσες μέσα στη νύχτα ή πολύ νωρίς.
        i. Ποτέ τον τελευταίο μήνα
        ii. Λιγότερο από 1 φορά την εβδομάδα
        iii. 1-2 φορές την εβδομάδα
        iv. 3 ή περισσότερες φορές την εβδομάδα
    c. Έπρεπε να σηκωθείς από το κρεβάτι για να πας στην τουαλέτα.
        i. Ποτέ τον τελευταίο μήνα
        ii. Λιγότερο από 1 φορά την εβδομάδα
        iii. 1-2 φορές την εβδομάδα
        iv. 3 ή περισσότερες φορές την εβδομάδα
    d. Είχες δυσκολίες στην αναπνοή.
        i. Ποτέ τον τελευταίο μήνα
        ii. Λιγότερο από 1 φορά την εβδομάδα
        iii. 1-2 φορές την εβδομάδα
        iv. 3 ή περισσότερες φορές την εβδομάδα
    e. Έβηχες ή ροχάλιζες δυνατά.
        i. Ποτέ τον τελευταίο μήνα
        ii. Λιγότερο από 1 φορά την εβδομάδα
        iii. 1-2 φορές την εβδομάδα

iv. 3 ή περισσότερες φορές την εβδομάδα

f. Κρύωνες πολύ.
   i. Ποτέ τον τελευταίο μήνα
   ii. Λιγότερο από 1 φορά την εβδομάδα
   iii. 1-2 φορές την εβδομάδα
   iv. 3 ή περισσότερες φορές την εβδομάδα

g. Ζεσταινόσουν πολύ.
   i. Ποτέ τον τελευταίο μήνα
   ii. Λιγότερο από 1 φορά την εβδομάδα
   iii. 1-2 φορές την εβδομάδα
   iv. 3 ή περισσότερες φορές την εβδομάδα

h. Έβλεπες άσχημα όνειρα.
   i. Ποτέ τον τελευταίο μήνα
   ii. Λιγότερο από 1 φορά την εβδομάδα
   iii. 1-2 φορές την εβδομάδα
   iv. 3 ή περισσότερες φορές την εβδομάδα

i. Πονούσες.
   i. Ποτέ τον τελευταίο μήνα
   ii. Λιγότερο από 1 φορά την εβδομάδα
   iii. 1-2 φορές την εβδομάδα
   iv. 3 ή περισσότερες φορές την εβδομάδα

j. Συνέτρεχε άλλος λόγος/λόγοι; Παρακαλούμε περίγραψε. (Αν όχι προχωρήστε στην ερώτηση 25):

24) Πόσο συχνά δυσκολεύτηκες να κοιμηθείς τη νύχτα τον τελευταίο μήνα εξαιτίας αυτού του λόγου / λόγων;
   a. Ποτέ τον τελευταίο μήνα
   b. Λιγότερο από 1 φορά την εβδομάδα
   c. 1-2 φορές την εβδομάδα
   d. 3 ή περισσότερες φορές την εβδομάδα

25) Τον τελευταίο μήνα, πόσο συχνά πήρες φάρμακα για να σε βοηθήσουν να κοιμηθείς τη νύχτα (είτε με συνταγή γιατρού είτε χωρίς;
   a. Πολύ καλή
   b. Αρκετά καλή

c. Αρκετά κακή
d. Πολύ κακή

26) Τον τελευταίο μήνα, πόσο συχνά πήρες φάρμακα για να σε βοηθήσουν να κοιμηθείς τη νύχτα (είτε με συνταγή γιατρού είτε χωρίς;
    i. Ποτέ τον τελευταίο μήνα
    ii. Λιγότερο από 1 φορά την εβδομάδα
    iii. 1-2 φορές την εβδομάδα
    iv. 3 ή περισσότερες φορές την εβδομάδα
27) Τον τελευταίο μήνα, πόσο συχνά δυσκολεύτηκες να μείνεις ξύπνιος/α ενώ οδηγούσες, έτρωγες ή συμμετείχες σε κοινωνικές δραστηριότητες;
    i. Ποτέ τον τελευταίο μήνα
    ii. Λιγότερο από 1 φορά την εβδομάδα
    iii. 1-2 φορές την εβδομάδα
    iv. 3 ή περισσότερες φορές την εβδομάδα
28) Τον τελευταίο μήνα, πόσο δύσκολο σας ήταν να έχετε αρκετή όρεξη και ενέργεια προκειμένου να ανταποκριθείτε στις καθημερινές σας υποχρεώσεις;
    a. Καθόλου δύσκολο
    b. Λίγο δύσκολο
    c. Αρκετά δύσκολο
    d. Πάρα πολύ δύσκολο

ΚΑΠΝΙΣΜΑ ΚΑΙ ΦΥΣΙΚΗ ΔΡΑΣΤΗΡΙΟΤΗΤΑ

29) Κάπνισες ποτέ συστηματικά;
    a. Ναι.
    b. Όχι.
30) Σε ποια ηλικία ξεκίνησες το κάπνισμα;
31) Τώρα καπνίζεις συστηματικά;
    a. Ναι.
    b. Όχι.
32) Αν όχι, πόσο καιρό έχεις διακόψει το κάπνισμα;
33) Αθλείσαι / γυμνάζεσαι;
    a. Ναι.
    b. Όχι. (Προχώρα στην ερώτηση 36)

34) Με ποιο άθλημα / φυσική δραστηριότητα ασχολείσαι κυρίως;

a. Ποδόσφαιρο
b. Πετόσφαιρα (Βόλεϊ)
c. Καλαθόσφαιρα (Μπάσκετ)
d. Κολύμβηση
e. Πολεμικές τέχνες
f. Γυμναστήριο / Όργανα
g. Στίβος (Αγώνισμα: _____)
h. Τροχάδην (jogging)
i. Ποδηλασία
    i. Πόσες ώρες την εβδομάδα;
        1. Λιγότερο από 1 ώρα
        2. 1 - 3 ώρες
        3. 3 - 6 ώρες
        4. 6- 9 ώρες
        5. Περισσότερο από 9 ώρες

35) Ασχολείσαι και με κάποιο άλλο άθλημα;

a. Ναι. Με ποιο;
b. Όχι (Προχώρα στην ερώτηση 36)
    i. Πόσες ώρες την εβδομάδα;
        1. Λιγότερο από 1 ώρα
        2. 1 - 3 ώρες
        3. 3 - 6 ώρες
        4. 6- 9 ώρες
        5. Περισσότερο από 9 ώρες

36) Τον τελευταίο μήνα **πόσες ώρες την ημέρα** αφιερώνεις για τα παρακάτω;

	Δραστηριότητα	**Ώρες**
Α	Χορός	
Β	Περπάτημα (με γρήγορο βήμα)	
Γ	Γεωργικές ή κτηνοτροφικές εργασίες, κηπουρική	
Δ	Καθιστική δραστηριότητα (τηλεόραση, ηλεκτρονικός υπολογιστής, ηλεκτρονικά παιχνίδια κ.α.)	
Ε	Σηκώνεις/κουβαλάς βαριά αντικείμενα ή κάνεις οποιαδήποτε χειρωνακτική εργασία	

ΠΟΙΟΤΗΤΑ ΖΩΗΣ

37) Βάζοντας ένα ✓ σε ένα κουτάκι κάθε ομάδας παρακάτω, παρακαλούμε σημειώστε ποιες δηλώσεις περιγράφουν καλύτερα την κατάσταση της υγείας σας **<u>ΣΗΜΕΡΑ</u>**.

a. **Κινητικότητα**

Δεν έχω κανένα πρόβλημα στο περπάτημα ❑

Έχω μερικά προβλήματα στο περπάτημα ❑

Είμαι καθηλωμένος/η στο κρεβάτι ❑

b. **Κινητικότητα**

Δεν έχω κανένα πρόβλημα με την αυτοεξυπηρέτησή μου ❑

Έχω μερικά προβλήματα στο να πλένομαι και να ντύνομαι ❑

Είμαι ανίκανος/η να πλυθώ ή να ντυθώ ❑

c. **Συνηθισμένες Δραστηριότητες** (*π.χ. δουλειά, μελέτη, νοικοκυριό, οικογενειακές δραστηριότητες ή δραστηριότητες ελεύθερου χρόνου)*

Δεν έχω κανένα πρόβλημα στο να εκτελώ τις συνηθισμένες δραστηριότητές μου❑

Έχω μερικά προβλήματα στο να εκτελώ τις συνηθισμένες δραστηριότητές μου ❑

Είμαι ανίκανος/η να εκτελώ τις συνηθισμένες δραστηριότητές μου ❑

d. **Πόνος/Δυσφορία**

Δεν έχω καθόλου πόνο ή δυσφορία ❑

Έχω μέτριο πόνο ή δυσφορία ❑

Έχω υπερβολικό πόνο ή δυσφορία ❑

e. **Άγχος /Θλίψη**

Δεν έχω άγχος ή θλίψη ❑

Έχω μέτριο άγχος ή θλίψη ❑

Έχω υπερβολικό άγχος ή θλίψη ❑

Για να βοηθήσουμε κάποιον να πει πόσο καλή ή κακή είναι μια κατάσταση υγείας, ζωγραφίσαμε μια κλίμακα (σαν ένα θερμόμετρο) πάνω στην οποία η καλύτερη κατάσταση που μπορείτε να φανταστείτε έχει βαθμό 100 και η χειρότερη κατάσταση που μπορείτε να φανταστείτε έχει βαθμό 0.

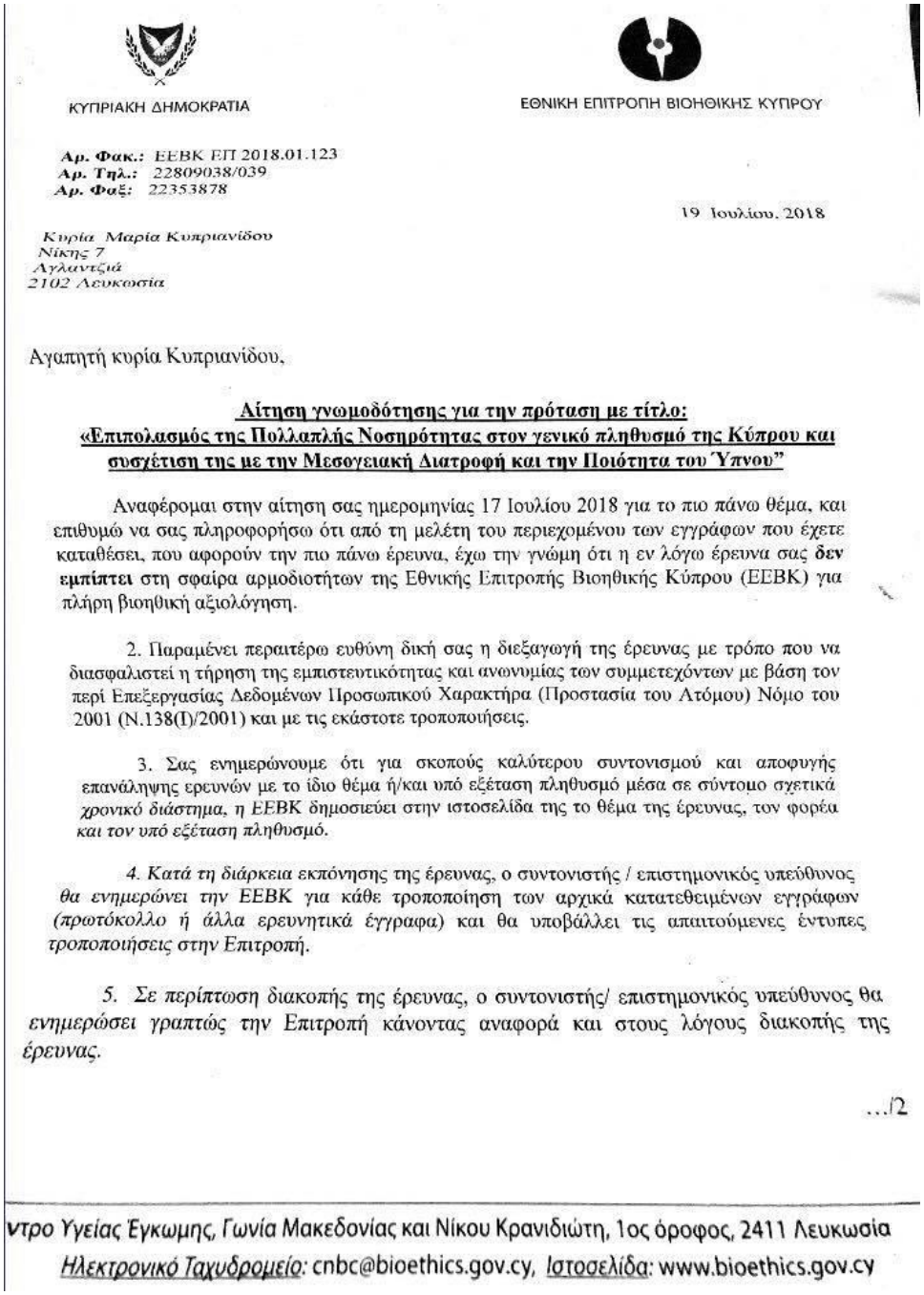
Θα θέλαμε να σημειώσετε πάνω σε αυτήν την κλίμακα πόσο καλή ή κακή είναι η υγεία σας σήμερα, κατά τη γνώμη σας. Παρακαλούμε κάντε το αυτό, **<u>τραβώντας μια γραμμή στο σημείο της κλίμακας που δείχνει πόσο καλή ή κακή είναι η κατάσταση της υγείας σας ΣΗΜΕΡΑ.</u>**

38) Οι ερωτήσεις της κλίμακας αυτής σας ρωτάνε για τα συναισθήματα και τις σκέψεις σας κατά τη διάρκεια του **ΤΕΛΕΥΤΑΙΟΥ ΜΗΝΑ**. Σε κάθε περίπτωση, επιλέξτε το τετράγωνο που αντιπροσωπεύει το πόσο συχνά αισθανθήκατε ή σκεφτήκατε με συγκεκριμένο τρόπο.

	Ποτέ	**Σχεδόν Ποτέ**	**Μερικές Φορές**	**Αρκετά συχνά**	**Πολύ συχνά**
Πόσο συχνά έχεις νιώσει αναστάτωση εξαιτίας κάποιου γεγονότος που συνέβη αναπάντεχα;					
Πόσο συχνά έχεις νιώσει ότι αδυνατούσες να ελέγξεις τα σημαντικά πράγματα στη ζωή σας;					
Πόσο συχνά ένιωσες νευρικός/η και στρεσαρισμένος/η;					
Πόσο συχνά έχεις αντιμετωπίσει επιτυχώς τα προβλήματα και τις ενοχλήσεις της καθημερινότητας;					
Πόσο συχνά ένιωσες να αντεπεξέρχεσαι αποτελεσματικά στις σημαντικές αλλαγές που συνέβαιναν στη ζωή σου;					
Πόσο συχνά νιώσατε πεπεισμένοι για την ικανότητά σας να χειριστείτε τα προσωπικά σας προβλήματα;					
Πόσο συχνά ένιωσες ότι τα πράγματα πήγαιναν με τον					
Πόσο συχνά ανακάλυψες ότι δεν μπορούσες να ανταπεξέλθεις στο σύνολο των υποχρεώσεων σου;					
Πόσο συχνά ήσουν σε θέση να ελέγξεις τους					
Πόσο συχνά ένιωσες ότι είχες τον απόλυτο έλεγχο των					
Πόσο συχνά εξοργίστηκες εξαιτίας κάποιων συμβάντων που δεν άπτονταν του ελέγχου σου;					
Πόσο συχνά έχεις πιάσει τον εαυτό σου να σκέφτεται για πράγματα που πρέπει να φέρεις εις πέρας;					
Πόσο συχνά ήσουν σε θέση να ελέγξεις τον τρόπο που ξοδεύεις τον χρόνο σου;					
Πόσο συχνά ένιωσες ότι οι δυσκολίες συσσωρεύονταν σε τέτοιο βαθμό ώστε να μην μπορείς να τις ξεπεράσεις;					

ΣΑΣ ΕΥΧΑΡΙΣΤΟΥΜΕ !

Approval of the study by the CNBC (ΕΕΒΚ ΕΠ 2018.01.123)



ΚΥΠΡΙΑΚΗ ΔΗΜΟΚΡΑΤΙΑ

ΕΘΝΙΚΗ ΕΠΙΤΡΟΠΗ ΒΙΟΗΘΙΚΗΣ ΚΥΠΡΟΥ

Αρ. Φακ.: ΕΕΒΚ ΕΠ 2018.01.123
Αρ. Τηλ.: 22809038/039
Αρ. Φαξ: 22353878

19 Ιουλίου, 2018

Κυρία Μαρία Κυπριανίδου
Νίκης 7
Αγλαντζιά
2102 Λευκωσία

Αγαπητή κυρία Κυπριανίδου,

Αίτηση γνωμοδότησης για την πρόταση με τίτλο:
«Επιπολασμός της Πολλαπλής Νοσηρότητας στον γενικό πληθυσμό της Κύπρου και συσχέτιση της με την Μεσογειακή Διατροφή και την Ποιότητα του Ύπνου"

Αναφέρομαι στην αίτηση σας ημερομηνίας 17 Ιουλίου 2018 για το πιο πάνω θέμα, και επιθυμώ να σας πληροφορήσω ότι από τη μελέτη του περιεχομένου των εγγράφων που έχετε καταθέσει, που αφορούν την πιο πάνω έρευνα, έχω την γνώμη ότι η εν λόγω έρευνα σας **δεν εμπίπτει** στη σφαίρα αρμοδιοτήτων της Εθνικής Επιτροπής Βιοηθικής Κύπρου (ΕΕΒΚ) για πλήρη βιοηθική αξιολόγηση.

2. Παραμένει περαιτέρω ευθύνη δική σας η διεξαγωγή της έρευνας με τρόπο που να διασφαλιστεί η τήρηση της εμπιστευτικότητας και ανωνυμίας των συμμετεχόντων με βάση τον περί Επεξεργασίας Δεδομένων Προσωπικού Χαρακτήρα (Προστασία του Ατόμου) Νόμο του 2001 (Ν.138(Ι)/2001) και με τις εκάστοτε τροποποιήσεις.

3. Σας ενημερώνουμε ότι για σκοπούς καλύτερου συντονισμού και αποφυγής επανάληψης ερευνών με το ίδιο θέμα ή/και υπό εξέταση πληθυσμό μέσα σε σύντομο σχετικά χρονικό διάστημα, η ΕΕΒΚ δημοσιεύει στην ιστοσελίδα της το θέμα της έρευνας, τον φορέα και τον υπό εξέταση πληθυσμό.

4. Κατά τη διάρκεια εκπόνησης της έρευνας, ο συντονιστής / επιστημονικός υπεύθυνος θα ενημερώνει την ΕΕΒΚ για κάθε τροποποίηση των αρχικά κατατεθειμένων εγγράφων (πρωτόκολλο ή άλλα ερευνητικά έγγραφα) και θα υποβάλλει τις απαιτούμενες έντυπες τροποποιήσεις στην Επιτροπή.

5. Σε περίπτωση διακοπής της έρευνας, ο συντονιστής/ επιστημονικός υπεύθυνος θα ενημερώσει γραπτώς την Επιτροπή κάνοντας αναφορά και στους λόγους διακοπής της έρευνας.

.../2

ντρο Υγείας Έγκωμης, Γωνία Μακεδονίας και Νίκου Κρανιδιώτη, 1ος όροφος, 2411 Λευκωσία
Ηλεκτρονικό Ταχυδρομείο: cnbc@bioethics.gov.cy, Ιστοσελίδα: www.bioethics.gov.cy

6. Ο συντονιστής/ επιστημονικός υπεύθυνος θα ενημερώσει την Επιτροπή σε περίπτωση αδυναμίας να συνεχίσει ως συντονιστής και θα υποβάλει τα στοιχεία επικοινωνίας του αντικαταστάτη του.

7. Με το πέρας της ερευνητικής πρότασης, ο συντονιστής / επιστημονικός υπεύθυνος θα ενημερώσει εγγράφως την Επιτροπή ότι το υπό αναφορά ερευνητικό πρωτόκολλο ολοκληρώθηκε.

8. Σας ευχόμαστε κάθε επιτυχία στη διεξαγωγή της έρευνάς σας.

Με εκτίμηση,

Καθ. Κωνσταντίνος Ν. Φελλάς
Πρόεδρος
Εθνικής Επιτροπής Βιοηθικής Κύπρου