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AGRICULTURAL UNIVERSITY OF ATHENS

Department of Food Science and Human Nutrition

PhD thesis

VITAMIN D INTAKE AND STATUS IN A REPRESENTATIVE SAMPLE OF GREEK ADULTS: THE HELLENIC NATIONAL NUTRITION AND HEALTH SURVEY

Ioannis G Dimakopoulos

Athens,

June 2019

Supervisor

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Τμήμα Επιστήμης Τροφίμων & Διατροφής του Ανθρώπου

Διδακτορική Διατριβή

ΔΙΑΤΡΟΦΙΚΗ ΠΡΟΣΛΗΨΗ ΚΑΙ ΚΑΤΑΣΤΑΣΗ ΒΙΤΑΜΙΝΗΣ D ΣΕ ΑΝΤΙΠΡΟΣΩΠΕΥΤΙΚΟ ΔΕΙΓΜΑ ΕΝΗΛΙΚΩΝ ΣΤΗΝ ΕΛΛΑΔΑ: ΣΤΟΙΧΕΙΑ ΑΠΟ ΤΗΝ ΠΑΝΕΛΛΑΔΙΚΗ ΜΕΛΕΤΗ ΔΙΑΤΡΟΦΗΣ ΚΑΙ ΥΓΕΙΑΣ

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Αθήνα,

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ΔΙΔΑΚΤΟΡΙΚΗ ΔΙΑΤΡΙΒΗ

ΤΙΤΛΟΣ: **ΔΙΑΤΡΟΦΙΚΗ ΠΡΟΣΛΗΨΗ ΚΑΙ ΚΑΤΑΣΤΑΣΗ ΒΙΤΑΜΙΝΗΣ D ΣΕ ΑΝΤΙΠΡΟΣΩΠΕΥΤΙΚΟ ΔΕΙΓΜΑ ΕΝΗΛΙΚΩΝ ΣΤΗΝ ΕΛΛΑΔΑ: ΣΤΟΙΧΕΙΑ ΑΠΟ ΤΗΝ ΠΑΝΕΛΛΑΔΙΚΗ ΜΕΛΕΤΗ ΔΙΑΤΡΟΦΗΣ ΚΑΙ ΥΓΕΙΑΣ**

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Περίληψη (στα Ελληνικά)

Γενική επισκόπηση: Παγκοσμίως ο επιπολασμός της έλλειψης βιταμίνης D στον ορό είναι ιδιαίτερα αυξημένος. Υπολογίζεται πως 1 δισεκατομμύριο άνθρωποι έχουν χαμηλή συγκέντρωση βιταμίνης D στον ορό. Ακόμα και σε χώρες της Μεσογείου, όπως η Ελλάδα, όπου η ηλιοφάνεια είναι αυξημένη, παρατηρείται αυξημένος επιπολασμός και χαμηλά επίπεδα βιταμίνης D στον ορό.

Ακόμη, σε παγκόσμιο επίπεδο, παρατηρείται χαμηλή πρόσληψη βιταμίνης D από την τροφή καθώς και από συμπληρώματα διατροφής. Η έλλειψη βιταμίνης D μπορεί να επιδράσει σημαντικά στη σκελετική υγεία σε όλες τις ηλικιακές ομάδες, όπως για παράδειγμα με ραχιτισμό στους ανήλικους καθώς επίσης και να αυξήσει την πιθανότητα για οστεομαλακία, οστεοπενία και οστεοπόρωση στους ενήλικες.

Επιπρόσθετα, την τελευταία δεκαετία αρκετές μελέτες έχουν συσχετίσει την έλλειψη βιταμίνης D και με άλλες παθήσεις, και η σχέση τους ερευνάται. Παραδείγματα αποτελούν η πιθανή σχέση μεταξύ της βιταμίνης D και χρόνιων ασθενειών όπως η παχυσαρκία, ο σακχαρώδης διαβήτης, τα αυτοάνοσα νοσήματα, τα καρδιαγγειακά νοσήματα και ο καρκίνος. Ακόμη, σχετίζεται με αυξημένη θνησιμότητα ανεξαρτήτου αιτίας.

Στόχοι: Δεδομένα από αντιπροσωπευτικό δείγμα του πληθυσμού της Ελλάδας, άνω των 18 ετών, από την Πανελλαδική Μελέτη Διατροφής και Υγείας χρησιμοποιήθηκαν σε αυτή τη διδακτορική διατριβή. Κύριος στόχος της διατριβής ήταν η καταγραφή του επιπολασμού έλλειψης βιταμίνης D στον ορό στον ενήλικο πληθυσμό της Ελλάδας καθώς επίσης και η συσχέτιση του με τους πιθανούς παράγοντες που επηρεάζουν τα επίπεδα της.

Δευτερεύων στόχος ήταν η καταγραφή της πρόσληψης βιταμίνης D από την τροφή και η σύγκριση αυτών των επιπέδων με το Estimated Average Requirement καθώς και το Recommended Dietary Intake. Τέλος, διερευνήθηκε πώς ένα θεωρητικό παράδειγμα εμπλουτισμού τροφίμου με βιταμίνη D θα βοηθούσε στην αύξηση διατροφικής πρόσληψης βιταμίνης D καθώς και πως θα βελτιωνόταν η πρόσληψη βιταμίνης D από την τροφή σε σύγκριση με τις συστάσεις.

Μεθοδολογία: Αντιπροσωπευτικό δείγμα 3773 ενηλίκων ηλικίας ≥18 ετών από την πλειοψηφία των νομών της χώρας χρησιμοποιήθηκε για αυτή τη μελέτη. Η επιλογή των εθελοντών έγινε τυχαιοποιημένα, σε συνεργασία με την Ελληνική Στατιστική Αρχή μετά από στρωματοποιημένη δειγματοληψία. Η Πανελλαδική Μελέτη Διατροφής και Υγείας εφάρμοσε πληθώρα ερωτηματολογίων στους εθελοντές, τα περισσότερα από τα οποία συμπληρώνονταν με τη βοήθεια ερευνητή.

Οι μετρήσεις που πραγματοποιήθηκαν έγιναν από εξειδικευμένο και εκπαιδευμένο με βάση το πρωτόκολλο της μελέτης επιστημονικό προσωπικό. Για τη συγκεκριμένη διδακτορική διατριβή και ανάλυση χρησιμοποιήθηκαν δεδομένα από: (1) Εξετάσεις αίματος (βιταμίνη D, παραθυρεοειδής ορμόνη, ασβέστιο, κτλ.), (2) ερωτηματολόγιο έκθεσης στον ήλιο, (3) Δυο ανακλήσεις 24ώρου ανά εθελοντή με βάση την Automated Multiple-Pass Method και με τη χρήση Computer Assisted Personal Interview, (4) Ερωτηματολόγιο λήψης φαρμάκων και συμπληρωμάτων διατροφής και (5) Ανθρωπομετρικές μετρήσεις.

Για την ανάλυση των δεδομένων από τις ανακλήσεις 24ώρου χρησιμοποιήθηκε η διεθνώς αποδεκτή μεθοδολογία για την εκτίμηση των εθελοντών που υπό- ή υπέρ-αναφέρουν τη διατροφική τους πρόσληψη (misreporters) καθώς επίσης και μεθοδολογία για τον υπολογισμό της συνήθους πρόσληψης των εθελοντών (Usual intake estimation).

Αποτελέσματα: Η διάμεσος πρόσληψη βιταμίνης D στον ορό ήταν 16.72 ng/ml για το σύνολο του δείγματος, 16.67 ng/ml για του άνδρες και 16.74 ng/ml για τις γυναίκες, χωρίς να παρατηρούνται στατιστικά σημαντικές διαφορές μεταξύ των δυο φύλων (P=0.923). Οι πιθανότητες να έχουν συγκέντρωση 25(OH)D στον ορό μικρότερη των 20 ng/ml μειωνόταν σημαντικά σε εκείνους που ήταν πολύ δραστήριοι (OR 0.55, 95% CI 0.35, 0.98), που είχαν αυξανόμενη έκθεση στον ήλιο 1-3 ώρες / CI 0.44, 0.80), >3 ώρες / ημέρα (OR 0.36, 95% CI 0.24, 0.55) και χρώμα δέρματος ανοιχτόχρωμο ή μέτρια ανοιχτόχρωμο (OR 0.47, 95% CI 0.24, 0.91), ελαφρώς σκουρόχρωμο (0.34, 95% CI 0.17, 0.67) και σκουρόχρωμο ή πολύ σκούρο χρώμα δέρματος (OR 0.34, 95% CI 0.15, 0.75), σε σύγκριση με τα αντίστοιχα επίπεδα σύγκρισης. Οι πιθανότητες αυξήθηκαν σημαντικά με την παχυσαρκία (OR 1.95, 95% CI 1.24, 3.08) και την άνοιξη ως περίοδο συλλογής δείγματος στο αίμα (OR 1.75, 95% CI 1.22, 2.50). Οι παραπάνω μετρήσεις στον ορό πραγματοποιήθηκαν σε υποδείγμα 1084 ατόμων του ενήλικου πληθυσμού της μελέτης όπου πραγματοποιήθηκαν και οι εξετάσεις αίματος.

Η διάμεσος πρόσληψη βιταμίνης D από τα τρόφιμα κυμάνθηκε από 1.16-1.72 mcg/ημέρα και 1.01-1.26 ανάλογα με την ηλικιακή ομάδα και το φύλο. Σημαντικές πηγές της βιταμίνης D από την τροφή ήταν τα ψάρια (46%), το κρέας (15%) και τα δημητριακά (12%). Ωστόσο, το 90% του πληθυσμού σε όλες τις ηλικιακές ομάδες δεν πληρούσε το Estimated Average requirement για τη βιταμίνη D.

Ο εμπλουτισμός τροφίμου/ τροφίμων με βιταμίνη D αποτελεί μια πολιτική υγείας που, αν εφαρμοστεί, θα μπορούσε να μειώσει σημαντικά το ποσοστό εκείνων που προσλαμβάνουν βιταμίνη D από την τροφή λιγότερη από το Estimated Average Requirement και κατά συνέπεια να βελτιώσει και τον επιπολασμό επιπέδων βιταμίνης D <20 ng/ml στον ορό.

Συμπεράσματα: Η ανεπάρκεια της βιταμίνης D είναι ιδιαίτερα αυξημένη στον ενήλικο πληθυσμό της Ελλάδας. Σχετικές πολιτικές δημόσιας υγείας συνιστώνται ιδιαίτερα, οι οποίες θα μπορούσαν να περιλαμβάνουν την ενίσχυση της βιταμίνης D καθώς και πρόταση για αυξημένη, αλλά ασφαλή έκθεση στον ήλιο. Οι πολιτικές δημόσιας υγείας για την αύξηση της κατανάλωσης τροφίμων με υψηλή περιεκτικότητα σε βιταμίνη D ή/ και τον εμπλουτισμό των τροφίμων μπορούν να μειώσουν σημαντικά το ποσοστό των ατόμων που δεν πληρούν τις συστάσεις καθώς και εκείνων που έχουν χαμηλά επίπεδα βιταμίνης D στον ορό.

Επιστημονικός τομέας: Επιδημιολογία της Διατροφής.

Λέξεις κλειδιά: βιταμίνη D, διατροφική πρόσληψη, επιδημιολογία, διατροφική πολιτική.

Abstract (in English)

Overview: Globally, the prevalence of low serum vitamin D is high. It is estimated that 1 billion people have low concentrations of serum vitamin D. Even in countries in the Mediterranean, like Greece, where sunlight exposure is increased, high prevalence of low serum vitamin D is observed. In addition, globally, low intake of vitamin D from food is observed as well as from nutritional supplements. Vitamin D deficiency can impact on skeletal health in all age groups, like for example with rickets in children as well as to increase the probability of osteomalacia, osteopenia and osteoporosis in adults.

Furthermore, the last decade several studies have associated vitamin D deficiency with other conditions, and their relationship is under investigation. Some examples are the probable relationship of vitamin D with chronic conditions such as obesity, diabetes mellites, autoimmune disease, cardiovascular diseases and cancer. It is also associated with increased mortality from all causes.

Objectives: Data from a representative sample of the population in Greece ≥18 years old from the Hellenic National Nutrition and Health Examination Survey were used for this doctoral thesis. Main objective of this thesis was the estimation of low serum vitamin D prevalence in Greek adults as well as its association with probable factors that can influence its levels.

Secondary objective was the estimation of vitamin D intake from food as well as the comparison of these levels with the Estimated Average Requirement as well as the Recommended Dietary Intake. An additional objective was to estimate how a theoretical example of food fortification could help increase vitamin D food intake as well as how much of an improvement this could offer when intake levels were compared with the guidelines.

Methods: A representative sample of 3773 adults, aged 18 years old and over, from most Greece's counties was used for this study. Selection of volunteers was randomized, in collaboration with the Hellenic Statistical Authority. In the Hellenic National Nutrition and Health Survey a plethora of questionnaires were applied, and most were completed with the help of field workers. The measurements/ clinical examinations were performed by specialized and trained personnel according to the study protocol. For this specific doctoral

thesis and analysis data were used from: (1) Blood results (serum vitamin D, parathyroid hormone, calcium, etc.), (2) Sunlight exposure questionnaire, (3) Two 24-hour recalls per volunteer based on the Automated Multiple-Pass Method and with the use of Computer Assisted Personal Interview, (4) Drug and nutritional supplement questionnaire and (5) Anthropometric measurements.

For the analysis of the 24-hour recall data methodology from the international knowledge base was used in order to estimate misreporters as well as the estimation of the usual intake.

Results: Median serum 25(OH)D was 16.72 ng/ml for the total sample, 16.67 ng/ml for males and 16.74 ng/ml for females with no significant differences between the two genders (P=0.923). The odds of having 25(OH)D <20 ng/ml significantly decreased with being very active (OR 0.55, 95% CI 0.35, 0.98), increasing length of sun exposure 1-3 hours/day (OR 0.59, 95% CI 0.44, 0.80), >3 hours/day (OR 0.36, 95% CI 0.24, 0.55)], and skin color light to medium skin (OR 0.47, 95% CI 0.24, 0.91), fairly dark skin colour (OR 0.34, 95% CI 0.17, 0.67) and dark or very dark skin colour (OR 0.34, 95% CI 0.15, 0.75)], compared to respective baseline levels. The odds significantly increased with obesity (OR 1.95, 95% CI 1.24, 3.08), and spring season of blood sample collection (OR 1.75, 95% CI 1.22, 2.50).

Median vitamin D intake from food was 1.23 mcg/day (0.60, 2.44), with 9.1% consuming supplements. Median vitamin D intake from food ranged from 1.16-1.72 mcg/day and 1.01-1.26 in different age group in males and females, respectively. Major food sources of vitamin D were fish (46%), meat (15%) and cereals (12%), however, over 90% of the population in all age groups did not meet the Estimated Average Requirement, even when supplemental use was accounted for. Vitamin D overall intake is below the average requirements.

Conclusion: Vitamin D deficiency is highly prevalent in Greek adults. Relevant public health policies are highly recommended, which could include vitamin D fortification. and suggestion for increased but safe sun exposure. Public health policies to increase the consumption of foods high in vitamin D and/or food fortification may significantly reduce the percentage of individuals that do not meet the recommendations.

Scientific field: Nutritional epidemiology.

Keywords: vitamin D, nutrition intake, epidemiology, nutrition policy.

Περιεχόμενα

Abbreviations

24hr	24-hour recall
25(OH)D	25-hydroxyvitamin D
AESAN	*A*gencia *E*spañola de *S*eguridad *A*limentaria y *N*utrición
AI	Adequate Intake
AMPM	Automated Multiple-Pass Method
ANSES	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail
ARCHES	Arkansas Cardiovascular Health Examination Survey
BMI	Body Mass Index
BRFSS	Behavioral Risk Factor Surveillance System
CAPI	Computer Assisted Personal Interview
CI	Confidence Interval
CVD	Cardiovascular disease
DNFCS	Dutch National Food Consumption Survey
EAR	Estimated Average Requirement
EDTA	Ethylenediaminetetraacetic acid
EFSA	European Food Safety Authority
EU	European Union
H/D	Hours per Day
HDPA	Hellenic Data Protection Authority (HDPA)
HNNHS	Hellenic National Health and Nutrition Examination Survey

IoM	Institute of Medicine
IPAQ	International Physical Activity Questionnaire
IU	International Units
KG/M^2	Kilograms per meters squared
LR TEST	Likelihood Ratio test
MED	Minimal Erythemal Dose
MG	Micrograms (µg)
NDNS	National Diet and Nutrition Survey
NDSR	Nutrition Data System for Research
NG/ML	Nanogram per milliliter
NHANES	National Health and Nutrition Examination Survey
NIAAA	National Institute on Alcohol Abuse and Alcoholism
OR	Odds Ratio
PG/ML	Picogram per milliliter
PTH	Parathyroid Hormone
RDA	Recommended Dietary Intake
SACN	Scientific Advisory Committee on Nutrition
SSM	Skeletal Muscle Mass
UK	United Kingdom
USA	United States of America
USDA	United States Department of Agriculture
WHO	World Health Organization

1. Introduction

1.1 Prevalence of serum 25(OH)D deficiency

In recent years vitamin D deficiency has become the most common nutritional deficiency in the world with more than 1 billion people having inadequate levels of serum vitamin D concentration (Holick 2007, Lips 2010). In populations living in low latitude where ultraviolet (UV) rays are assumed adequate for vitamin D skin synthesis or in industrialized nations where some foods are fortified with vitamin D, deficiency still persists (Palacios and Gonzalez 2014) across all age groups and subgroups (Hilger et al. 2014, Manios et al. 2017, Spiro and Buttriss 2014).

These levels are observed in the national (Katrinaki et al. 2016, Manios et al. 2017, Papadakis et al. 2015), European (Cashman et al. 2016, Hilger et al. 2014, Manios et al. 2017, Spiro and Buttriss 2014) and International level (Hilger et al. 2014, Palacios and Gonzalez 2014). Apart from low serum concentrations, published data have also reported high prevalence of low vitamin D intake even at levels that are far below the recommended reference intake, as per the Institute of Medicine (IoM) (Ross et al. 2011, Spiro and Buttriss 2014).

In more detail, several studies in the Greek adult population show a high prevalence of vitamin D deficiency. In 625 healthy and free-living adults, aged 18-85 years old, living in a latitude of 38^{o} the prevalence of vitamin D deficiency was high (57.7%) (Singhellakis et al. 2011). Authors reported that this could possibly be explained by inadequate sun exposure, use of commercial sunscreens, that can reduce vitamin D skin synthesis by up to 99%, as well as air pollution (Singhellakis et al. 2011). Another study, that included 279 elderly individuals in Greece also reported high levels of vitamin D deficiency where only 6.5% could be considered having sufficiency during winter and 35% during summer (Papapetrou et al. 2007).

Similar levels of deficiency, ranging from 50-80%, have been reported in the Greek dataset of elderly individuals of a multicenter study; even peasants and farmers that are supposed to work outdoors and therefore be exposed to the sun daily (van der Wielen et

al. 1995). One possible explanation could be that they cover most of their body with clothes, even during the summer months.

Numerous other studies in the Greek population have reported similar levels of deficiency. For example a study in healthy young/ middle-aged men reported vitamin D deficiency of 50.3% (Kassi et al. 2015). In addition, high prevalence of deficiency has been observed in studies that included individuals <18 years old (Gonzalez-Gross et al. 2012, Karras et al. 2013, Manios et al. 2017, Nicolaidou et al. 2006).

Studies from other countries in the mediterranean region, in European countries as well as internationally, reported increased levels of deficiency which however vary from country to country (Lips 2010, Manios et al. 2017, Spiro and Buttriss 2014). This variability was expected as there are many factors that influence vitamin D status. For example, sun exposure is influenced by factors such as geographical latitude, season, urban vs. rural location, clothing, skin colour, air pollution and sunscreen use (SACN 2016). Even in Southern European countries where there is a relative abundance of UVB availability, in comparison to Northern European countries, increased prevalence of vitamin D deficiency can be observed (Manios et al. 2017).

1.2 Prevalence of low intakes from food and supplements

Apart from the high prevalence of low serum vitamin D deficiency, which is considered the main source for the majority of the population (Calvo et al. 2005), dietary intakes of vitamin D are also very low (Spiro and Buttriss 2014). Many studies, from Greece but also internationally, reported low intakes of vitamin D from food; intakes that are well below the Estimated Average Requirement (EAR) (Au et al. 2013, Bailey et al. 2010, Freisling et al. 2010, Manios et al. 2014, Moore et al. 2004, Ross et al. 2011, Spiro and Buttriss 2014).

More specifically, a European Food Safety Agency (EFSA) study, that included intakes from 14 European countries, reported a mean dietary intake ranging from 1.1 to 8.2 mcg/day (EFSA 2012). This level of intake is explained in the literature as a result of very few foods naturally containing vitamin D (SACN 2016). Some examples are fish, especially fatty fish; milk, meat, eggs and fortified products, such as cereals (Spiro and Buttriss 2014). In more

detail, egg yolk contains approximately 12.6 mcg per 100g, oily fish, such as salmon, herring, sardines and mackerel, contains 5-16 mcg per 100g whereas animal products such as meat, liver and kidneys contain 0.1-1.5 mcg per 100g (SACN 2016).

In addition vitamin D_3 can be found in some species of plants however wide variation has been reported and is not yet known if the edible portions contain it; some wild mushrooms are also rich sources of vitamin D_2 (13-30mcg per 100g) (SACN 2016).

With regards to contribution of different food groups to vitamin D intake in European countries fish contributes 70% of vitamin D from food intake in Spain (18-64 years old) (AESAN 2011), 38% in France (ANSES 2013), 25% in the UK (19-64 years old) (Bates et al. 2015), 12-16% (12% for those 18-64 years, 16% for those ≥65 years) in Ireland (Spiro and Buttriss 2014) and only 8-11% in the Netherlands (8% in 7-69 years old and 11% in ≥70 years old) (DNFCS 2011, Ocke et al. 2013). Meat contributes 22% of vitamin D from food intake (19-64 years old) (Bates et al. 2015), in Ireland 22-30% (30% for 18-64 years old, 22% for ≥65 years old) (Spiro and Buttriss 2014), in Spain 2% (AESAN 2011) and in the Netherlands 12-20% (20% in those 7-69 years old and 12% in those aged ≥70 years old) (DNFCS 2011, Ocke et al. 2013). Another example, cereals, contributed 12% in males and 13% in females in the UK (Spiro and Buttriss 2014), 4% in Spain (AESAN 2011) and to 2-5% in Irish adults (Spiro and Buttriss 2014).

Supplements offer a further option in order to increase intake. This has been particularly important in (1) countries where sunlight availability is low, (2) during the winter months irrespective of the country when sunlight availability is lower and/or (3) for people with very low sunlight exposure (Cashman and Kiely 2014).

With respect to nutritional supplement consumption great variability has been observed between different countries; especially between those living a more northern latitude compared to those living in the mediterranean (Skeie et al. 2009). More specifically, a gradient, in consumption, is observed between countries in the south and countries in the north and as an example nutrition supplement consumption in Norway was as high as 61.7% whereas the lowest was observed in Greece (6.7% in females and 0.5% in males) (Skeie et al. 2009). These observations highlighted the further need to explore vitamin D intakes (from food and supplements) in Greece.

With respect to mandatory food fortification, regulations differ between countries. For example, according to European Union law directive infant and follow-on formula must be fortified with vitamin D (SACN 2016). In the United States of America (USA), although on a voluntary basis, almost all milk products are fortified. Other foods that are also, but to a lesser extent, fortified include yoghurt, breakfast cereals, cheese as well as few other food products (Yetley 2008). Law in Canada also requires that milk and margarine are fortified on a mandatory basis as well as soy milk and infant formula (Calvo et al. 2004). In Greece, there is no mandatory fortification law at the moment.

1.3 Vitamin D metabolism

1.3.1 Vitamin D synthesis

Vitamin D is a fat-soluble vitamin that humans obtain naturally via few foods that contain it as well as through exposure of the skin to sunlight and from its precursor 7-dehydrocholesterol. Vitamin D produced in the skin is referred as vitamin D_3 (cholecalciferol) whereas its dietary form can be either vitamin D_3 or a similar molecule of plant origin called vitamin D_2 (ergocalciferol) (FAO 2002). Cholecalciferol and ergocalciferol can be considered metabolically equal (FAO 2002).

In addition, humans obtain vitamin D from nutritional supplements as well as from fortified foods. Vitamin D from all mentioned sources is inert (IOM 2011). It must undergo two hydroxylation reactions in order to be converted to its active form, 1,25-dihydrovitamin D. The first reaction takes place in the liver where vitamin D is converted to 25-hydroxyvitamin D (25(OH)D) the major circulating form; also known as calcidiol. This form is also the main biomarker of vitamin D status. The second reaction takes place in the kidneys were it is converted to 1,25-dihydroxyvitamin D; its active form, also known as calcitriol (IOM 2011).

Although named a “vitamin”, vitamin D is a steroid prohormone that has endocrine, paracrine and autocrine functions. The most known (endocrine) function of vitamin D is to regulate calcium absorption and homeostasis (Spiro and Buttriss 2014). Its active form circulates in the blood with vitamin D binding protein. It can cross the plasma membrane

and subsequently interact with the vitamin D receptor, binds to a specific vitamin D responsive element and together with associated transcription factors enhances transcription of mRNAs which in turn code for calcium-transporting proteins, bone matrix proteins or cell cycle-regulating proteins (SACN 2016).

As a result, it stimulates the intestinal absorption of calcium and phosphate and stimulates calcium resorption. These functions help restore serum levels of calcium and phosphorus when their concentrations are low. With regards to maintaining this homeostasis of calcium and phosphorus 1,25-dihydroxyvitamin D acts along with parathyroid hormone (PTH).

1.3.2 Factors affecting serum 25(OH)D concentration

Currently serum 25(OH)D levels are considered the best available indicator of vitamin D status, i.e. the best indicator of body content as well as the amount available for cellular use and it is used as a marker upon which to decide if an individual has sufficient or deficient serum concentration (SACN 2016).

Adipose tissue has been suggested as a place where vitamin D can be stored in the body, however the physiological mechanisms which regulate this process are currently unknown (IOM 2011). The same could be hypothesized for skeletal muscle but our understanding is currently limited and it has been described in the literature as a research gap to be studied further (Cashman and Kiely 2011).

Furthermore, when vitamin D enters the circulation is cleared by the liver in a few hours and we rely only on measuring serum 25(OH)D concentration as it is not feasible to measure vitamin D concentration in adipose tissue, muscle or the liver (SACN 2016). However, as vitamin D and its metabolites stored in adipose tissue as well as other bodily sites, from where they could also be mobilized, what is usually examined, in reality, is the relationship between serum concentration and other factors, such as sunlight exposure and dietary intake (IOM 2011, SACN 2016).

As previously mentioned, serum 25(OH)D has been suggested as the best indicator of status as well as the main form of storage in the body since it is easily available for cellular use. It reflects intake from diet (foods and supplements) as well as skin synthesis (SACN 2016). Serum $1,25(OH)_2D$ may not be considered the best indicator, although it is the main driver of physiological responses to vitamin D, as even in cases of extreme deficiency serum $1,25(OH)_2D$ concentration can be normal (Holick 2004, IOM 2011). Hence, 25(OH)D is used as the indicator of vitamin D status by most health authorities (IOM 2011, SACN 2016) although is not clear if serum 25(OH)D can act as the ideal indicator of the association between health outcomes and vitamin D status (IOM 2011).

For example, low serum 25(OH)D concentrations have been associated with chronic inflammatory conditions and therefore some researchers have suggested possible reverse causality, i.e. that low serum 25(OH)D concentration could be an effect of an inflammatory state rather than the cause (Reid et al. 2011). Similar associations have also been observed in other studies (Silva and Furlanetto 2015).

In addition, a number of other factors can influence serum 25(OH)D concentration such as season, geographical location, sun exposure, skin colour, sunscreen use, BMI, serum PTH concentration as well as some genetic factors (Cashman and Kiely 2011, Holick et al. 2011, IOM 2011, SACN 2016).

1.3.2.1 Influence of dietary intake on serum 25(OH)D concentration

With regards to food intake and its influence on serum levels, both vitamin D_2 and D_3 can increase serum 25(OH)D levels (Seamans and Cashman 2009), however it is not clear if they have the same effect (SACN 2016). In addition, it has been suggested that the simultaneous presence of dietary fat in the intestines can increase absorption of vitamin D (Weber 1981). An individual's stored body fat, as estimated by the Body Mass Index (BMI), also seems to negatively influence the elevation of serum 25(OH)D concentration following supplementation (Forsythe et al. 2012).

Although there is a great variability between trials and not all were dose-response, meta-regression analyses of data from randomized controlled trials in adults show that for every

1 mcg of vitamin D consumed serum concentrations increased by 0.25 ng/ml (Cranney et al. 2007); an estimate that is very close to reports from other studies as well (Heaney and Weaver 2003). However, the effect of increasing intakes of vitamin D from food and supplements on serum 25(OH)D intake is linear and steeper up to vitamin D intake of 1000 IU/day (25 mcg/day), but decreases with intake ≥1000 IU/day (IOM 2011).

In addition, these results could be affected by the latitude and season were the respective studies were conducted as some other researchers have reported higher increases in serum 25(OH)D concentration, on average 0.8 ng/ml (compared to 0.25 ng/ml previously mentioned) for every 1 mcg intake per day (SACN 2016).

Similar, results were observed in an Institute of Medicine (IoM) analysis between randomized controlled trials conducted in populations of different latitudes. In order to ensure that the guidelines by the IoM will take into account the most vulnerable, in terms of low serum 25(OH)D concentration, individuals in the formulation of their guidelines they used data from higher latitudes where it is assumed that skin synthesis is at its lowest (IOM 2011).

1.3.2.2 Influence of sunlight exposure on serum 25(OH)D concentration

The effect of sunlight exposure to serum 25(OH)D concentration is influenced by many factors such as season of the year, time of the day, amount of skin exposed, skin colour, geographical latitude, sunscreen use as well as genetic factors (IOM 2011, SACN 2016).

In comparison with dietary vitamin D that is associated with chylomicrons and low density lipoprotein and is subsequently metabolized in the liver, vitamin D synthesized in the skin following sunlight exposure is more efficient in raising serum 25(OH)D concentrations probably because it diffuses slowly in the bloodstream (Fraser 1983, Haddad et al. 1993). Unfortunately, due to heterogeneity, in study design and populations studied, it is not possible to quantitively and accurately report the effect of sun exposure on serum 25(OH)D concentration (Cranney et al. 2007). However, the lower the serum 25(OH)D concentration the higher the increase in serum levels following exposure to sunlight (Bogh et al. 2010). In

the same study, researchers reported that with higher the surface area of the skin exposed lower doses of exposure are adequate to elevate serum 25(OH)D levels.

Some researchers have tried to quantify the effect of sun exposure to serum concentration and suggested that exposure of approximately one quarter of the total body surface 2-3 times per week to ¼ Minimal Erythemal Dose (MED) during spring to autumn season is equal to an oral dose of 1000 UI vitamin D (SACN 2016). One MED is defined as the minimum dose of ultraviolet radiation that produces erythema in that person's skin. However, this as well as similar studies do not always take into account normal life situations where people naturally adopt different postures and are randomly oriented to the sun and differ in the season when data was collected as well as in the ethnic groups studied, making therefore generalization of these results difficult (Farrar et al. 2011, Farrar et al. 2013, Webb et al. 2011).

Furthermore, latitude can influence skin synthesis following sunlight exposure. At latitudes below 37^{o}C sunlight is adequate for year round synthesis, whereas at higher latitudes vitamin D cannot be synthesized during the winter months (SACN 2016). A study which compared serum concentrations in different geographic latitudes (57^{o}N vs. 51^{o}N) reported a difference of approximately 4 ng/ml (Macdonald et al. 2011). However, it should also be considered that the weather in northern latitudes is colder and therefore individuals might spend much less time outdoors as well as have most of their skin covered with clothes, therefore reducing exposure of skin to the ultraviolet radiation.

For the same reason, contribution of skin synthesis to serum 25(OH)D status might be more limited during the winter months. However, irrespective of being outdoors during winter in higher latitudes ultraviolet radiation is even more limited and in northern countries not enough to produce biologically relevant quantities of vitamin D in the skin (Webb et al. 1989, Webb et al. 1988). A seasonal variation in serum 25(OH)D concentrations has been observed in many countries (IOM 2011, Kasahara et al. 2013, Manios et al. 2017, O'Neill et al. 2016, Papadakis et al. 2015, SACN 2016).

Skin colour can also affect skin synthesis and it has been observed that individuals with darker skin colour have lower serum 25(OH)D concentrations; although it is not entirely clear if this is the result of cultural and lifestyle, rather than physiological, reasons (Clemens

et al. 1982, SACN 2016, Webb 2006). Studies that have examined the role of skin melanin on skin synthesis have led to contradictory findings (Armas et al. 2007, Libon et al. 2013).

Another factor that could potentially influence skin synthesis of vitamin D is age. In some studies, individuals with increased age have lower serum 25(OH)D concentrations compared to those of younger age (MacLaughlin and Holick 1985). However, as previously mentioned for latitude and those living in northern areas/ countries, this could be the effect of going less outdoor with increasing age and therefore being less exposed to ultraviolet radiation. Furthermore, this lower serum 25(OH)D concentrations observed in older people could be a consequence of diminishing liver and/ or kidney function which could in turn influence one or both hydroxylation steps that take place in these two organs.

Apart from geographical and physiological factors, other factors can also have an impact on skin synthesis. For example, public health policies are in place to prevent skin cancer and therefore use of sunscreen can reduced skin synthesis of vitamin D. Relevant studies reported that although sunscreen use could block completely skin synthesis, it does not because sunscreens are not applied by individuals in the recommended dosage (Norval and Wulf 2009, Springbett et al. 2010). Therefore, vitamin D skin synthesis could be reduced but not completely prevented.

1.4 Health conditions associated with vitamin D deficiency

Low serum 25(OH)D levels have been associated with several health conditions of public health concern. Serum 25(OH)D levels, as previously mentioned, are analogous to an individual's sunlight, and more specifically UVB light, exposure as well as intake from food and supplements (SACN 2016).

The most widely studied role of vitamin D is the one that is related to bone health. During an individual's lifetime bone undergoes significant stages of growth, replacement and repair (IOM 2011). Bone is broken down, in a process called resorption, and new is formed, in a process called ossification (SACN 2016). Bone develops rapidly during infancy, less rapidly during childhood until another period of rapid growth that takes place during adolescence.

Peak is reached in the early 20s, however with increasing age bone resorption slowly but steadily predominates bone ossification. Later in life rate of bone loss increases, especially in women after menopause 4-8 years after which there is an acceleration of bone loss (Harel et al. 2002).

Vitamin D helps absorb calcium in the gastrointestinal tract as well as to maintain adequate serum calcium and phosphate concentrations for normal bone growth and remodeling (Holick 2004). Serum 25(OH)D deficiency is implicated in three different conditions related to bone health: rickets, osteomalacia and osteoporosis (IOM 2011). Serum 25(OH)D deficiency can lead to development of rickets in children.

Vitamin D supplementation can reverse the skeletal changes if it is diagnosed and prevented before the bone plates have begun to mature (SACN 2016). In adults, osteomalacia can develop as a result of vitamin D deficiency and impaired bone mineralization. Usually, it is also linked to hyperparathyroidism or caused by damage to the liver and/ or kidneys which could interfere with the respective hydroxylation reactions in the metabolic pathway to convert vitamin D to its active metabolite (IOM 2011).

In addition, osteoporosis can be developed as a result of ageing and is linked with micro-architectural deterioration of bone mass and increased risk of fractures (IOM 2011, SACN 2016). Many factors, that can influence bone mass, along with vitamin D deficiency or insufficiency can play a role in the development of osteoporosis (SACN 2016).

Apart from its effect on skeletal health, vitamin D has been studied for its probable effect in more than a hundred health outcomes including a very wide range of diseases like malignant, cardiovascular, autoimmune, infectious and metabolic diseases (Theodoratou et al. 2014). However, due to the nature of results in observational studies, and their accompanying limitations, no results offer highly convincing evidence of a role of vitamin D for any outcome (IOM 2011, SACN 2016, Theodoratou et al. 2014).

Therefore, apart from beneficial effects of vitamin D supplementation (along with calcium) on skeletal health, concerning other outcomes, vitamin D supplementation is probably linked to decrease in dental caries in children as well in parathyroid hormone in patients with chronic kidney disease (Holick 2005, Theodoratou et al. 2014).

Suggestive, but not conclusive, evidence also exists with regards to adequate vitamin D concentration in serum with cardiovascular disease, stroke, hypertension, depression, metabolic syndrome, cognition, type 2 diabetes and high body mass index, among other less common outcomes (Theodoratou et al. 2014).

1.5 Recommendations for vitamin D serum levels and intake

Although the major source for vitamin D in humans is skin synthesis following exposure to sunlight, many; especially those living in Northern countries, rely on body stores (which are not yet defined) and dietary intake (Cashman and Kiely 2014). However, as the ideal method to measure vitamin D study is measuring serum 25(OH)D levels, which is influenced by skin synthesis as well as intake – and the first source (skin synthesis) is in turn influenced by a number of factors such as latitude, pollution, skin colour, etc. (SACN 2016), setting recommended dietary intakes for vitamin D is not an easy task (Cashman and Kiely 2014).

In addition, our understanding of the role of serum levels of 25(OH)D and several health outcomes, as previously mentioned, is limited (Theodoratou et al. 2014); which could be an additional factor upon which requirements could be established. The strongest indicator, currently, is the association of 25(OH)D levels with skeletal health.

In recent years and in response to the epidemic of low serum 25(OH)D levels globally, many governmental authorities have tried to establish recommendations regarding vitamin D intake from food. One of the most comprehensive reviews was the one by the Institute of Medicine regarding calcium and vitamin D requirements (IOM 2011). IoM used a risk assessment framework in order to derive the Dietary Reference Intake (DRI) values for the first time; an approach described in the literature (Cashman 2012, Taylor 2008).

Similarly, other authorities, like the Scientific Advisory Committee on Nutrition (SACN) as well as the European Food Safety Authority followed a similar approach to set the reference intakes by appraising the evidence and using mostly evidence from independent systematic evidence-based reviews (Cashman and Kiely 2014, EFSA 2018, SACN 2016).

1.5.1 Recommendations for 25(OH)D serum levels

In this risk assessment approach, mentioned earlier, committees considered several outcomes (e.g. clinical, functional) as well as biomarkers (e.g. of effect, of exposure) in order to derive the Dietary Reference Intakes for vitamin D (Cashman 2012). Using mostly data regarding the association between vitamin D and skeletal health reference serum 25(OH)D was initially proposed; where a concentration ≥20 ng/mL was a suggested to meet the requirements for almost all healthy individuals (97.5%) (Cashman and Kiely 2014). The IoM committee named this concentration as the Recommended Dietary Allowance (RDA)-like concentration (IOM 2011).

The IoM committee explicitly reported that the Dietary Reference Values (DRVs) for vitamin D were based on the best available evidence at the time it was written and suggested that new DRVs should be derived when a much larger body of evidence is available, including more randomized controlled trials (IOM 2011). However, due to the fact that the available evidence is sometimes controversial and incomplete a lot of controversy was generated among scientists and some criticized the recommendations as conservative (Cashman and Kiely 2014).

Therefore, in response to the IoM guidelines the Endocrine Society, in the USA, also published guidelines for the evaluation, treatment and prevention of vitamin D deficiency (Holick et al. 2011). Although, they had similar views the Endocrine Society suggested categories of serum 25(OH)D which were based on “deficiency”, “insufficiency” and “sufficiency” (Holick et al. 2011) rather than the relative serum 25(OH)D concentration that would be “adequate” for 97.5% of the healthy population as IoM suggested (IOM 2011).

Both authorities (IoM and the Endocrine Society) agree that the evidence is limited for a causative link between serum 25(OH)D concentration and any outcome not related to skeletal health (Holick et al. 2011, IOM 2011).

1.5.2 Recommendations for food intake

Using meta-regression of data from randomized controlled trials, regarding the dose-response relationship of serum 25(OH)D to intake from food and supplements, the IoM translated the suggested serum 25(OH)D levels into Dietary Reference Intakes (Cashman and Kiely 2014, IOM 2011). This is how the Estimated Average Requirement (EAR) for vitamin D was set at 10 mcg/day for all adults and the Recommended Dietary Requirement (RDA) at 15 mcg/ day for adults 18-70 years old and at 20 mcg/day for those ≥71 years old. (IOM 2011). The Tolerable Upper Intake Level (UL) was set at 100 mcg/day for adults ≥18 years old (IOM 2011).

The EAR is defined as the nutrient intake level that is estimated to meet the requirements of half healthy individuals of the specified age and gender group (IOM 2011). The RDA is defined as the nutrient intake level that is estimated to meet the needs of nearly all (97.5%) healthy individuals of the specified age and gender group (IOM 2011). The UL is defined as the maximum daily intake unlikely to cause any adverse health effects (IOM 2011).

Similar strategy in the development of reference intakes has been used by EFSA (EFSA 2010) where an Adequate Intake (AI) was set at 15 mcg/day (EFSA 2018). The AI is usually set when evidence is insufficient to develop an RDA and is set at a level assumed to ensure nutritional adequacy for a population (IOM 2011). Hence, the AI by EFSA is comparable and equal to the RDA set by the IoM.

1.6 Gaps in knowledge

Based on the above several gaps in knowledge remain. Firstly, there is need to identify the prevalence of low serum 25(OH)D concentration in a representative sample of the Greek adult population. In addition, there is need to explore probable correlations between serum 25(OH)D concentration and several factors that may influence it.

Some of these factors are dietary intake from food and supplements, sunlight exposure, skin colour, season of the year when data was collected, body mass index, gender, age, parathyroid hormone concentration, other dietary factors and sunscreen use.

In addition, there is need to identify the level of intake from food and supplements in the Greek population as well as the main food contributors of vitamin D in the Greek diet. From all the factors named above those that are modifiable are food and supplement intake as well as sunlight exposure, with the latter also influencing the risk of melanoma.

Hence, an additional aim of this study was to examine the theoretical effect of food fortification on improving vitamin D intake from food, and more specifically in comparison to the EAR and RDA.

All the above have been the scope of this PhD thesis and a detailed methodology was followed in order to explore all potential factors that may influence the results.

2. Scope of PhD thesis

The scope of the current PhD thesis was to measure the prevalence of low serum vitamin D intakes of Greek adults, in a representative sample of the Greek population, as well as the factors that may influence its levels.

An additional scope of this thesis was to estimate vitamin D intake from food and supplements, identify the main food sources of vitamin D intake in Greek adults and show how an example of food fortification might help increase dietary intake and improve serum 25(OH)D status.

2.1 Specific aims by paper in support to PhD thesis

1st paper aims: To estimate the prevalence of low serum vitamin D levels in a representative sample of Greek adults as well as identify the factors that could possibly influence serum levels like for example sun exposure, nutritional intake, body mass index and intake from supplements.

2nd paper aims: To estimate vitamin D intake from food as well as the main foods that contribute to vitamin D food intake in the adult Greek population. In addition, to compare intake levels with the EAR and the RDA as well as to describe the measurable benefits (in comparison with the mentioned reference values) of an example of food fortification towards increasing dietary intake at population level.

3rd paper aims: To report in detail the methodology used to develop all questionnaires and procedures that were developed in the Hellenic Nutrition and Health Study. In addition, to report some preliminary findings of the study and population's descriptive characteristics.

3. Presentation of papers

3.1 Presentation of paper I

Dimakopoulos, I., Magriplis E., Mitsopoulou, AV.., Karageorgou, D., Bakogianni, I., Micha, R., Michas, G., Chourdakis, M., Ntouroupi, T., Tsaniklidou, S.M., Argyri, N., Panagiotakos, D.B., Zampelas, A., (2019) Association of serum Vitamin D status with dietary intake and sun exposure in adults

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Association of serum Vitamin D status with dietary intake and sun exposure in adults

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Shortened title: Vitamin D levels of the Greek population

Abbreviations:

25(OH)D: 25-hydroxyvitamin-D, AMPM: Automated Multiple Pass Method, ARCHES: Arkansas BMI: Body Mass Index, Cardiovascular Health Examination Survey, BRFSS: Behavioural Risk Factor Surveillance System, CAPI: Computer Assisted Personal Interview, EFSA: European Food Safety Authority, HDPA: Hellenic Data Protection Authority, HNNHS: Hellenic National Nutrition & Health Study, IoM: Institute of Medicine, iPAQ: International Physical Activity Questionnaire, ML: milliliter, NDNS: National Diet & Nutrition Survey, NG: nanograms, NHANES: National Health & Nutrition Examination Survey, NIAAA: National Institute on Alcohol Abuse and Alcoholism, OR: Odds ratio, UV: ultraviolet.

Abstract

Background & aims: Serum 25(OH)D deficiency is becoming an epidemic. The aim was to assess vitamin D status of the adult Greek population in relation to intake, sun exposure and other factors, using data from the Hellenic National Nutrition and Health Survey (HNNHS).

Methods: Data from 1084 adult participants (37,8% males) were analyzed. Vitamin D intake was assessed using 24-hour recalls. Serum 25(OH)D concentration was evaluated and related to anthropometric measurements and other covariates including supplements used, by sex. Variables significantly associated with 25(OH)D <20ng/ml were assessed using simple and multiple logistic regression.

Results: Median vitamin D intake from food was 1.23 mcg/day (0.60, 2.44), with 9.1% consuming supplements. Median serum 25(OH)D was 16.72 ng/ml, with no sex differences (P=0.923). The odds of having 25(OH)D <20 ng/ml significantly decreased with being very active (OR 0.55, 95% CI 0.35, 0.98), increasing length of sun exposure [1-3 hours/day (OR 0.59, 95% CI 0.44, 0.80), >3 hours/day (OR 0.36, 95% CI 0.24, 0.55)], and skin color [light to medium skin (OR 0.47, 95% CI 0.24, 0.91), fairly dark skin colour (OR 0.34, 95% CI 0.17, 0.67) and dark or very dark skin colour (OR 0.34, 95% CI 0.15, 0.75)], compared to respective baseline levels. The odds significantly increased with obesity (OR 1.95, 95% CI 1.24, 3.08), and spring season of blood sample collection (OR 1.75, 95% CI 1.22, 2.50).

Conclusions: Vitamin D deficiency is highly prevalent in Greek adults. Relevant public health policies are highly recommended, which could include vitamin D fortification. and suggestion for increased but safe sun exposure.

Keywords: Vitamin D, 25-hydrovitamin D, diet, public health, nutrition survey, Greece.

Introduction

In recent years vitamin D deficiency has become the most common nutritional deficiency in the world with more than 1 billion people having inadequate levels of serum vitamin D concentration [1, 2]. In populations living in low latitude where UV rays are assumed adequate for vitamin D skin synthesis or in industrialized nations where some foods are fortified with vitamin D, deficiency still persists [3] across all age groups and subgroups [4-6]. These levels are observed in the national [4, 7-10], European [4-6, 11] and International level [3, 5]. Apart from low serum concentrations, published data have also reported high prevalence of low vitamin D intake even at levels that are far below the recommended reference intake, as per the Institute of Medicine (IoM) [6, 12].

Vitamin D has many physiological roles, including being a facilitator for calcium absorption, maintaining bone health and regulation of cell growth. Recently, its role to other health conditions, such as cardiovascular disease and diabetes have also been investigated [13], emphasizing on the importance of a high prevalence of vitamin D deficiency at the population level.

Vitamin D is primarily produced endogenously following skin exposure to ultraviolet (UV) and its synthesis is influenced by a plethora of factors, such as geographical location, use of sunscreen and type of clothing, time spent outdoors and time of the day, age, skin pigmentation as well as environmental pollution [14].

In parallel, dietary intake is also important and significantly contributes to maintaining serum 25-hydroxyvitamin D (25(OH)D) concentration above 20 ng/ml. Vitamin D is found in a few foods, mainly in the form of cholecalciferol (vitamin D_3) which is highly

bioavailable. It can also be found as ergocalciferol (vitamin D_2) from plant sources. Vitamin D supplementation from various forms can also be added to the intake and should therefore be considered when evaluating vitamin D status.

Given the significant prevalence of vitamin D deficiency worldwide, in all age groups, irrespectively of sunlight prevalence, as well as the number of factors that influence vitamin D status, studies addressing vitamin D population status are warranted. In Greece, to our best knowledge, a study on the population prevalence of vitamin D deficiency in adults, using a national representative sample, has not been performed.

The aim of this study is therefore to assess vitamin D status of the adult Greek population, using serum 25(OH)D concentration, in relation to total vitamin D intake (from diet and supplements) and sun exposure.

Materials & methods

Study design & Sample

Data from the Hellenic National Nutrition and Health Survey (HNNHS), was used in this study, whereas collection took place from September 2013 to May 2015. Details of HNNHS's methods have been reported elsewhere [15]. Eligible for participation were males and females ≥6 months old that reside in Greece who were (i) not pregnant/ breastfeeding, (ii) not institutionalized (e.g. military service, hospital, other institution) and selection was performed using a random stratified design based on the 2011 census data.

A total of 3836 adults (≥18 years, 40.8% males) were initially enrolled in the HNNHS, for whom anthropometric and medical history was assessed by trained interviewers and according to the International Classification of Diseases (ICD-10) codes. All participants were also invited to provide blood samples for biochemical – hematological evaluation and anthropometric measurements. Of them, 1197 (26.2% of total population; 28.7% of adult population) agreed; no age distribution differences were found between the total population and those who provided blood sample (p= 0.677). A total sample of 1084 adults (23.7% participation; 37.8% males) with available data on serum 25(OH)D concentration were included.

Data collection

In HNNHS data collection included (i) an initial household Computer Assisted Personal Interview (CAPI) consisting of multiple questionnaires and a 24hr recall, (ii) additional validated questionnaires, (iii) a second 24hr recall via telephone 8-20 days after the first interview, selecting a different non-consecutive day, as specified by HNNHS study-protocol and (iv) a visit to a mobile unit in order to perform the medical, biochemical and anthropometric examinations/ measurements. HNNHS fieldwork protocol. Interviews were performed throughout all seasons of the year, to account for season vitamin D status and decrease error in results.

The list of questionnaires used, relevant to this study, included information on demographic, psychosomatic health, vitamin and subscribed drug intake. These can be found in detail in the methodology HNNHS paper [15]. All questionnaires included in this study

were adapted from previously validated and used by other large National Health Surveys [16].

Blood samples in the morning, between 8:00 and 10:00 am, upon having fasted for at least 10 hours. To assure compliance all individuals were asked if they had fasted and when their last meal was. These were collected using BD vacutainer® safety blood collection set 21G and holder 21G and Greiner vacuette K_3EDTA. After centrifugation with the Nuve® NF400 centrifuge samples were stored in cryovials in -80^o C. Plasma 25(OH)D concentration was measured on a COBAS e411 immunoassay analyzer (place) using the Elecsys Vitamin D total assay (Roche Diagnostics, place) [17].

Dietary intake was assessed using a detailed interviewer-administered 24-hour dietary recall using the Automated Multiple-Pass Method (84.5% completed both 24-hour recalls) [18]. The FoodEx2 food classification and description system developed by the European Food Safety Authority (EFSA) was used and recommendations for the harmonization of data across European Union countries were followed [19]. Food quantification was performed with the use of validated food atlases as the primary option along with standardized household measures. The Nutrition Data System for Research (NDSR) developed by the University of Minnesota was used for nutrient analysis. From the initial n=1964 24-hour recalls there were 62 recalls with extreme intakes (<600 or >6000 kcal per day) which were excluded from the analysis (67.7% females, 32.3% males).

A drug and supplement questionnaire was developed using validated questionnaires from other studies, mainly from the United States [15]. The questionnaire was applied twice, during the initial interview as well as during the mobile unit visit. From this data, vitamin D

supplement intake was categorized as follows: “no supplement use” or “supplement use”. Although initially thought appropriate to have three categories (no supplement use, <10 μg/day and ≥10 μg/day), as those receiving ≥10 μg/day are supposed to intentionally seek vitamin D supplementation [20] rather than obtaining it as part of a multivitamin supplement, the number of observations in the ≥10 μg/day category was too small (males=2, females=45). Although the ideal method to assess sun exposure is dosimetry [21] in HNNHS, due to limited funding, sun exposure was assessed using a questionnaire; statistically significant correlations have been reported between the two methods [22]. The questionnaire’s aim is to evaluate the amount of sun exposure as well as the parameters that could influence vitamin D skin synthesis to rank individuals accordingly. It included questions relating to sun exposure for each of the four seasons (weekends and weekdays), exposure for the last 30 days, sunscreen use and skin colour.

Physical activity was measured using the International Physical Activity Questionnaire (IPAQ) short form for those ≥18 years - <65 years and a modified version for those ≥65 years old. Alcohol was assessed using questionnaire from NHANES, BRFSS, Arkansas Cardiovascular Health Examination Survey (ARCHES) and Recommended Alcohol Questions by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) were used [15]. Volunteers were classified as “alcohol” or “non-alcohol” consumers, based on their intake over the past 30 days.

Anthropometric measurements were performed according to the NHANES study protocol [23] with the use of Seca 213 portable stadiometer, and InBody 270 Biospace analyser was used to measure body weight following the required preparation. Height was

measured by asking the volunteer to (i) remove any ornaments, jewelry, etc. from the top of the head, (ii) stand up straight against the backboard with the body weight evenly distributed from feet flat on the platform, (iii) stand with the heels together and toes apart at approximately a 60^{o} angle and (iv) field researcher made sure that the back of the head, shoulder blades, buttocks and heels made contact with the backboard. Weight was measured by asking the volunteer to (i) remove heavy clothing and objects as well as shoes and (ii) to stand in the center of the scale platform facing the recorder with hands at the sides and looking straight ahead. Each of these individuals visited one of the 5 mobile units where medical and anthropometric measurements were completed.

Statistical analyses

Normality of continuous data was checked using P-P and kernel density plots. Categorical variables were expressed as frequencies and percentages (N %), whereas continuous variables were expressed as mean with standard deviation (SD) if normal and median if skewed and interquartile range (25%, 75%). Differences in categorical variables were derived using chi square test and Kruskal-Wallis test for sex differences between continuous variables, since continuous variables used in this analysis were not normally distributed.

The 25(OH)D cut-off for logistic regression chosen was 20 ng/ml as values <20 ng/ml reflect inadequate (12 to <20 ng/ml) or deficient (<12 ng/ml) levels for bone and overall health in healthy individuals [24].

Univariate logistic regression analysis for each potential factor associated with 25(OH)D, based on a-priori knowledge was assessed, in total and by sex. Variables that were

found significantly associated with the odds of serum 25(OH)D levels <20 ng/ml were included in the multivariate regression, as well as a-priory known factors. The Likelihood Ratio test (LR test) was used to check the significance of the models with significance level at 0.05.

All analyses were performed in STATA statistical software (STATA 13.1, Stata Corp LP, Texas, USA) with a significance level set at P<0.05.

Ethical statement

The study was approved by the Ethics Committee of the Department of Food Science and Human Nutrition of the Agricultural University of Athens. It was also approved by Hellenic Data Protection Authority (HDPA). All members of the staff signed confidentiality agreements. All volunteers were asked to sign a detailed consent form.

Results

Demographic and general characteristics of the population

The baseline characteristics of this subgroup of the HNNHS population are presented in **Table** 1 in total as well as by sex. According to the Shapiro-Wilk test for normality continuous variables did not follow a normal distribution. Statistically significant sex differences were found for dietary vitamin D intake, Body Mass Index (BMI) category, activity level, vitamin D supplement use, sun exposure and skin colour (P for all <0.05).

The median (interquartile range) age of the total sample was 36 years (27, 52), 35 (28, 48) for males and 36.5 (26, 54) for females. With regards to BMI category of the total population, 57.8% normal weight or were underweight (4.9% underweight), 28.6% overweight and 13.6% obese. Furthermore, males' prevalence of overweight (38% vs.

22.8%) and obesity (16.1% vs. 12.0%) were significantly higher compared to that of female participants (P<0.001) (**Table** 1).

Serum 25(OH)D concentration, dietary intake and skin synthesis

Median (interquartile range) serum 25(OH)D concentration for the total population was 16.7 ng/ml (9.8, 23.6), 16.67 ng/ml (11.1, 23.46) for males and 16.74 ng/ml (9.72, 23.64) for females. According to the IoM cut-off levels for vitamin D deficiency, 28.8% of the total sample was found deficient (<30 ng/ml), 36.0% insufficient (<20 ng/ml), 35.1% sufficient (>30 ng/ml and <50 ng/ml) and only 0.1% being in the high (≥50 ng/ml) category. There were no significant differences in serum 25(OH)D concentration between males and females. In addition, there were no significant differences in serum 25(OH)D concentration in different age groups (≥18 years, data not shown). However, there were significant differences in serum 25(OH)D concentration for the total sample (P<0.01) as well as for males (P=0.003) and females (P=0.007) per month of blood sample collection (**Figure 1**) with higher prevalence of 25(OH)D levels <20 ng/ml during March (end of Winter, beginning of Spring season). In addition, there were significant differences in serum 25(OH)D concentration for the total sample (P=0.03) as well as for males (P=0.002) and females (P=0.03) per season of blood sample collection (data not shown) with higher prevalence of 25(OH)D concentration <20 ng/ml during Spring, as per total sample.

Median (interquartile range) vitamin D intake from food for the total population was 1.23 μg/day (0.60, 2.44), 1.45 μg/day (0.66, 3.07) for males and 1.16 μg/day (0.56, 2.05) for females. Regarding vitamin D supplement use, 9.1% reported taking a supplement containing vitamin D (Table 1). Among those, 4.8% reported taking <10 μg/day vitamin D,

mostly from multivitamins, and 4.3% reported taking ≥10 μg/day. There was statistically significant difference in vitamin D supplement intake between sexes (P<0.001) as 94.1% of males and 88.9% of females reported not taking a supplement containing vitamin D. Additionally, a low 0.5% of males reported taking a supplement containing ≥10 μg /day compared to the 6.7% of females.

Most of the total sample reported sun exposure for the last 30 days (before the blood sample collection) of 0-1 h/day (49.2%) and 1-3 h/d (36.7%) compared to 13.0% that reported >3 h/d. On the other hand, 45.2% and 36.9% of males reported 0-1 h/d and 1-3 h/d of sun exposure respectively compared to 51.7% and 36.7% of females. In addition, 17.9% of males and 11.7% of females reported sun exposure >3 h/d. There was statistically significant difference in sun exposure between the two sexes (P=0.020).

There were no statistically significant differences in season of blood sample collection between the two sexes (P=0.442). For 28.6% of the total sample blood collection was performed during summer, 11.6% during fall, 29.4% during winter and 30.4% during spring.

In terms of skin colour 60.2% of the total sample had light colour/ medium light as (56.4% of total males and 62.5% of total females), 25.6% had dark skin (31.2% of males and 22.2% of females), 7.4% had dark or very dark skin colour, and 6.8% very light skin colour (Table 1). There was statistically significant difference in skin colour between males and females (P<0.001).

Odds of having 25(OH)D concentration <20 ng/ml

As can be seen in **Table** 2 the odds of having 25(OH)D levels <20 ng/ml were lower for the total sample with high activity, with supplement use, increased hours of sun exposure and darker skin colour. On the other hand, spring season of blood sample collection was associated with increased odds of having 25(OH)D concentration <20 ng/ml as was being obese. In more detail, very active individuals had 41% reduced odds (OR 0.59, 95% CI 0.35, 0.98, P=0.044). Individuals using vitamin D supplements were 46% less likely of having insufficient serum vitamin D concentration (OR 0.54, 95% CI 0.34, 0.86, P=0.010). One to three hours of sun exposure per day reduces the odds of 25(OH)D <20 ng/ml by 41% (OR 0.59, 95% CI 0.44, 0.80, P=0.001), >3 hours/day by 64% (OR 0.37, 95% CI 0.24, 0.55, P<0.001) as compared with 0-1 hours/day of sun exposure dy. Compared to very light skin coloured individuals, those with light to medium light colour had 53% lower odds of 25(OH)D concentration <20 ng/ml (OR 0.47, 95% CI 0.24, 0.91, P=0.025), those with fairly dark 66% reduced odds (OR 0.34, 95% CI 0.17, 0.67, P=0.002) as those with dark or very dark skin (OR 0.34, 95% CI 0.15, 0.75, P=0.007). Furthermore, blood samples collected during spring compared to those collected during summer were related with 87.5% increased odds of 25(OH)D concentration <20 ng/ml (OR 1.73, 95% CI 1.22, 2.48, P=0.002). This model was adjusted for age. The likelihood ratio test for the whole model was 88.85 with a p value <0.001.

For males (**Table** 2) smoking status was associated with increased odds of 25(OH)D concentration <20 ng/ml (OR 1.74, 95% CI 1.04, 2.90, P=0.034) as was spring season of blood sample collection (OR 2.91, 95% CI 1.52, 5.53, P=0.001). On the other hand, compared to 0-1 hours per day of sun exposure individuals with 1-3 hours per day had 44%

reduced odds (OR 0.56, 95% CI 0.32, 0.95, P=0.033), >3 hours per day 80% reduced odds (OR 0.21, 95% CI 0.11, 0.42, P<0.001). The model was adjusted for age, BMI category, activity level, vitamin D supplement use and skin colour. The likelihood ratio test for the model was 68.09 with P<0.001.

For females (**Table** 2) being obese was associated with increased odds of 25(OH)D concentration <20 ng/ ml (OR 2.22, 95% CI 1.19, 4.16, P=0.012). In contrary, supplement use compared to no supplement use was associated with 51% reduced odds (OR 0.49, 95% CI 0.29, 0.85, P=0.012) as was sun exposure 1-3 hours/day (OR 0.61, 95% CI 0.42, 0.89, P=0.012), >3 hours/day (OR 0.50, 95% CI 0.29, 0.89, P=0.019) compared to 0-1 hours/day of sun exposure. Furthermore, light to medium skin colour (OR 0.44, 95% CI 0.21, 0.89, P=0.023), fairly dark skin colour (OR 0.33, 95% CI 0.15, 0.70, P=0.004) and dark to very dark skin colour (OR 0.28, 95% CI 0.11, 0.75, P=0.011) were associated with reduced odds of 25(OH)D concentration <20 ng/ ml compared to individuals with very light skin colour. The model was adjusted for age, season of blood sample collection and PTH levels. The likelihood ratio test for the whole model was 55.23 with P<0.001.

Several demographic variables (marital status, health insurance and income) as well as other variables, mentioned in the literature, such as alcohol intake, serum cholesterol, serum magnesium, serum creatinine, serum lead (Pb) levels, dietary factors (e.g. Ca, Vitamin K), skeletal muscle mass and sunscreen use were not significantly associated with 25(OH)D levels (data not shown). Fiber (OR 1.00, 95% CI 1.00, 1.01, P=0.046) and magnesium intake (OR 1.00, 95% CI 1.00, 1.00, P=0.035) were significantly associated with the odds of having

serum 25(OH)D <20 ng/ ml in males and in crude analyses but were excluded as there was no clinical significance (OR=1).

Discussion

To our knowledge this is the first study that aims to identify factors associated with 25(OH)D concentration <20 ng/ml in Greek adults. HNNHS' measurements revealed that 64,8% of adults had insufficient serum 25(OH)D concentration and 28.8% were deficient. Many factors associated with vitamin D status are modifiable, including dietary intake, sunlight exposure and supplement use.

Vitamin D deficiency and insufficiency have been of concern recently with a worldwide review reporting that 37.3% of studies found mean values of 25(OH)D concentration <20 ng/ml with the subtotal for males being 22.3 ng/ml and for females 21.3 ng/ml [5]. In accordance to our study, high prevalence of deficiency has been reported in previous studies [5-9, 11, 25] with a review reporting 35-75% of adults from Mediterranean countries having serum 25(OH)D concentration <20ng/ml (54% of Greek adults) [4]. These studies have taken place in more than 40 countries worldwide many of which in Europe [5, 6]. Included studies were cross-sectional or cohort where vitamin D status was measured, whereas studies where status was estimated, rather than measured, were excluded. Most studies included a random sample.

In addition, other reports from Greece [7, 8], Europe [25] and non-European counties [9, 26-28] showed that the highest prevalence of serum 25(OH)D concentration <20 ng/ml was during March. In our study (**Figure** 1) no blood samples were collected during August and September compared to others [25] which reported lowest prevalence during July-

September. Lowest prevalence was observed in October after which it increases and peaks in March. This is explained by higher sun exposure during summer and spring where 24% & 13% have sun exposure >3 h/d compared to 7% during fall and winter.

Vitamin D food intake in our sample was low, a finding that seems reasonable as few foods contain vitamin D and there is no fortification law in Greece; a strategy that is reported to have a positive effect in other regions [29, 30]. Our results are similar or lower compared to levels reported elsewhere [6, 31, 32]. In the United States, were milk and cereals are fortified, intakes are higher (3.9-7.0 μg/day) [33]. Higher intakes are also observed in European countries except Spain where there is also no fortification law and intake is 1.6-1.7 μg/day [6]. Although, dietary assessment methodologies vary between European countries, a notable discrepancy between intakes and recommendations exists [6].

Although, 0-1 or 1-3 hours/day might seem adequate and Greece has adequate UVB availability all year round [34] we have to consider that data is self-reported, that the majority of the skin might be covered by clothing, especially during the winter months, and that little might be exposed to the sun rays. Also, participants might have also included time exposed in the sun when behind a glass (e.g. inside a building or a car) that acts as a barrier of UVB rays submission [35]. Furthermore, for cultural or health reasons people might be avoiding sun exposure. Similar trends have been reported in sunny countries in the past [1, 36, 37].

Only approximately 6% of males and 11% of females reported consuming supplements, and <1% of males & 6.7% of females receiving ≥10 μg/ day (data not shown). The significant sex difference can be explained by the higher prevalence of osteoporosis in women compared to men as reported in previous findings (8.3% vs. 0.8% in adults) [15].

Considering that intake and synthesis is low it is reasonable to observe serum 25(OH)D concentration being low. Based on the IoM cut-offs [24], 28.8% is characterized deficient, 35.9% has insufficient concentration, 35.1% sufficient concentration and 0.1% high concentration. These are comparable with studies from Greece [7, 8], Europe [11] and the rest of the world [3, 38]. There were no significant differences in serum 25(OH)D concentration observed between males and females as in other reports [39].

In our study, factors associated with lower odds of serum 25(OH)D concentration <20 ng/ml were being very active, supplement intake, increased sun exposure and darker skin colour. Spring season of blood sample collection was associated with higher odds of deficiency. Although, darker skin is associated with lower odds, which is contradictory to other findings, this cannot be explained by longer sun exposure as it is the same across all skin colour categories (Pearson's chi-square test P=0.064). This controversy might be because almost all subjects are of Caucasian origin in contrast with other countries where a higher proportion is of non-Caucasian origin who differ physiologically and culturally [14]. Only 7% of the sample has dark or very dark skin compared to 60% that has light or medium light and therefore associations could be influenced by sample size.

Other studies reported a positive effect of physical activity on 25(OH)D concentration adequacy which is hypothesized to be due to increased sun exposure [14] however there seems to be an effect irrespective of sun exposure as the same has been observed for indoor activity [40]. The main factors that influenced the odds of having 25(OH)D levels <20ng/ml were sun exposure and season of blood collection. With increasing sun exposure, the odds of vitamin D deficiency were lower. Spring season of

blood sample collection was associated with higher odds of vitamin D (25(OH)D) deficiency/insufficiency, probably because of the low levels of sun exposure during preceding months. As previously suggested [41], this seasonal difference in 25(OH)D concentrations could possibly be improved with the consumption of fortified products. Supplement use might not have been significantly associated with lower odds of deficiency due to the small sample size of males that were receiving supplements with content ≥10 μg/day (n=2). This can be explained by the lower prevalence of osteoporosis in males and/or lower degree of actively checking for osteoporosis in comparison to females, and hence reduced supplemental intake. Smoking as per other reports was associated with higher odds of serum 25(OH)D concentration <20 ng/ml and it is hypothesized that smoking impairs conversion of 25(OH)D to 1,25(OH)D [42].

In females, obesity was associated with higher odds of 25(OH)D concentration <20 ng/ml. The lipophilic nature of adipose tissue is hypothesized to act as sequester of vitamin D, rather than storage, and studies have reported increases in 25(OH)D concentration with weight reduction in obese individuals [14]. The exact mechanisms remain unclear [24]. Supplement use and sun exposure were associated with lower odds as was darker skin. In accordance with other studies, our biochemical data also show a negative correlation between serum PTH concentration and 25(OH)D concentration [43-45] but it was not significant in the model. Supplement use was also significant, in contrast with males, which could be explained by higher supplemental intake in females. Season of blood sample collection was not significantly correlated with 25(OH)D concentration however a seasonal difference in supplement intake was observed. Women taking ≥10 μg/day via supplements

were more likely to be taking it during Spring (43.2%) and Winter (25%) than during the Summer (18.2%) and Fall (13.6%) (data not shown). This could be the result of their perception that during Summer sunlight exposure is adequate for synthesis.

In both sexes dietary intake was not significantly associated with the odds of having 25(OH)D concentration <20 ng/ml probably because 94.6% had very low intakes. In another recent study, it was showed that in European participants with higher intakes of vitamin D from food had higher 25(OH)D concentrations [46].

Due to the nature of the study, some limitations should be considered. Firstly, no causal relationships can be drawn, since it is a cross-sectional study. Most participants lived in urban areas and therefore we were unable to explore differences between urban vs. semi-urban regions (0.37% from non-urban regions). However, in Greece, the vast majority of the population reside in metropolitan areas. In addition, we did not explore ethnic differences as <1% of the sample were of non-Caucasian race.

In conclusion, serum 25(OH)D deficiency is high in Greek adults of both sexes. Given vitamin D's possible link to several diseases, relevant actions and policies to correct deficiency and reduce prevalence, need to be taken. Food fortification and vitamin D supplements are two options towards that goal. Longer but safe sun exposure could offer an additional effective and low-cost strategy for 25(OH)D deficiency prevention.

Statement of authorship

AZ conceptualized, designed and was the Principal Investigator of the HNNHS study. AZ and RM coordinated the design of the data collection instruments, coordinated

and supervised data collection. GM supervised medical data collection. ID, DK, AVM and IB were involved in every step of the study and made substantial contributions to the design and methodology of data collection as well as the acquisition of data and training of field workers. TN coordinated mobile unit data collection. SMT and KA contributed to the mobile unit data collection and analysis. DBP coordinated sample collection methodology. ID conceptualized this study, carried out all statistical analyses and drafted the manuscript. EM supervised the preparation of the database and carried out the statistical analyses and together with MC revised the manuscript. GD, CG, EF, EMT, ET, TES, AV, ES, MC, AK, GK, SZ and AP contributed to parts of methodology. All the authors approved the final manuscript as submitted.

Contributors: EF, ET, TS, AV, ES, AT, GK, SZ, AP contributed to the writing of the protocols and the data collection on the field. All contributors approved the final manuscript as submitted.

Advisory Committee: GC, GD, GD, IM and ER acted as external advisory committee. All the Advisory Committee members approved the final manuscript as submitted.

Conflict of interest

RM reports grants from NIH/NHLBI, grants from Unilever R&D, grants from Bill and Melinda Gates Foundation, personal fees from World Bank and personal fees from Bunge.

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Table 1: Descriptive characteristics of study participants (Median values and interquartile ranges (25%, 75%), numbers and percentages)

	Total		**Males**		**Females**		**P value**[a]
	n=1084		n=410		n=674		
	median	Range	median	Range	median	Range	
Age (years)	36	27, 52	35	28, 48	36.5	26, 54	0.972
Dietary vitamin D intake (μg/d)[b]	1.23	0.60, 2.44	1.45	0.66, 3.07	1.16	0.56, 2.05	<0.001***
Serum 25(OH)D levels (ng/ml)	16.72	9.8, 23.6	16.67	11.1, 23.46	16.74	9.72, 23.6	0.923
Serum PTH levels (pg/ml)	38.04	28.7, 49.8	38.06	28.9, 51.3	38.04	28.0, 49.7	0.987
	n	%	n	%	n	%	
BMI category							<0.001***
Normal weight[c]	627	57.8	188	45.7	439	65.1	
Overweight	310	28.6	156	38.0	154	22.8	
Obese	147	13.6	66	16.1	81	12.0	
Education level							0.068
Primary school	50	4.6	12	2.9	38	5.6	
Secondary school	374	34.5	157	38.3	217	32.2	
Professional/Private higher education	98	9.0	31	7.6	67	9.9	
University degree	402	37.1	153	37.3	249	36.9	
MSc or PhD	160	14.8	57	13.9	103	15.3	
Activity level							0.048*
Sedentary	120	11.1	36	8.8	84	12.6	

Little active	197	18.3	80	19.5	117	17.5	
Moderately active	436	40.4	155	37.8	281	42.0	
Very active	326	30.2	139	33.9	187	27.9	
Smoking status (last 30 days)							0.471
Not smoking	700	64.7	260	63.4	440	65.6	
Smoking	381	35.2	150	36.6	231	34.4	
25(OH)D status[d]							0.886
<12 ng/ml (Deficient)	312	28.8	118	28.8	194	28.8	
12-19.9 ng/ml (Insufficient)	390	36.0	149	36.3	241	35.8	
20-49.9 ng/ml (Sufficient)	381	35.1	143	34.9	238	35.3	
≥50 ng/ml (High)	1	0.1	0	0.0	1	0.1	
Vitamin D supplement use							<0.001***
No supplement use	985	90.9	386	94.1	599	88.9	
Supplement use	99	9.1	24	5.9	75	11.1	
Sun exposure (last 30 days)							0.020*
0-1 h/d	520	49.2	179	45.2	341	51.7	
1-3 h/d	388	36.7	146	36.9	242	36.7	
>3 h/d	148	13.0	71	17.9	77	11.7	
Skin colour							<0.001***
Very light	72	6.8	11	2.8	61	9.2	
Light colour/Medium light	638	60.2	224	56.4	414	62.5	
Fairly dark	271	25.6	124	31.2	147	22.2	
Dark or very dark	78	7.4	38	9.6	40	6.0	

Season of blood sample collection							0.442
Summer	309	28.6	116	28.4	193	28.7	
Fall	125	11.6	51	12.5	74	11.0	
Winter	318	29.4	128	31.3	190	28.3	
Spring	329	30.4	114	27.9	215	32.0	

µg/d, micrograms/day. 25(OH)D, 25-hydroxyvitamin D. ng/ml, nanograms per milliliter. PTH, Parathyroid hormone. pg/ml, picogram per milliliter. BMI, Body Mass Index. kg/m^2, kilograms per meters squared. €, euros. h/d, hours/day.

[a]Categorical variables depicted as frequencies and percentages, continuous variables depicted as medians and 95% confidence intervals (because they are not normally distributed). Normality was tested using the Shapiro-Wilk test. P values indicate sex differences. Kruskal-Wallis test was used in the case of continuous variables and Peason's chi square in the case of categorical variables. [b]Excluding 24-hour recalls with extreme energy intake (<600 or >6000 kcal/ day. [c]Due to the small sample size of underweight individuals (n=53) they were merged with normal weight individuals.

[d]Based on Institute's of Medicine cut-off points. Values are rounded to the first decimal (except for p values).

*P<0.5, **P<0.01, ***P<0.001.

Table 2: Regression analyses examining the associations of 25(OH)D <20 ng/ml (deficiency & insufficiency based on IoM cut-off points) in the total sample and by sex.

Variables	**Total** 25(OH)D levels <20 ng/ml						**Males** 25(OH)D levels <20 ng/ml						**Females** 25(OH)D levels <20 ng/ml					
	Crude			Model[a]			Crude			Model[b]			Crude			Model[c]		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Age (years)	0.99	0.98, 1.00	0.213	0.98	0.97, 0.99	0.010*	0.97	0.96, 0.99	0.004**	0.96	0.95, 0.98	<0.001***	1.00	0.99, 1.01	0.593	0.99	0.98, 1.00	0.632
BMI category																		
Normal weight	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-
Overweight	1.07	0.80, 1.42	0.617	1.21	0.88, 1.66	0.235	0.96	0.61, 1.49	0.863	1.21	0.71, 2.04	0.468	1.14	0.78, 1.68	0.480	1.22	0.78, 1.89	0.369
Obese	1.84	1.22, 2.78	0.003**	1.95	1.24, 3.08	0.044*	1.36	0.74, 2.52	0.313	1.66	0.79, 3.46	0.173	2.33	1.32, 4.12	0.003**	2.22	1.19, 4.16	0.012*
Activity level																		
Sedentary	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-
Little active	0.81	0.48, 1.35	0.431	0.85	0.49, 1.47	0.566	1.01	0.42, 2.44	0.975	1.03	0.38, 2.76	0.951	0.72	0.38, 1.35	0.308	0.74	0.38, 1.47	0.403
Moderately active	0.60	0.38, 0.95	0.031*	0.66	0.40, 1.08	0.100	0.74	0.33, 1.64	0.462	0.74	0.30, 1.85	0.529	0.55	0.31, 0.95	0.033*	0.59	0.32, 1.09	0.094

Very active	0.51	0.32, 0.82	0.006**	0.59	0.35, 0.98	0.044*	0.53	0.24, 5.39	0.129	0.55	0.21, 1.39	0.209	0.52	0.29, 0.92	0.026*	0.57	0.30, 1.08	0.089
Education level																		
Primary school	Ref.	-	-	-	-	-	Ref.	-	-	-	-	-	Ref.	-	-	-	-	-
Secondary school	0.95	0.51, 1.78	0.886	-	-	-	2.99	0.90, 9.90	0.072	-	-	-	0.59	0.27, 1.29	0.195	-	-	-
Professional/Private higher education	0.84	0.41, 1.73	0.654	-	-	-	1.93	0.50, 7.48	0.337	-	-	-	0.63	0.26, 1.53	0.319	-	-	-
University degree	0.98	0.52, 1.83	0.963	-	-	-	2.88	0.87, 9.54	0.083	-	-	-	0.65	0.30, 1.40	0.277	-	-	-
MSc or PhD	0.88	0.45, 1.71	0.712	-	-	-	2.06	0.58, 7.32	0.259	-	-	-	0.66	0.29, 1.52	0.334	-	-	-
Vitamin D intake from food (µg/day)	0.97	0.93, 1.00	0.053	-	-	-	0.96	0.92, 1.01	0.101	-	-	-	0.97	0.92, 1.02	0.274	-	-	-
Vitamin D supplement use																		
No supplement use	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-
Supplement use	0.54	0.35, 0.82	0.004**	0.54	0.34, 0.86	0.010*	0.61	0.26, 1.40	0.250	0.56	0.22, 1.44	0.233	0.52	0.32, 0.84	0.008**	0.49	0.29, 0.85	0.012*

Sun exposure (last 30 days)																		
0-1 h/d	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-
1-3 h/d	0.58	0.44, 0.77	<0.001***	0.59	0.44, 0.80	0.001**	0.52	0.32, 0.84	0.008**	0.56	0.32, 0.95	0.033*	0.60	0.43, 0.86	0.005**	0.61	0.42, 0.89	0.012*
>3 h/d	0.37	0.26, 0.55	<0.001***	0.36	0.24, 0.55	<0.001***	0.25	0.14, 0.46	<0.001***	0.21	0.11, 0.42	<0.001***	0.49	0.30, 0.82	0.007**	0.50	0.29, 0.89	0.019*
Skin colour																		
Very light	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-
Light colour/Medium light	0.48	0.26, 0.88	0.019*	0.47	0.24, 0.91	0.025*	0.84	0.21, 3.27	0.804	0.55	0.10, 3.09	0.506	0.41	0.21, 0.82	0.012*	0.44	0.21, 0.89	0.023*
Fairly dark	0.33	0.17, 0.62	0.001**	0.34	0.17, 0.67	0.002**	0.53	0.13, 2.12	0.375	0.32	0.05, 1.81	0.199	0.29	0.14, 0.60	0.001**	0.33	0.15, 0.70	0.004**
Dark or very dark	0.36	0.17, 7.66	0.008**	0.34	0.15, 0.75	0.007**	0.57	0.13, 2.52	0.463	0.33	0.05, 2.07	0.240	0.33	0.13, 0.81	0.017*	0.28	0.11, 0.75	0.011*
PTH (pg/ml)	1.00	1.00, 1.01	0.046*	1.00	0.99, 1.01	0.098	1.00	0.99, 1.01	0.813	1.00	0.99, 1.01	0.416	1.01	1.00, 1.01	0.015*	1.00	0.99, 1.01	0.068
Season of blood sample collection																		

Summer	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-
Fall	1.34	0.87, 2.07	0.176	1.18	0.74, 1.88	0.479	1.02	0.52, 1.98	0.944	0.68	0.32, 1.44	0.321	1.71	0.95, 3.09	0.072	1.69	0.90, 3.18	0.101
Winter	1.19	0.86, 1.65	0.269	1.04	0.73, 1.49	0.801	1.85	1.09, 3.12	0.021*	1.63	0.89, 3.00	0.109	0.91	0.60, 1.37	0.661	0.83	0.53, 1.32	0.452
Spring	1.84	1.32, 2.57	<0.001***	1.75	1.22, 2.50	0.002**	2.71	1.53, 4.77	0.001**	2.91	1.52, 5.53	0.001**	1.49	0.99, 2.62	0.054	1.45	0.93, 2.27	0.097
Smoking status																		
Not smoking	Ref.	-	-	-	-	-	Ref.	-	-	Ref.	-	-	Ref.	-	-	-	-	-
Smoking	1.19	0.91, 1.55	0.186	-	-	-	1.63	1.05, 2.52	0.027*	1.74	1.04, 2.90	0.034*	0.98	0.70, 1.37	0.944	-	-	-
	LR test for the model: 88.85, p<0.001***						LR test for the model: 68.09, p<0.001***						LR test for the model: 55.23, p<0.001***					

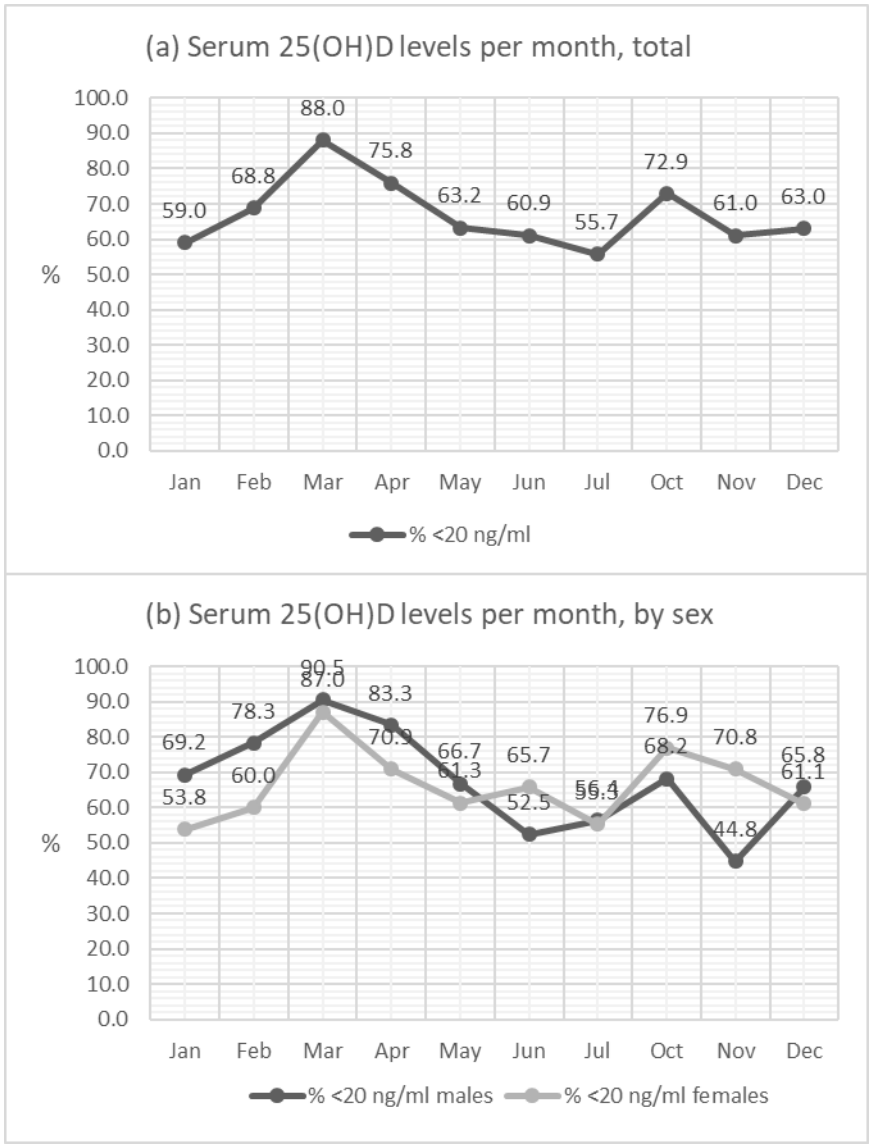
25(OH)D. 25-hydroxyvitamin D. ng/ml, nanograms per milliliter. OR, Odds Ratio. CI, Confidence Interval. BMI, Body Mass Index. h/d, hours/ day. µg/day, micrograms per day. PTH, Parathyroid hormone. Pg/ml, picogram per milliliter. LR test, Likelihood Ratio test. *P<0.05, **P<0.01, ***P<0.001.

[a]Model 1: was adjusted for covariates having p values <0.05 in crude analyses for the total sample which were age, BMI, activity level, vitamin D supplement use, sun exposure, skin colour, PTH and season of blood sample collection.

[b]Model 2: model 1 plus adjustment for smoking status which had a p value <0.05 only in crude analyses for males.

[c]Model 3: model 1.

Figure 1 Prevalence of serum 25(OH)D levels <20ng/ml and per month[a] of blood sample collection (a) total (P<0.01[b]), (b) for males (P=0.003[b]) and females (P=0.007 [b]).



[a] There were no blood samples collected during August and September.

[b]P values indicate differences by month.

3.2 Presentation of paper II

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Intake and contribution of food groups to vitamin D intake in a representative sample of the adult Greek population.

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Abstract

Background

Globally, vitamin D intake from food and supplements is low, consistent with the high prevalence of low serum 25(OH)D concentration. The aim of the study was to assess vitamin D intake and major relevant food contributors, among Greek adults, as well as to propose subsequent policies.

Methods

Vitamin D from diet and supplements was estimated. Two 24-hour recalls (≥19 years old), using the Automated Multiple Pass Method, and a drug and supplement questionnaire. Over- and under- reporters were identified using the Goldberg cut-off. A total of 2218 individuals were included in the final analysis. The National Research Council method was used to account for within- and between-person variation. Vitamin D food intake adequacy was estimated based on the Estimated Average Requirement (EAR) of 10 mcg/day, set by the Institute of Medicine. Major foods contributing to intake were identified and the effect on meeting EAR, of a potential food fortification example was examined.

Results

Median vitamin D intake from food ranged from 1.16-1.72 mcg/day and 1.01-1.26 in different age group in males and females, respectively. Major food sources of vitamin D were fish (46%), meat (15%) and cereals (12%), however, over 90% of the population in all age groups did not meet the EAR, even when supplemental use was accounted for. Vitamin D overall intake is below the average requirements.

Conclusion

Public health policies to increase the consumption of foods high in vitamin D and/or food fortification may significantly reduce the percentage of individuals that do not meet the recommendations.

Key words: Vitamin D, Greece, adults, diet, fortification.

Abbreviations (in alphabetical order)**:** 25(OH)D: 25-hydroxyvitamin D, AMPM: Automated Multiple-Pass Method, BMR: Basal Metabolic Rate, CAPI: Computer Assisted Personal Interview, DRI: Dietary Reference Intake, EAR: Estimated Average Requirement, EFSA: European Food Safety Authority, EIrep: Energy Intake reported, FG: Food Group, HDPA: Hellenic Data Protection Authority, IoM: Institute of Medicine, iPAQ: International Physical Activity Questionnaire, NCI: National Cancer Institute, NDSR: Nutrition Data System for Research, NRC: National Research Council, RDA: Recommended Dietary Intake, UL: Upper Level, USDA: United States Department of Agriculture.

Introduction

Vitamin D plays an important role in the regulation of serum calcium and phosphate which in turn is crucial for bone mineralization [1]. It is well known that such a deficiency can lead to the development of rickets in children and osteoporosis in adults, and recent studies have shown that it may be associated with chronic diseases, such as obesity, diabetes, autoimmune and cardiovascular disease and cancer [1, 2] as well as all-cause mortality [3]. More than one billion people worldwide have low concentration of serum 25-hydroxyvitamin D (25(OH)D), suggesting a potential deficiency [4, 5]; this comprises a health problem worldwide [6-9], including Greece [7, 10, 11] across all age groups [6, 7, 12].

Vitamin D is synthesized in the skin but can also be obtained from foods and supplements. Apart from health issues related to a systematic sun exposure for individuals, including the associated higher risk of melanoma [13], a single general population guideline is difficult to be set since vitamin D skin synthesis is influenced by skin colour, geographical location, season and other factors [14].

Overall, the intake of vitamin D from foods is also very low worldwide and well below the Estimated Average Requirement (EAR) of 10 mcg/day [6, 15-20]. This is reasonable as very few foods naturally contain vitamin D, such as fish and eggs [1]. Supplementation can be an option, especially in cases of extreme deficiency, however it might not be a viable strategy for long-term use across all age groups of the population. In contrast, increasing consumption of foods that naturally contain vitamin D, as well as food

fortification of commonly consumed foods, might offer a plausible strategy to curb this pandemic.

Therefore, knowledge of vitamin D intake from food and supplements is required to potentially tackle vitamin D deficiency pandemic at the population level, through public health policies.

The aim of this study was, therefore, to primarily assess vitamin D intake in a representative sample of the adult Greek population across both genders and different age groups, and to determine the foods that primarily contribute to vitamin D food intake. A secondary aim of this study was to identify possible public health policies to correct low serum 25(OH)D concentration at population level.

Materials & Methods

Study design

Data from the Hellenic National Nutrition and Health Survey (HNNHS), were used in this study [21]. Data collection took place from September 2013 to May 2015, throughout the area of Greece and was stratified by prefecture according to the National 2011 Census. All adults from HNNHS were included (N=3773, ≥19 years; 40.8% males), from 4,574 HNNHS participants. Pregnant and breastfeeding women, as well as institutionalized (e.g. military service, hospital, other institution) individuals, were excluded, due to their different requirements.

More information on the design and study sampling have been already published [21]. The Ethics Committee of the Department of Food Science and Human Nutrition of the Agricultural University of Athens, and the Hellenic Data Protection Authority, approved the HNNHS study. All participants were asked to provide a written informed consent prior to inclusion.

Data collection

Sociodemographic and anthropometric data were collected by trained health professionals using Computer Assisted Personal Interview (CAPI) software. Dietary intake was assessed from two 24-hour recalls. The first interview was administered using the Automated Multiple-Pass Method [22], which is a USDA validated tool for estimating energy and nutrient intake and can be applied during a face-to-face interview. The second interview was conducted via telephone, 8-20 days after the first in a different day.

The FoodEx2 food classification and description system developed by the European Food Safety Authority (EFSA) was used and recommendations for the harmonization of data across European Union countries were followed [23]. Food quantification was performed primarily with the use of age-specific validated food atlases as the primary option, along with standardized household measures as the secondary tool. The Nutrition Data System for Research (NDSR) developed by the University of Minnesota was used for nutrient analysis. This is a database containing more than 18000 foods, including 7000 branded products. For traditional Greek recipes, Greek food composition tables were used [24].

Total energy intake was calculated from both recalls for all individuals, using these validated databases. Individuals reporting extreme energy intakes (<600 kcal/day & >6000 kcal/day) were excluded (n=326, 4.8%) from the analysis. Furthermore, under- and over-reporters were identified using the Goldberg equation [25, 26]. In summary the Energy Intake (EIrep) to Basal Metabolic Rate (BMR) ratio, multiplied with the Physical Activity (estimated using the International Physical Activity Questionnaire) [27], was compared to specific cut-offs established according to EFSA methodology [26]. A total of 1,297 individuals were identified as under-reporters (36.1%; 37.1% males and 35.5% of females) and 72 as over-reporters (2%; 1.5% of males and 2.3% of females). A total of 2218 individuals (907; 40.9% males) were, therefore, included in the main analysis, to account for potential recall error. A secondary analysis, including under- and over-reporters (3587 in total; 1478, 41.2% males) was also conducted, to examine the effect of misreporting on vitamin D intake [Results shown in Table A2].

Estimation of usual vitamin D intake

To remove the effects of within- and between- subject variation in dietary intake and to estimate the usual intake distribution of vitamin D for each age and gender group the National Research Council method was used [28]. This methodology involves several steps. First, data were checked for normality. As vitamin D intake was not normally distributed (Shapiro-Wilk test $P<0.001$) data were log transformed to approach normality. Then, the within- and between- person variance was estimated for each age and gender group and individual adjusted intakes of vitamin D were estimated. Last, the adjusted data was back transformed.

The above method was applied to estimate the percentages below and above selected Dietary Reference Intakes (DRIs) such as the EAR, Recommended Dietary Allowance (RDA) and the Tolerable Upper Intake Level (UL). The DRIs used in this study are suggested by the Institute of Medicine (IoM) to assess the adequacy of dietary intake [1]. EAR is defined as the average daily level of intake estimated to meet the requirements of 50% of healthy individuals, RDA as the average daily level of intake estimated to meet the requirements of nearly all (97-98%) of healthy individuals, and UL is the maximum daily intake unlikely to cause adverse health effects.

Percentage food group contribution

To estimate the contribution of each food group (FG) to the vitamin D food intake, foods reported in 24hR were categorized into 42 FG (Appendix, Table 1). Foods included in recipes/ mixed dishes were assigned to multiple food groups according to the different foods that they consisted of. The dishes in FG42 were not disaggregated due to their high energy and low micronutrient intake. The assumption was made that the ingredients of recipes/ mixed dishes equally contributed to the total nutrient content.

The percentage of the contribution of each FG to the vitamin D intake was derived by the following formula: % contribution of FG to vitamin D = (sum of vitamin D intake for that FG / sum of total vitamin D intake)*100. This was calculated separately for each age and gender group.

A drug and supplement questionnaire was developed using validated questionnaires from other studies, mainly from the United States, and more details of this have been

published previously by our group [29]. From these data, vitamin D supplement intake was categorized as follows: “None”, “≥10 mcg/day” and “<10 mcg/day”.

Forecasted vitamin D intake levels following fortification of milk as an example

To estimate the new vitamin D intake data per 24hR following fortification intake of milk from two different FGs was used. First, “FG10 Milk”, as well as part of “FG32 Coffee”. The latter was used because a significant amount of milk consumed during the day was with coffee (cappuccino in particular). As cappuccino was under the FG32 group only as a recipe (rather than shared between FG10 and 32), although it contained milk, FG32 had also to be used in order to complete the fortification estimation.

With regards to “FG10 Milk” the new data after fortification was derived by adding the prespecified amount for food fortification (1, 2, 5, 7, 10, 12, 15 and 20 mcg) per 100g of milk to the initially reported amount. With regards to the FG32 Coffee category and specifically cappuccino, the amount added to the initially reported amount was estimated using the assumption that 58% of the total amount of cappuccino in grams comes from milk, as it is usually prepared in Greece.

Then, the NCI method for usual vitamin D intake estimation was applied, as previously described, for each fortification scenario. Based on these levels, the percentages below the EAR and RDAs were estimated.

Statistical analyses

Normality of the distribution of continuous variables was evaluated using the Shapiro-Wilk test. Age and vitamin D food intake were not normally distributed and were expressed as median and interquartile range. Levels of vitamin D intake following

fortification were an estimation, rather than actual data, and, therefore, were expressed as means and standard deviations. Categorical variables were presented as frequencies. Kruskal-Wallis test was used to assess gender differences in vitamin D food intake. The Wilcoxon Sign test was used to assess differences in median vitamin D intake between vitamin D intake estimates with and without misreporters. Two sample Kolmogorov-Smirnoff test was used to check distribution equality between normal and misreporters. The level of statistical significance was set at $P<0.05$. All analyses were performed in STATA statistical software (STATA 13.1, Stata Corp LP, Texas, USA) and Microsoft Excel software (Excel 2016, Microsoft Corp).

Ethical approval

The study was approved by the Ethics Committee of the Department of Food Science and Human Nutrition of the Agricultural University of Athens. It was also approved by Hellenic Data Protection Authority (HDPA). All members of the staff signed confidentiality agreements. All volunteers were asked to sign a detailed informed consent form.

Results

Vitamin D food intake

Data from 24hR was available for Group 1 (n=2218) individuals (40.9% males). Baseline median vitamin D food intake data ranged from 1.01 mcg/ day in females ≥71 years old to 1.72 mcg/ day for males 19-30 years old (Table 2). Ninety nine percent of the population (99.6% for males and 99.9% for females) had levels below the EAR and 100%

percent below the RDA (Recommended Dietary Allowance), with no individual exceeding the UL (Tolerable Upper Intake Level) across all age groups and genders.

Vitamin D intake including all individuals, other than those reporting extreme intakes (<600kcal/day & >6000kcal/day; N=3587) in the analysis, was also assessed. Overall, median vitamin D intake from food was lower in all gender and age groups in this group (noted in table as Group 2, see Appendix) compared to the sample calculated according to Goldberg criteria (Group 1)

Vitamin D supplement intake

Vitamin D containing supplement use was also low (Table 2) for most age and gender groups. Ninety four percent of males and 92% of females did not take any supplements containing vitamin D. Supplement use with ≥10 mcg/ day of vitamin D was at its highest in females in the 51-70 years old group (11.6%), as well as in females ≥71 years old age group (5.9%). Supplement use with ≥10 mcg/ day of vitamin D ranged from 0.0-1.0% in males among the different age groups. Individuals consuming multivitamin supplements were categorized at the <10 mcg/ day level, as these contain minimal vitamin D amounts.

Percent contribution of different foods to vitamin D intake

Overall, major sources of vitamin D food intake in our population were fish (46%); 43% of vitamin D food intake was contributed from fresh fish whereas 3% from processed fish. Meat contributed 15% of vitamin D from food intake (11% red meat, 1% white meat, and 3% processed red meat). Cereals also contributed 12% of vitamin D from food intake (Table 3). Most of the vitamin D food intake from cereals was from processed cereals (9%

of total contribution) compared to all bran cereals (3% of total contribution). The major vitamin D food contributors are shown in Table 3 for the total population and by gender. As per the contribution of FG subcategories similar to the total sample, results were found in males and females.

Fish contribution to vitamin D food intake was at its lowest for the 19-30 years old category in both males (36%) and females (34%) (Table 3). It reached a peak at the 51-70 years old category for both genders (60% male, 58% female) and was maintained in the ≥71 years old category. A similar trend was observed for the sub-category of fresh fish, but not processed fish from which vitamin D food intake contribution peaked at the 31-50 years old category for both genders (6% male and 5% female).

Meat contribution to vitamin D food intake was higher in the 31-50 years old (17%) and same in the 19-30- and 51-70- years old categories (16%) in males. It was lower in the males ≥71 years old category (11%). In females, meat contribution to vitamin D food intake was 18% in the 31-50 years old category, 14% in the 19-30 years old category, 11% in the 51-70 years old category and 6% in the ≥71 years old category.

The contribution of cereals to vitamin D food intake was higher in the younger age group of 19-30 years old (19% in males and 20% in females), but was reduced with increasing age reaching a lowest of 5% and 8% in the 51-70 years old category for males and females, respectively.

In all other FGs contribution to vitamin D food intake was generally low and similar between the genders as well as between age groups of the same gender (Table 3).

Effect of vitamin D fortification of milk to vitamin D intake

Progressive fortification of milk with vitamin D from low to extreme levels reduced the percentage of participants below the EAR and the RDA (Figures 1 & 2). The higher the amount of fortification of milk, the higher the percentage below the EAR and RDA. The purpose of progressive simulation of milk fortification was to identify the levels at which vitamin D fortification would provide improvements in vitamin D intake at group level but would still be safe for all age groups. However, in our example even at extreme levels of fortification (e.g., 20 mcg/ 100g of milk) no participant exceeded the UL of 100 mcg/ day for vitamin D (maximum reached 76.6 mcg/ day; these amounts refer to adjusted vitamin D intakes following the application of the NCI method for each level of fortification).

Discussion

The main finding of this study was that less than 1% of the Greek population enrolled in the study met the EAR for vitamin D intake across all ages and gender groups, whereas none met the RDA, highlighting the need for prevention programs. This was demonstrated with an example of milk fortification, a food consumed regularly by most individuals in all age and gender groups, where a moderate fortification (about 7 mcg/ 100g of milk) would cover EAR recommendations for over half of the population, in respect to their current estimated vitamin D intakes.

Similar finding have been reported from other studies in Greece and in other countries where intakes were well below the EAR of 10 mcg/ day [6, 15-20]. It is noteworthy that in an EFSA report, including intakes from 14 European countries, a mean dietary intake ranging from 1.1 to 8.2 mcg/day was observed [30].

The low vitamin D intake can be explained as very few foods naturally contain vitamin D [1], and include fish, especially fatty fish; other sources are milk, meat, eggs and fortified products, such as cereals [6]. Requirements, however, were developed to cover population's needs for health, hence other means to cover these requirements, through food and or supplements are potentially needed. Major contributors to dietary vitamin D intake in our study were fish, meat and cereals, with these varying between gender. Compared to other European countries fish contributes 70% of vitamin D from food intake in Spain (18-64 years old) [31], 38% in France [32], 25% in the UK (19-64 years old) [33], 12-16% (12% for those 18-64 years, 16% for those ≥65 years) in Ireland [6] and only 8-11% in the Netherlands (8% in 7-69 years old and 11% in ≥70 years old) [34, 35], compared to 46% in HNNHS. In our study, the dietary contribution of meat was 15% whereas in the UK meat contributes to 22% of vitamin D from food intake (19-64 years old) [33], in Ireland 22-30% (30% for 18-64 years old, 22% for ≥65 years old) [6], in Spain 2% [31] and in the Netherlands 12-20% (20% in those 7-69 years old and 12% in those aged ≥70 years old) [34, 35]. Finally, cereals contributed 12% to the vitamin D intake in our study, as in the UK (12% in males and 13% in females) [6], compared to 4% in Spain 4% [31] and to 2-5% in Irish adults [6].

Vitamin D can also be obtained via exposure to sunlight, many avoid sun exposure or use sunscreens due to reduce the risk of melanoma. Supplements are also an option, especially during the winter months or for people with minimal sunlight exposure [36]. The latter were accounted for in the study, and intake remained extremely low, demonstrating again the need for preventive programs. Specifically, and noteworthy, 92% of females and 94.6% of males in our study did not receive any supplement vitamin D containing, approximately 4% were adding minimally to their intake through multivitamin supplements (<10 mcg/day), and 3.9% of females and 0.4% of males solely consumed a high amount (>10 mcg/ day) of vitamin D, to cover requirements. Regarding other European countries a gradient between countries in the south and those in the north has been reported with regards to use of dietary supplements [37]. In more detail, the highest consumption was observed in Norway (61.7% in females) and the lowest in Greece (6.7% in females and 0.5% in males).

Milk was chosen as the most appropriate and practical example for Greece, as it can be consumed daily by all age groups and is also a very good source of calcium, and phosphorus, nutrients with a vital role in bone health. Fish and meat cannot be fortified. Cereals could be fortified, however, as most of the cereal products consumed in Greece are imported, this would complicate the implementation of such a policy. In addition, cereals, in general, contain high amounts of sugar and any public health policy to increase their intake could provoke controversial results. Another potential food for fortification, which does not contribute vitamin D, could be flour. Nevertheless, most consumers in Greece buy bread from many different local bakeries and producers rather than from a few companies as is the case in other countries and implementation would be much more difficult and impractical.

According to our estimations, even a low (7-10 mcg/ day, which is approximately 100ml) milk fortification could improve vitamin D intake of the population without increasing the risk of toxicity (UL of vitamin D is 100 mcg/day). A higher level of fortification (e.g. 20 mcg/ 100g of milk) could increase the risk of toxicity in some age and gender groups, especially in female individuals ≥71 years old, who regularly consume vitamin D supplements for osteoporosis at a level of 25-75 mcg/day. Our study examined other fortification scenarios for the adult (≥19 years) population where the UL is set at 100 mcg/ day (for those ≥9 years). However, milk is a food product that is consumed regularly by children as well, where the UL is 63 mcg/ day for children 1-3 years old and 75 mcg/ day for children 4-8 years old. Therefore, when considering the implementation of fortification scenarios, safe consumption data also referring to children must be taken into consideration not to exceed the UL in any population group. Likewise, one should take into account the presence of subjects with lactose intolerance and milk protein allergies, in whom food vitamin D should be taken via other foods or as a supplement.

The results of this study, although cross-sectional in nature, are strengthened by its design. It included a representative sample of the Greek population, in all age groups, and dietary intake was assessed using the most advanced research tools and standardized procedures following European and International guidelines (e.g. AMPM, food atlases). In addition, assessment of intake included all days of the week, as well as all twelve months and, therefore, effects due to seasonal variation in consumption of foods is minimized, and the NRC method was used in determining final intake to account for within and between individual variation. Moreover, fortification scenarios were performed based on actual

consumption data, to provide specific results that public health officials can use as primary information. Also, sunlight exposure and complete vitamin D status need to be accounted for before implementation. The geographical latitude of Greece, despite the amount of sunlight, require those residing in Greece to have a larger amount of sunlight exposure for synthesis, an area of contradiction with skin health.

However, there are also limitations in our study. Results must be interpreted with caution, as this is a cross-sectional survey. Although extreme intakes and misreporters were excluded this could have created a biased sample as some misreporters could have been reporting true intake. Additionally, blood status was not reported, although the aim of this study was to report food adequacy and not vitamin D status.

Conclusion

Vitamin D deficiency is a widespread population problem observed in many countries, including Greece. Dietary intake among the Greek population, is extremely low, below the EAR levels, placing the population at multiple risks. Food fortification policies have not yet been formulated, potentially because of insufficient data. This study increases public health awareness on the need for preventive public health strategies, even in areas where sunlight is found in abundance.

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Table 3 Basic demographic characteristics of study participants.

	Males	**Females**	**All**
	907	1311	2218
	Mean ± SD	**Mean ± SD**	**Mean ± SD**
Age (years)	40.8±16.8	40.9±17.2	40.8±17.0
	N (%)	**N (%)**	**N (%)**
Ethnicity			
Greek	883 (97.4)	1276 (97.3)	2159 (97.3)
Other	24 (2.6)	35 (2.7)	59 (2.7)
Marital status			
Married	394 (43.4)	537 (41)	931 (42)
Unmarried	481 (53)	608 (46.4)	1089 (49.1)
Divorced/ Separated	19 (2.1)	73 (5.6)	92 (4.2)
Widowed	13 (1.4)	91 (7)	104 (4.7)
Educational level			
Primary	75 (8.3)	110 (8.4)	185 (8.4)
Secondary	371 (41.0)	447 (34.1)	818 (37)
Diploma	69 (7.6)	125 (9.5)	194 (8.8)
Bachelor's degree	308 (34.1)	486 (37.1)	794 (35.9)
Postgraduate degree	81 (9.0)	141 (10.8)	222 (10)

SD: Standard Deviation.

Table 4 Vitamin D food intake levels in the Hellenic National Nutrition and Health Survey (2013-2015).

Age group (years)	**N**[1] Group 1	**Vitamin D from food**[2,5] (mcg/day) Group 1: excluding recalls with extreme energy intakes & misreporters	% **Vitamin D from supplements** (mcg/day)			% **below selected DRIs**		
		Median (25, 75)	**None**	**≥10**	**<10**[3]	**EAR**	**RDA**	**UL**
Males	**907**	**-**	**94.6**	**0.4**	**5.0**	**99.6**	**100.0**	**100.0**
19-30	315	1.72 (1.26, 2.48)	94.9	0.0	5.1	99.0	100.0	100.0
31-50	340	1.53 (1.22, 1.99)	92.1	0.6	7.4	100.0	100.0	100.0
51-70	191	1.59 (1.25, 2.01)	97.4	1.0	1.6	100.0	100.0	100.0
≥71	61	1.16 (0.81, 1.89)	98.4	0.0	1.6	100.0	100.0	100.0
Females	**1311**	**-**	**92.4**	**3.9**	**3.7**	**99.9**	**100.0**	**100.0**
19-30	491	1.26 (1.03, 1.56)	95.1	0.4	4.5	100.0	100.0	100.0
31-50	433	1.17 (0.86, 1.52)	94.2	2.1	3.7	100.0	100.0	100.0
51-70	302	1.24 (0.92, 1.61)	85.4	11.6	3.0	100.0	100.0	100.0
≥71	85	1.01 (0.65, 1.66)	92.9	5.9	1.2	98.8	100.0	100.0

[1]Total number of participants used for the Group 1 analysis is n=2218.
[2]Group 1: Median and interquartile range estimated by excluding recalls with extreme energy intakes (<600kcal/day and >6000kcal/day) and misreporters (based on the Goldberg cut-off) as well as by using adjusted vitamin D intake levels based on the NRC methodology [28] for usual intake estimation. P value for age differences in Vitamin D intake from food according to the Kruskal – Wallis test is <0.001 for both genders (n=2218).
[3]Includes those that reported taking <10 mcg/ day as well as those that reported unknown quantity of vitamin D from supplements.
mcg: micrograms, %: percentage, Median (25, 75): Median and interquartile range, DRI: Dietary Reference Intakes, EAR: Estimated Average Requirement, RDA: Recommended Dietary Allowance, UL: Tolerable Upper Intake Level.

Table 5 Percentage contribution of food groups to average total intake of vitamin D from food by age and gender of respondent.

	All	Males aged (years)				All males	Females aged (years)				All females
		19-30	31-50	51-70	≥71		19-30	31-50	51-70	≥71	
	%	%	%	%	%	%	%	%	%	%	%
Fish, total	**46**	**36**	**53**	**60**	**60**	**49**	**34**	**38**	**58**	**58**	**43**
Fresh fish	43	34	46	58	60	46	32	33	58	58	41
Processed fish	3	3	6	2	0	4	3	5	1	0	3
Meat, total	**15**	**16**	**17**	**16**	**11**	**16**	**14**	**18**	**11**	**6**	**14**
Red meat	11	12	12	13	8	12	10	13	8	4	10
White meat	1	2	1	1	2	1	1	1	1	1	1
Processed red meat	3	3	3	2	2	3	3	3	2	1	3
Cereals, total	**12**	**19**	**8**	**5**	**6**	**11**	**20**	**12**	**8**	**9**	**14**
All bran cereals	3	2	3	1	0	2	5	3	2	4	4
Processed cereals	9	17	5	3	6	9	15	8	6	5	10
Desserts	**7**	**8**	**5**	**5**	**4**	**6**	**9**	**8**	**7**	**8**	**8**
Cheese	**6**	**5**	**6**	**5**	**7**	**6**	**6**	**8**	**5**	**5**	**6**
Egg	**4**	**4**	**3**	**4**	**3**	**4**	**5**	**4**	**4**	**6**	**5**
Baked Products	**3**	**4**	**3**	**2**	**0**	**3**	**4**	**4**	**2**	**3**	**3**
Milk	**2**	**3**	**2**	**1**	**3**	**2**	**2**	**2**	**1**	**2**	**2**
Animal fat	**2**	**2**	**2**	**1**	**1**	**2**	**3**	**2**	**1**	**1**	**2**
Other[1]	**2**	**2**	**2**	**1**	**3**	**2**	**2**	**2**	**1**	**2**	**2**
Yoghurt	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**2**	**2**	**2**	**1**

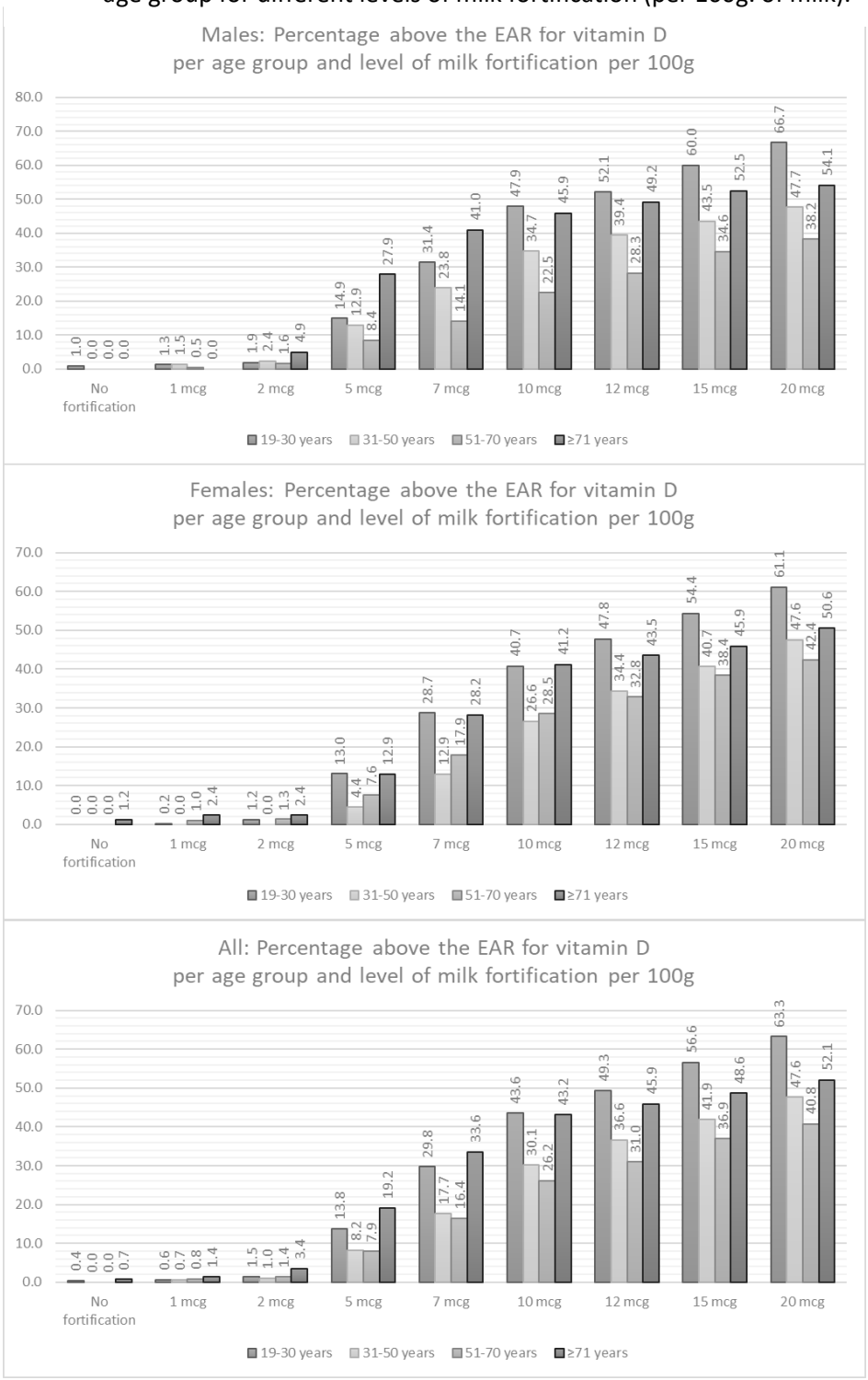
[1]Includes vegetables, sauces, olive oil and olives, other vegetable fat that contribute ≤0.5% each to vitamin D intake.

Table 6 Level of vitamin D intake from food after fortification of milk.

	Fortification level per 100g of milk							
	1 mcg	**2 mcg**	**5 mcg**	**7 mcg**	**10 mcg**	**12 mcg**	**15 mcg**	**20 mcg**
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Males								
19-30 years	3.25 ± 1.72	4.18 ± 2.12	6.59 ± 3.44	8.03 ± 4.37	10.07 ± 5.76	11.37 ± 6.67	13.26 ± 8.04	16.27 ± 10.26
31-50 years	2.75 ± 2.22	3.55 ± 3.08	5.55 ± 5.00	6.77 ± 6.19	8.52 ± 7.97	9.66 ± 9.16	11.32 ± 10.94	14.01 ± 13.89
51-70 years	2.50 ± 1.57	3.06 ± 2.12	4.45 ± 3.43	5.28 ± 4.25	6.44 ± 5.47	7.19 ± 6.28	8.28 ± 7.51	10.03 ± 9.55
≥71 years	2.69 ± 1.65	3.83 ± 2.74	6.74 ± 5.5	8.56 ± 7.34	11.20 ± 10.12	12.93 ± 11.98	15.49 ± 14.75	19.68 ± 19.34
Females								
19-30 years	2.49 ± 1.41	3.37 ± 2.01	5.71 ± 3.74	7.16 ± 4.89	9.24 ± 6.6	10.59 ± 7.73	12.57 ± 9.42	15.78 ± 12.18
31-50 years	2.10 ± 1.12	2.75 ± 1.56	4.42 ± 2.87	5.43 ± 3.75	6.88 ± 5.06	7.80 ± 5.92	9.15 ± 7.20	11.33 ± 9.28
51-70 years	2.29 ± 1.71	2.92 ± 2.17	4.53 ± 3.45	5.50 ± 4.31	6.88 ± 5.61	7.77 ± 6.48	9.06 ± 7.77	11.14 ± 9.89
≥71 years	2.51 ± 2.55	3.35 ± 3.23	5.62 ± 5.16	7.04 ± 6.49	9.11 ± 8.56	10.46 ± 9.97	12.46 ± 12.09	15.73 ± 15.65

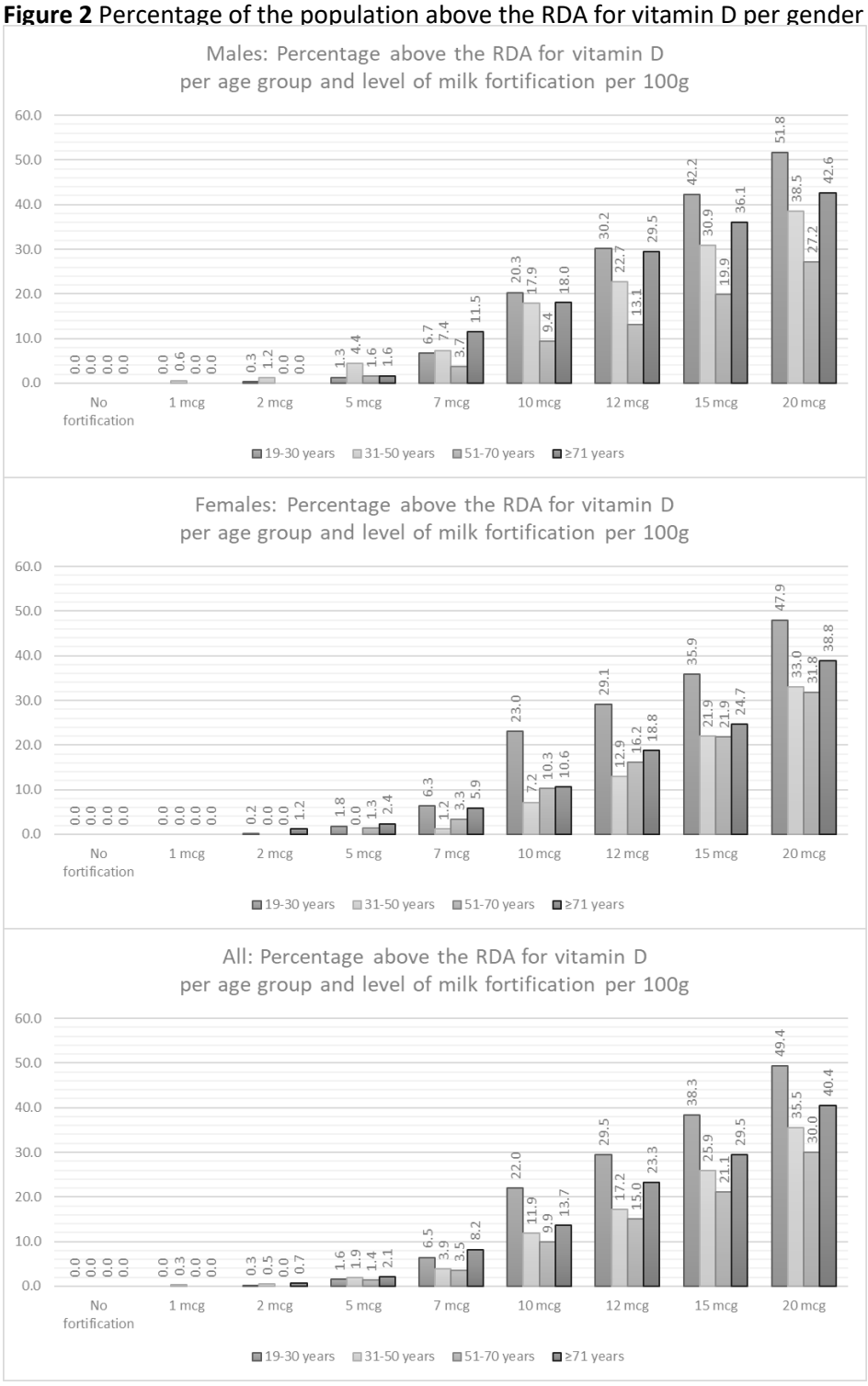
Mean and SD estimated using adjusted vitamin D intake levels based on the NRC methodology [28] for usual intake estimation.
g: grams, SD: Standard Deviation, mcg: micrograms.

Figure 1 Percentage of the population above the EAR for vitamin D by gender and age group for different levels of milk fortification (per 100g. of milk).



EAR: Estimated Average Requirement, g: grams, mcg: micrograms. EAR for vitamin D: 10 mcg/ day.

Figure 2 Percentage of the population above the RDA for vitamin D per gender



RDA: Recommended Dietary Intake, g: grams, mcg: micrograms.
RDA for vitamin D: 15 mcg/ day for individuals 19-70 years, 20 mcg/ day for individuals >70 years.

Appendix

Table A1 List of food groups used for the estimation of % food contribution to vitamin D intake.

FG01 Fruits (fresh, dried, canned)
FG02 Natural fruit juices
FG03 Non-starchy vegetables
FG04 Starchy vegetables (except potato)
FG05 Potato
FG06 All bran cereals
FG07 Processed cereals
FG08 Lentils, beans, meat substitute
FG09 Nuts, peanut butter, almond milk
FG10 Milk
FG11 Yoghurt
FG12 Cheese
FG13 Egg
FG14 Fish (fresh)
FG15 Seafood, snails
FG16 Red meat (including offal)
FG17 White meat
FG18 Processed red meat
FG19 Processed white meat (e.g. chicken nuggets)
FG20 Processed fish
FG21 Olive oil, olives
FG22 Other vegetable oils (e.g. coconut oil, margarine/ butter mix)
FG23 Animal fat (e.g. mayonnaise, white sauce)
FG24 Alcoholic beverages
FG25 Beverages with sugar, soft drinks, fruit juices with added sugar
FG26 Beverages with sugar substitutes except fruit juices
FG27 Salty snacks (e.g. potato crisps, cracker)
FG28 Desserts
FG29 Herbs and spices
FG30 Salt
FG31 Water
FG32 Coffee
FG33 Tea
FG34 Artificial sweeteners
FG35 Sugar, honey, syrup
FG36 Baked products (e.g. cakes, biscuits, croissant)
FG37 Fruit juices with sweetener
FG38 Cooking cube, sauce
FG39 Salad dressing
FG40 Baby food

FG41 Dairy substitutes
FG42 Fast food (e.g. souvlaki, burger, fries)

Table A2: Median dietary intakes of vitamin D in sample excluding recalls with extreme energy intakes & misreporters (Group 1) and sample excluding recalls with extreme energy intakes only (Group 2).

Age group (years)	**N**[1] Group 1	**Vitamin D from food**[2] (mcg/day) Group 1: excluding recalls with extreme energy intakes & misreporters	**N**[3] Group 2	**Vitamin D from food**[4] (mcg/day) Group 2: excluding recalls with extreme energy intakes only.	**P value**[5]	**P value**[6]
		Median (25, 75)		**Median (25, 75)**		
Males	**907**	**-**	**1478**	**-**		
19-30	315	1.72 (1.26, 2.48)	480	1.44 (1.02, 2.07)	<0.001	<0.001
31-50	340	1.53 (1.22, 1.99)	524	1.30 (1.03, 1.67)	<0.001	<0.001
51-70	191	1.59 (1.25, 2.01)	335	1.13 (0.80, 1.48)	<0.001	<0.001
≥71	61	1.16 (0.81, 1.89)	139	0.91 (0.64, 1.51)	0.0128	0.0128
Females	**1311**	**-**	**2109**	**-**		
19-30	491	1.26 (1.03, 1.56)	713	1.15 (0.91, 1.45)	<0.001	<0.001
31-50	433	1.17 (0.86, 1.52)	641	1.00 (0.74, 1.34)	<0.001	<0.001
51-70	302	1.24 (0.92, 1.61)	555	1.01 (0.74, 1.30)	<0.001	<0.001
≥71	85	1.01 (0.65, 1.66)	200	1.00 (0.63, 1.49)	0.0128	0.001

[1]Total number of participants used for the Group 1 analysis is n=2218.
[2]Group 1: Median and interquartile range estimated by excluding recalls with extreme energy intakes (<600kcal/day and >6000kcal/day) and misreporters (based on the Goldberg cut-off) as well as by using adjusted vitamin D intake levels based on the NRC methodology *[28]* for usual intake estimation. P value for age differences in Vitamin D intake from food according to the Kruskal – Wallis test is <0.001 for both genders (n=2218).
[3]Group 2: Excluding recalls with extreme energy intakes (<600kcal/day and >6000kcal/day) but not misreporters. Total number of participants used for analysis is n=3587.
[4]Group 2: Estimated as in 2 but without excluding misreporters of energy intake according to the Goldberg cut-off (n=3587).
[5]P values estimated using the Wilcoxon Sign test for measures with and without misreporters.
[6]P: Based on Kolmogorov-Smirnoff two sample test significant mean differences (by reporting status) were found in total adjusted intakes (p<0.001).

3.3 Presentation of paper III

Aims, design and preliminary findings of the Hellenic Nutrition and Health Survey.

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BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

Aims, design and preliminary findings of the Hellenic National Nutrition and Health Survey (HNNHS)

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Abstract

Background: The aim of the Hellenic National Nutrition and Health Survey was to assess nutritional intake, health status and various behaviors in a representative sample of the Greek population.

Methods: Data collection took place from 01.09.2013 to 31.05.2015. Random stratified sampling was performed by (a) geographical density criteria of Greece (7 regions), (b) age group of the reference population (< 19, 20–64 and > 65 years) and (c) gender distribution. The final population enrolled included (throughout Greece), 4574 individuals (42.5% men; 57.5% women of who 47.2% were from Athens metropolitan area, 18.5% from Central Macedonia, and the remaining 34% almost equally scattered throughout the country (p for the comparisons with official statistics by region, age group and sex > 0.7). Questionnaires developed were based on extensive review of the literature, following a validation procedure when necessary.

Results: Preliminary analyses revealed that 32% of the adult population were overweight and 15.5% were obese, with significant gender differences in total and per age group ($p < 0.001$, for all). The majority of the adult population reported being active smokers (50.4%) or regular alcohol consumers (72.4%); with significant gender differences ($p < 0.001$, for all). Prevalence of hyperlipidemia was 16.7%, cardiovascular disease 13.9%, hypertension 13.3%, thyroid disease 13.8%, and Diabetes Mellitus 3.6%. Significant gender and age group differences were found in various diseases.

Conclusions: Study's preliminary results provide valuable information about the Hellenic population's health. Findings from this survey could be used to detect disease risk factors for public health prevention policies and programs.

Keywords: Diet, Public health, Nutrition survey/ methods, Cross-sectional study, Greece

Background

The evaluation of current population's mental and physical health and the identification of the most important modifiable risk factors for disease prevention and treatment is mandatory in assuring a healthy and productive population [1–5].

During the last few decades, a pharmacological approach for public health promotion was widely used, hence focusing mostly on disease treatment rather than prevention. This approach allowed increased prevalence of various health risk factors, and led to an increase in health care costs, and a decrease in gross production. World data have shown that 8 out of the 20 main causes of morbidity and mortality are due to unhealthy nutrition [1, 4, 5]. Recent findings showed that the three leading factors of global disease burden were high blood pressure, smoking, and high alcohol consumption [4, 5], however when globally assessed their geographical variations on the magnitude of their effect of these risks

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varied with alcohol being the leading risk factor in Eastern Europe and high blood pressure in central Europe, for example. Additionally, overweight and obesity, physical inactivity and other modifiable risk factors (dietary fats) represent substantial risk factors too, with their risk burden varying on diseases by gender, and dietary fats by age (children, adults, elderly) [4, 5]. More specifically, older ages had a higher consumption of fish oils, while younger individuals had a higher trans-fat intake [5].

Therefore, well-designed country specific studies are necessary for the assessment and evaluation of major modifiable risk factors in different geographic regions, which will enable a focused (per region's needs) promotion of public health. Additionally, data should also focus in gender and age specific differences.

Efficiently performed well-designed nationally representative cross-sectional studies have adequately evaluated the population's health and nutrition habits. Examples from such programs include the National Health and Nutrition Examination Survey (NHANES) and the National Diet and Nutrition Survey (NDNS). During the last several decades, findings from NHANES have been used in the United States of America (USA) for status and the development of health policies to safeguard public health, including policies for prevention of lead poisoning and folic acid deficiency through compulsory food fortification [6, 7].

The present Hellenic National Nutrition and Health Survey (HNNHS) is the first national cross-sectional study that takes place in Greece, which encompasses a representative sample of all ages, and following standards established by NHANES (USA) and NDNS (United Kingdom).

The aim of the HNNHS was to assess nutritional intake, health status and various behaviors in the Greek population, which could be used to help promote public health through the design and implementation of related policies and intervention programs. In the present paper, the aims, the design and some preliminary findings of the HNNHS are explained below in detail.

Methods

Study design

This is a cross-sectional observational survey. Responders' selection was performed with a random stratified design based on the 2011 census data. Stratification was made according to (a) geographical density criteria by Greek region (7 regions), as provided by the Hellenic Statistical Authority, (b) age group of the reference population (< 19, 20–65 and > 65 years) and (c) gender distribution. A random selection of more than one individual per household was possible but no more than one individual from the same age group could be enrolled in the study. If households had children < 6 years of age, one (if more were present) was randomly selected to be included in the study, upon consent. The sample required to accurately evaluate measures of effect for common risk factors and prevalence of chronic diseases (a priori estimated to equal to 1.2), at 0.05 level (alpha) was 3634 individuals, to achieve a statistical power equal to 85%. To maintain 85% power in the estimation of prevalence rates of chronic diseases or morbidities equal to 15%, with 1 standard deviation (SD) of the referent population (N = 11,000,000), at 0.05 significance, a sample size of 4658 was needed.

Sample

Invitations were sent to approximately 6000 individuals (anticipating a 70–75% response rate) in to achieve the required sample size, based on a feasibility and volunteer basis in all Greek regions, by the study's investigators from 01.09.2013 to 31.05.2015. A total 4574 (42,5% men and 57.5% women) finally agreed to participate. The sample was distributed throughout Greece, with 47.2% of it residing in the Athens Metropolitan area, 18.5% in the region of Central Macedonia, whereas the rest was almost equally scattered throughout the country (Table 1; p for the comparisons with Official statistics by region, age group and sex > 0.7). Post-hoc assessment, accounting for large population (N > 10,000) resulted in a 92% study power, for an effect size of 1.2 (OR = 1.2). When the 15% probability of chronic disease was accounted for, the power was reduced to 84%.

Age standardization was performed using the 2011 Census as the reference population's data to check a-posteriori that the sampled population was representative of the Greek population, as per the aim of the study (calculations are provided in the excel file provided in the Additional files 1 and 2). The population was stratified by 10 years and statistical analyses were performed.

Table 1 Distribution of the sample within Greece

Prefecture	N	%
Attica	2160	47.2
Central Macedonia	844	18.5
Epirus	59	1.3
Eastern Macedonia, Thrace	193	4.2
Peloponnese	144	3.1
Western Macedonia	99	2.2
Thessaly	238	5.2
Central Greece	104	2.3
Western Greece	219	4.8
Crete	262	5.7
Ionian Islands	51	1.1
North Aegean Islands	92	2
South Aegean Islands	87	1.9

The sampled population was representative for the age groups 0–19, 20–65 and 65+, and, hence were used in the analysis. Furthermore, the prevalence of chronic diseases (surveyed) of the actual Greek population (as per census), through direct standardization, was compared to the prevalence found in the study population. The crude and adjusted odds ratios (OR) calculated by age group in total and by gender did not significantly differ, hence allowing increasing generalizability of the results.

Inclusion – Exclusion criteria

Total HNNHS sample population included volunteers ≥6 months old that reside in Greece. Exclusion criteria included individuals (i), that did not speak Greek, (ii) women who were at that time breastfeeding or pregnant, (iii) members of the armed forces (including those that are currently undergoing their compulsory military service), (iv) individuals that reside in institutions (e.g. nursing homes, rehabilitation centers, hospice centers, psychiatric institutions, prisons, monasteries), (v) those that were unable to provide informed consent due to any cause (e.g., mental impairment, psychiatric condition, drug abuse, vision or hearing loss) unless a first degree relative was able to assist in the process.

Data collection

Information was collected via a series of previously validated questionnaires, from the entire population sampled (details given in "Questionnaires in brief" section). All of the questionnaire types used in HNNHS are provided in supplementary tables, along with their validation references in Additional file 1: Tables S1-S3. Additional references are listed for those questionnaires that are not relevant in this study's results.

Clinical examinations were performed on a subsample. More specifically, an initial interview took place at the volunteer's house, with the use of a specially designed computer software (i.e. Computer Assisted Personal Interview (CAPI)), to minimize response biases and misclassification (minimize volunteer burden and maximize reliability of collected data). The list of questionnaires applied can be seen in the Additional file 1: Tables S1 and S2. In summary, the interviewing process included data on (i) demographics, (ii) quality of life (QoL), (iii) medical history (i.e. chronic & autoimmune diseases, depression, anxiety), (iv) breastfeeding, (v) vitamin and subscribed drug intake, (vi) memory impairment, (vii) eating habits, (viii) alcohol intake, (ix) smoking habits, (x) physical activity, (xi) sleeping habits, (xii) overall patient health, and (xiii) effects of economic crisis. The questionnaires were chosen according to the volunteer's age, as designated by the study's protocol (Additional file 1: Tables S1-S3).

A detailed 24-h dietary recall was obtained during this process. The volunteers were also interviewed for a second 24-h dietary recall via telephone 8–20 days after the first interview, selecting a different day, and non-consecutive, as specified by HNNHS study-protocol. Specific questionnaire structure and validated food atlases for food quantification were used depending on volunteer's age (≥1.5–4 years old, ≥4- < 10 years old, ≥10- < 12 years old and ≥ 12 years old) in order to maximize response accuracy. More specifically, dietary intake data were collected using two automated multiple-pass 24-h dietary recalls and a Food Propensity Questionnaire (FPQ). To harmonize data collection, we based our food classification and description system on FOOdEx2 developed by EFSA [8], based on volunteers age (< 2 years old and ≥ 2 years old). Main differences between the two versions was the food list, (was shorter for the < 2 year old's), as well as the frequency response section. The latter referred to the frequency of food intake over the last 30 days for volunteers < 2 years old, or to the past year for those ≥2 years old. Both FPQs were developed based on the Hellenic, European and International guidelines. Overall, the methods of dietary assessment were chosen as per EFSA recommendations for the harmonization of data across countries member states of the European Union [8]. Data on eating patterns and behaviors were also collected (timing of food intake, number of meals, activities performed during food consumption, place of consumption, and others) to account for their effects on individuals weight status as studies support [9–11]. The Nutrition Data System for Research (NDSR) (developed by the University of Minnesota) was used for nutrient analysis.

At the end of the interview, volunteers were provided with a list of questionnaires (hard copy) with specific instructions, to self-complete, based on the volunteer's age and their primary response to disease state during the interviewing process (Additional file 1: Table S2). These were to be fulfilled within a specific time period, to further reduce volunteer burden (time related) and to decrease interviewer and response bias because of the nature of the nature of the questionnaires (sensitive personal information). These questionnaires included (i) qualitative FPQ (asked to be completed by all volunteers, as explained above), (ii) perceived stress scale, (iii) perception of health control, (iii) eating behavior (iv) chronic disease specific information (onset, treatment, medical follow ups, and others), (v) pregnancy and infantile information (i.e., smoking during pregnancy, number of children, weight gain per pregnancy, infant's birth weight/length, breastfeeding (type & duration), and others), (vi) environmental exposure, (vii) social readjustment factors due to the economic crisis, (viii) asthma related information, and (vi) gastrointestinal disorders (the Greek version of Rome III FGID questionnaires for both children and adults was completed).

Interview based questionnaires and those to be self-completed were addressed to volunteers ≥12 years old. Questionnaires related to volunteers, less than 12 years old, were addressed to his/her parent or primary guardian.

In the case of volunteers being unable to self-respond (i.e., with inhibiting health complications, adolescents with lack of knowledge in specific questions) a parent/ guardian was asked to assist in the interview. The economic crisis questionnaire was answered only by one adult member per household. Information on primary respondent, or on potential help received during the process was recorded ("interviewee assistant"). A small list of questionnaires where exempt from this procedure (where the main respondent has to be the volunteer himself), due to the nature of the related questions. These included questions on (i) memory impairment, (ii) screen time and alcohol use, (≥12 years - < 18 years), (iv) smoking habits (≥12 years - < 18 years) and (v) patient health questionnaire.

Completed questionnaires were handed to the participants nearest mobile unit or were given to the experienced field investigator (who performed their initial interview), when completed. To achieve a maximum response rate, the study's trained personnel performed kind reminders via phone calls. A total of 3180 volunteers (2682 adults and 498 children and adolescents) completed all questionnaires (67% in total; 71% for adults and 62.6% for children & adolescents). Field investigators completed a quality control check-list upon checking the completed questionnaires.

Blood samples were taken from a sub-sample of the population. More specifically, all participants were invited to provide blood samples for biochemical – hematological evaluation. Of them, 1197 (26.2% of total population; 28.7% of adult population) agreed; no age distribution differences were found between the total population and those who provided blood sample ($p = 0.677$). Each of these individuals visited one of the 5 mobile units where medical and anthropometrics were completed (please see Additional file 1: Table S3). All samples were collected in the morning, between 8:00 and 10:00 am, upon having fasted for at least 10 h. To assure compliance all individuals were asked if they had fasted and when their last meal was.

Experienced field investigators were from various scientific fields (dietitians, physicians, sociologists as well as dietetic and medical students), and received specialized training on the HNNHS fieldwork protocol. These specialists were involved in the development, methodology and application of study questionnaires and protocol procedure attainment was assessed with quality control testing, during field-investigation.

Ethical approval and consent form

The study was approved by the Ethics Committee of the Department of Food Science and Human Nutrition of the Agricultural University of Athens. It was also approved by Hellenic Data Protection Authority (HDPA). All members of the staff signed confidentiality agreements. Adult volunteers were asked to sign the consent form. For minors < 13 years of age the parent or primary guardian signed the form and for volunteers between 13 and 18 years of age the consent form was asked to be signed by both (parent/ guardian and volunteer).

Questionnaires in brief

All questionnaires used in HNNHS, were derived based on a priori knowledge and from components of previously validated questionnaires. For this process. The outcome of interest and previous work performed in the Greek population were also considered.

For demographic characteristics (marital status, education, health insurance, employment, income and changes in employment and/or income during the economic crisis) components from NHANES [12], Behavioral Risk Factor Surveillance System (BRFSS) study [13] and NDNS [14], questionnaires were used.

The Quality of Life (QoL) questionnaire included components of (i) QoL and chronic pain components of the Healthy Days Module developed by the Center for Disease Control (CDC) [15], (ii) questions with regards to self-reported height, weight and oral health, from the Health Survey for England and the Activity Limitations Module (also CDC developed) [16].

Two questionnaires were developed for alcohol consumption; one for minors and the second for adults. For minors (≥12 years old and < 18 years old) the questionnaire was developed based on questions from the Youth Risk Behavior Survey [17], the European School Survey Project and other Drugs [18] and the Global School-based Student Health Survey (GSHS) [19]. For the adult questionnaire data from NHANES study [12], BRFSS [13], Arkansas Cardiovascular Health Examination Survey (ARCHES) [20] and Recommended Alcohol Questions by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) [21] were used. Volunteers were classified as alcohol or non-alcohol consumers, based on their intake over the past 30 days. Frequency of alcohol intake among "consumers" was categorized as daily, weekly or monthly, based on their response on (i) total drinks per month consumed, (ii) drinks per week and/or (iii) drinks per month. For minors, the total number of individuals that reported having consumed an alcoholic drink at some point in life (and not just few sips) was reported.

As in the case of alcohol consumption, smoking habits questionnaire(s) were also based on volunteer's age. In

particular, for adults questionnaires used were from the NHANES [12] and BRFSS [13] studies; for minors from the Youth Behavior Survey [17], NHANES [12] and the European School Survey Project on Alcohol and other Drugs [18]. Volunteers were grouped into (i) current smokers, if they responded that they had smoked the past month, (ii) ever smokers, if they had smoked at any point in their life, and (iii) non-smokers, if they had never smoked. Frequency of smoking, among current smokers, was also recorded as "daily" or "sometimes". Among minors, the question referred as to whether they had ever tried to smoke (aged up to 19 years).

Weight status was evaluated according to BMI. Body mass Index (BMI) is defined as the weight (in kg) over height (in meters squared). Cut-offs used (all in kg/m^2) for assessment are widely used and are the following (adults): < 18.5, underweight; 18.5–24.9, normal weight; 25–29.9, overweight; > 30, obese.

Physical activity has a well-known role as a health determinant hence the aim was to assess physical activity levels in all ages. Questionnaires on physical activity were modified based on age groups as per a priori knowledge, including (i) ≥2- < 12 years old of the questionnaire was based on questions from the NHANES survey [22] and Preschool-aged Children Physical Activity Questionnaire (Pre-PAQ Home Version) [23] (ii) ≥12- < 18 years old, the International Physical Questionnaire – Adolescents (IPAQ-A) [24], (iii) ≥18 years- < 65 years old the IPAQ short form was used [25] and (iv) for ≥65 years of age a modified version of the IPAQ has been suggested [26]. Preliminary results reported in this study include level of physical activity as perceived by the adult volunteers (sedentary, low, moderate and active) or by the primary care giver if the volunteer was < 12 years old.

Information about medical history for disease prevalence among the Greek population, related medical treatment and insurance coverage were collected. The synthesis of this questionnaire was based on the National Health Survey, NHANES [12], ARCHES [20], and the Million Women Study [27]. The definition of clinical investigated outcomes was based on the International Classification of Diseases (ICD)-10th version, recorded by experienced study investigators. Diabetes was defined as fasting blood glucose> 125 mg/dl or if on diabetic medication; dyslipidemia if total triglycerides> 150 mg/dl and/or total cholesterol> 200 mg/dl or on lipid-lowering medication; hypertension as average blood pressure greater or equal to 140/90 mmHg, or on antihypertensive treatment.

Further details on specific disease states (hypertension, dyslipidemia, diabetes) with specific questionnaires [20], were collected once the volunteer declared as having such a condition. In particular, data on prevalence of Chronic Obstructive Pulmonary Disease (COPD) was obtained using the COPD Population Screener [28] and Asthma using the questionnaire from the Hellenic Thoracic Society (for adults), and the Greek version of the questionnaire International Study of Asthma and Allergies in Childhood (ISAAC) [29] (minors 6–18 years old). Following a literature review the Rose Questionnaire for Angina [30] and the Edinburgh Claudication Questionnaire were used in HNNHS [31].

Additional the types of questionnaires used in the study can be viewed in the Additional files 1 and 2 and they included information on breastfeeding, drug and supplement use, memory impairment (≥45 years old), eating habits and behavior (as previously reiterated), sleeping habits, data on depression, stress (acute and chronic) & health locus of control, gestational & childbirth related questions, environmental exposure, functional gastrointestinal disorders, vitamin D intake status & sun exposure, and economic crisis, to acquire adequate and substantial information on the population's exposures and risks. Details for each of these questionnaires will be provided upon analysis.

Clinical/ physical evaluation and biochemical variables

HNNHS also included physical examination (temperature, spirometry, blood pressure, etc.), anthropometry (weight, height, waist and hip circumference, body composition, and grip strength), and several blood tests (glucose, HbA1c (diabetics), insulin, total lipid profile, thyroid hormones, thyroglobulin, PTH, complete blood count, folic acid, iron, ferritin, B_{12}, 25OH-vitamin D, creatine, urea, albumin, total protein, ALT, AST, bilirubin, uric acid, calcium, magnesium, manganese, selenium, hs-CRP, cortisol, and heavy metals, namely As, Cd, Co, Hg, Mo, Pb, Pt, Sb, W, Zn, Ce, La, Th, U) in a subsample of the population, to examine correlations with various health indices in later analyses (Additional file 1: Table S3).

Statistics

Prior to analysis, data were cross checked for missing values and outliers. Missing information was corrected if the information was derived from other questionnaires and/or measurements (non-reported values of weight and height were completed if the individual was measured at the CAPI). Also, individuals responding as non-diseased but reported taking a disease related medication, were classified as with disease outcome. Baseline socio-demographic are presented as frequencies and percentage (N, %) per gender. Variables of interest are presented in total and per gender and age-group (i.e., population's weight status, smoking, alcohol, physical activity, prevalence of chronic disease), while physical activity is presented by specific age groups (as per questionnaires). Chi-square test was used to assess gender differences by age group for weight status, smoking and

alcohol intake, and for total prevalence of chronic disease by gender. Tukey's paired means test was used to detect differences between age groups (for each chronic diseases). All reported p-values were based on two-sided hypothesis tests, with significance level at 5%. The statistical models were computed using STATA 12.0 (STATA corp. Texas).

Results

Demographic data

The sample was distributed in all different regions of Greece (Table 1). 47.2% was in the region of Attica, 18.5% Central Macedonia, and the rest of the sample being scattered through various regions of Greece (1.3% Epirus, 4.2% Eastern Macedonia and Thrace, 3.1% Peloponnese, 2.2% Western Macedonia, 5.2% Thessaly, 2.3% Central Greece, 4.8% Western Greece, 5.7% Crete, 1.1% Ionian islands, 2% North Aegean and 1.9% South Aegean).

The total number of participants is 4574 volunteers of which 1943 were males and 2629 females. Table 2 shows distribution per gender, age and socioeconomic parameters. Age distribution was representative of the 2011 Census, with 19% ($N = 869$) of the sampled population being 0–19 years old, 67% ($N = 3064$), 20–64 years old, and 14% ($N = 639$) were ≥ 65 years old. Marital status was as follows: 40.6% of the population was unmarried (43.3% males and 38.5% females), 48.4% married (51.4% males and 46.4% females) and 0.1% having a cohabitation agreement 6.2% were widowers (2.2% males and 9.2% females), 3.8% divorced and 0.7% separated.

Educational level greatly varied with approximately 32% having a University degree or greater, 7.1% had completed secondary education. Approximately 17% of the population had limited to low education, 27.1% completed lyceum (12 years of schooling), 5% technical secondary school and 8.3% private post-lyceum college. A large percentage of the population (78.3%; 77.8% males and 78.8% females) reported having public health insurance whereas only 4.3% had private insurance and 8.9% both types. A total of 8% males and 6.2% females were not insured (Table 2).

In terms of net monthly income (Table 2), 13,5% had low income (<€300–850), 11.4% had €851–1050, approximately 18% had moderate high income (€1051–1500), 10.6% had €1501–1900, 9.1% had €1901–2400, and 10.7% had high income (€2401–3800 and > €3801).

Weight status and behavioral data

Sample's self-reported weight status in total by age group (> 20 years old) and gender based on Body Mass Index (BMI) can be found in Table 3. A total prevalence of 47.5% of the adult population was overweight (32%) and obese (15.5%), with the prevalence increasing with age in both genders. A significant body weight status difference was found in each age group, with males having a higher prevalence of overweight compared to females ($p < 0.001$) in all age groups.

Frequency of alcohol consumption among adults was 72.4% (Table 4), with approximately 7% reporting daily consumption, 33% weekly and 60% on a monthly basis. A significant greater percentage of males reported of being alcohol consumers than females (81.1% compared to 67%, respectively; $p < 0.001$) and being more frequent alcohol consumers as well ($p < 0.001$). Among minors (12 to 19 years of age, inclusive), 111 out of 340 individuals (32.6%) reported as having consumed an alcoholic drink at some point before, and not only a few sips (Table 4). No significant differences were found between genders among minors in alcohol consumption ($p = 0.121$).

Smoking frequency in the total population among adults and minors, per gender, is being shown in Table 5. Approximately 34% of the population were current smokers, whereas 50.9% reported on having smoked at some point in their life. Significant gender differences were found in both cases with a higher proportion of males reporting to have smoked (59% compared to 44%) or of being current smokers (38.3% compared to 30.8; $p < 0.001$ for all). Among current smokers 87.3% reported to smoke daily with a borderline difference found between genders ($p = 0.046$). A total of 22% of minors (up to 19 years of age, inclusive) reported of having tried to smoke at some point. No significant gender differences were found ($p = 0.229$).

Preliminary results of physical activity level were self-reported as sedentary, low activity, moderately and very active (Table 6). The highest proportion of the population being very active was in young children (2–12 years old, 68.6%) and among adolescents (48.5%). Twenty – 5 % (25%) of adults aged 18–65 and > 65 years old reported being very active whereas 20% of the elderly (> 65) reported of having a completely sedentary lifestyle.

Prevalence of chronic disease

In Table 7, the prevalence of various chronic diseases is presented in total and per age group (20–39, 40–64, and 65+) in adults. In each category, gender specific rates can also be viewed. The highest prevalence (16.7%) was reported for hyperlipidemia (increased cholesterol or triglycerides), with prevalence increasing in both genders with age (Tukey's test $p < 0.001$ between groups). The same pattern was found for hypertension with the prevalence mounting to 56% (51.2% in males, 61% in females; $p < 0.05$) in the elderly compared to 1.7% in adults aged 20–39 and 17.3% in the 40–65 age group (Tukey's test not significant). Accordingly, age patterns were seen in all CVD (CHD, angina, MI, heart failure, arrhythmia and stroke), with significant age group differences found only

Table 2 Volunteer baseline socio-demographic characteristics by gender

	Males		Females	
	N	%	N	%
	1943	42.5	2629	57.5
Age				
0–19	426	21.9	443	16.9
20–64[a]	1259	64.8	1805	68.7
20–39	*797*	*41.0*	*1040*	*39.6*
40–65	*462*	*23.8*	*765*	*29.1*
65+	258	13.3	381	14.5
Marital status				
Unmarried	841	43.3	1012	38.5
Married	998	51.4	1217	46.3
Cohabitation agreement	2	0.1	2	0.1
Widower	43	2.2	241	9.2
Divorced	47	2.4	127	4.8
Separated	10	0.5	23	0.9
Don't know	–	–	1	0
Refused	–	–	4	0.2
Educational level				
No or little education	25	1.6	90	4
Primary school	128	8.2	224	9.9
Gymnasium	81	5.2	99	4.4
Lyceum	418	26.7	621	27.3
Technical school	133	8.5	57	2.5
Private college (Post Lyceum)	114	7.3	204	9
University degree (AEI)	336	21.5	517	22.7
University degree (TEI)	144	9.2	219	9.6
Master's degree	109	7	188	8.3
PhD	31	2	22	1
Refused	4	0.3	3	0.1
Net monthly income (€)				
≤ 300	76	3.9	106	4
301–650	148	7.6	285	10.8
651–850	171	8.8	264	10
851–1050	237	12.2	283	10.8
1051–1250	172	8.9	236	9
1251–1500	178	9.2	237	9
1501–1900	222	11.4	264	10
1901–2400	183	9.4	231	8.8
2401–3800	177	9.1	202	7.7
> 3801	51	2.6	59	2.2
Don't know	122	6.3	214	8.1
Refused	204	10.5	246	9.4
Health insurance				
Uninsured	156	8	162	6.2
Insured, private	91	4.7	105	4
Insured, public	1511	77.8	2071	78.8
Insured, both private and public	157	8.1	252	9.6
Don't know	10	0.5	20	0.8
Refused	4	0.2	3	0.1

[a]The sampled population (N%) in the age group 20–64, was further categorized to 20–39 years and 40–65 to cross-reference with further analysis performed in these sub-categories

in heart failure (Tukey's test $p = 0.014$ for 65+ compared to 20–39 years). Diabetes prevalence and osteoporosis was also considerably higher in the older age group (16,8%) compared to 3.8% in total population and 16.2% compared to 5.4%, respectively. Only osteoporosis was significantly different between age groups ($p < 0.001$ for 65+ and 20–39 and 40–64). The prevalence of thyroid disease was high in all age groups, especially in females and significantly different between the 65+ and 20–39-year-old age groups (Tukey's test $p = 0.026$). A significant difference was also found in cancer prevalence between the older and younger adult age groups (Tukey's test, $p = 0.033$).

Gender differences and chronic disease

Significant gender differences were found in hyperlipidemia, arrhythmia, cancer, thyroid disease, osteoporosis, arthritis/rheumatoid arthritis, irritable bowel syndrome, depression, and chronic stress, with females having a significantly higher proportion in each one of them. Prevalence of asthma and cancer was also higher in females, more specifically in the 40–64 age group (4.8% vs. 1.7%; $p < 0.05$ and 3.7% vs. 0.6%; $p < 0.01$, respectively). Gender difference was also found in CHD with males having a higher prevalence in the total adult sample and in the older group ($p < 0.001$, for all). The prevalence of MI did not differ in the total sample but was significantly higher in males over 65 years old than females in the same age group (9.1% vs. 1.9%; $p < 0.001$). Diabetes mellitus was significantly higher in males aged 40–64 years old than females of the same age group (5.9% vs. 2.7%; $p < 0.01$).

Discussion

The HNNHS was set up in 2013 with the aim to provide comprehensive, nutrition and health information, on a representative sample of the Greek population. Preliminary results of the HNNHS study showed an elevated

Table 3 Population's weight status in total by age group and gender based on Body Mass Index (BMI) categorization

Weight status categorization[d]	Total		By age group[e] and gender					
	Total adult population[e]		20-39[a]		40-64[b]		65+[c]	
			N (%)		N (%)		N (%)	
	N	%	M	F	M	F	M	F
Underweight	175	4.7	12 (1.5)	88 (8.5)	5 (1.1)	25 (3.3)	8 (3.1)	37 (9.8)
Normal weight	1772	47.9	420 (52.7)	722 (69.5)	139(30.2)	335 (43.8)	60 (23.3)	94 (24.8)
Overweight	1183	32.0	285 (35.8)	160(15.4)	212 (46.0)	244 (31.9)	127 (49.2)	154 (40.6)
Obese total	572	15.5	80 (10.0)	69 (6.6)	105 (22.8)	161 (21.1)	63 (24.4)	94 (24.8)

N (%) Frequency (percentage), *M* males, *F* Females
By gender: % of males or females in question compared to total number of males or females, respectively
[a]Chi square test for difference in weight status between genders in 20–39-year-old group ($p < 0.001$)
[b]Chi square test for difference in weight status between genders in 40–65-year-old group ($p < 0.001$)
[c]Chi square test for difference in weight status between genders in 65+ year-old group ($p < 0.006$)
[d]Based on BMI (kg/m^2) categorization: < 18.5 = underweight; 20–25 = normal weight; > 25–30 = overweight; > 30 = obese
[e]Study population ≥ 20 years of age; Chi square test for difference in weight status between age groups in total ($p < .001$) and per gender ($p < .001$)

prevalence of overweight and obesity in adults as well as dyslipidemia and hypertension. Among the adult population prevalence of overweight & obesity was almost 47%, significantly varying by gender, 17% of the total population had dyslipidemia, 13% hypertension and about 4% had diabetes and 14% were affected by a form of thyroidism. All outcomes significantly increased with age with prevalence of dyslipidemia and hypertension reaching 45 and 57% in the elderly, respectively. Furthermore, the prevalence of osteoporosis in Greek women over 65 year of age was 25.8%, a disease that is highly preventable.

In more detail, prevalence of overweight and obesity as well as chronic diseases increased with age with males having overall a higher weight status than females. This is in accordance with data from NHANES showing increased levels of obesity in adults, by sex, age and ethnicity. Hyperlipidemia prevalence in 2011 in Greece was 15% [32], and results from the ATTICA study reported that 1 in 2 adults (45 ± 15) years old was dyslipidemic [33].This is in accordance with current results from HNNHS (44,8% in total; 39.9% in males and 48.3% in females). High levels of hypertension and hyperlipidemia were also found in other studies [34, 35]and policies targeting the reduction of these public health outcomes are warranted as were developed by other countries upon findings [34, 35]. Participation rate was higher in females than males, as has been reported in most European countries [36].

Table 4 Frequency of alcohol consumption habits in minors and adults in total and by gender

Adults (20+ years)	Alcohol consumption*						
	Total		Males		Females		Level of significance [a]
	N	%	N	%	N	%	
The past 30 days*							
No	998	26.9	285	18.8	713	32.8	$p < 0.001$
Yes	2685	72.4	1229	81.1	1454	67.0	
Frequency							
Everyday	183	6.8	128	10.4	55	3.8	$p < 0.001$
Weekly	874	32.6	456	37.1	418	28.8	
Monthly	1628	60.6	645	52.5	981	67.5	
Minors (12–19 years) **							
Ever consumed							
No	229	67.4	142	89.3	153	84.5	$p = 0.121$
Yes	111	32.6	17	10.7	28	15.5	
Don't know	1	0.5					
Refused	–	–					

*For adults (20 + years of age: $N = 3705$ in total, 7 missing): any alcohol consumption the past 30 days and frequency of consumption
**For minors (12–20 years of age, $N = 340$, 159 males and 181 females): whole alcoholic drink consumed at some point in life (and not just few sips). 66 minors were < 18 years and 45 18 &19 years old
[a]Tested via chi square test for gender differences in adult population (20 years +) and in minors (up to 19 years); *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$;

Table 5 Frequency of smoking habits in total population among adults and minors by gender

Adults (20+ years)	Smoking**						
	Total		Males		Females		Level of significance[b]
	N	%	N	%	N	%	
Ever smoked							
No	1935	52.4	620	41.0	1215	56.0	$p < 0.001$
Yes	1878	50.9	893	59.0	955	44.0	
The past 30 days*							
No	2433	65.7	934	61.5	1497	68.5	$p < 0.001$
Yes	1252	33.8	580	38.2	672	30.8	
Frequency							
Every day[a]	1093	87.3	519	89.5	574	85.4	$P = 0.046$
Some days[a]	158	12.6	60	10.3	98	14.6	
Don't know	1	0.1					
Refused	–	–					
Minors (10–19 years)							
Ever smoked							
No	100	76.3	33	70.2	67	79.8	$p = 0.229$
Yes	29	22.1	12	25.5	17	20.2	
Don't know	1	0.8					
Refused	1	0.8					

*For adults (> 19 years of age: 3705 in total): ever smoking; for minors specified if they even tried it (then response yes)
[a]For adults smoking the past 30 days (frequency (%) of smoking for smokers $N = 1252$)
[b]Tested via chi square test for gender differences in adult population (20 years +) and in minors (up to 19 years); *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$;

The proportion of alcohol consumption and current smoking status was high, although the latter, prevalence of smoking, was lower compared to previous findings in the Hellenic population [37]. An alarming proportion of minors had tried alcohol or had smoked at some point. Smoking is a known risk factor for many chronic diseases, including cardiovascular disease, many forms of cancer, asthma and COPD. Alcohol, although has been found to have protective effects on CVD, when consumed in moderation [38], it is forbidden in minors.

Regarding arterial hypertension, the present study's preliminary results are comparable with other studies where hypertension was self-reported (13.1% vs. 13.3%, respectively, $n = 5003$) [39]. As hypertension is a common risk factor of cardiovascular disease, data on level of awareness is warranted. Efstratopoulos et al., found an awareness level of 60.2% among Greek hypertensive individuals [40], therefore, further investigation is warranted. The prevalence of hypertension in the NHANES study, for those ≥20 years old was also close to the EPIC and HYPERTENSHELL studies (33.5%) [41]. A 4% prevalence of diabetes mellitus was found in this study, reaching 6.3% for adults over 30 years of age, compared to 7–11% prevalence reported in Greece among adults [33, 42, 43]. HNNHS included information on thyroid and renal function, for which there are no data available in the Greek population. Respective prevalence levels of 13.7 and 0.6% of those ≥20 years old were reported. The increased prevalence in all types of thyroid

Table 6 Physical activity levels among different age groups based on self reported data

Physical activity*	≥2 - < 12 years		≥12 - < 18 years		≥18 - < 65 years		≥65 years old	
	N	%	N	%	N	%	N	%
Secentary way of life	–	–	–	–	–	–	128	20
Low activity	15	3.2	24	11.7	584	18.3	117	18.3
Moderate active, average	126	26.7	74	35.9	1357	42.4	205	32.1
Very active	324	68.6	100	48.5	812	25.4	160	25
Don't know	–	–	1	0.5	2	0.1	1	0.2
Refuse to respond	–	–	–	–	2	0.1	–	–

*Individuals were asked to report their perceived physical activity status or to state their child's if they responded on their behalf

Table 7 Prevalence of chronic disease in adult population sampled, in total, by gender and by gender and age group

Presence of disease/condition	Total				By gender and age group[a]					
	Total sample		By Gender[b] N (%)		20–39 N (%)		40–64 N (%)		65+ N (%)	
	N	%	M	F	M	F	M	F	M	F
Increased cholesterol or triglycerides[c]	765	16.7	297*** (15.2)	468 (17.8)	62** (7.8)	48 (4.6)	127 (27.6)	226 (29.5)	103* (39.9)	183 (48.3)
Don't know	175	3.8								
Hypertension	608	13.3	241 (12.4)	367 (14.0)	21* (2.6)	11 (1.1)	88 (19.1)	124 (16.2)	132* (51.2)	231 (61.0)
	47	1.0								
Coronary Heart Disease	69	1.8	53*** (3.4)	16 (0.7)	0 (0)	1 (0.1)	17 (3.7)	1 (0.1)	36*** (14.0)	14 (3.7)
Don't know	32	0.8								
Angina	36	0.9	19 (1.2)	17 (0.8)	6 (0.8)	4 (0.4)	6 (1.3)	2 (0.3)	7 (2.7)	10 (2.6)
Don't know	31	0.8								
Myocardial Infarction (Heart attack)	49	1.3	37 (2.4)	12 (0.5)	0	0	16** (3.3)	5 (0.7)	21*** (8.1)	7 (1.9)
Don't know	13	0.3								
Heart failure	42	1.1	16 (1.0)	26 (1.1)	0	3 (0.3)	2 (0.4)	8 (1.1)	14 (5.0)	15 (4.0)
Don't know	27	0.7								
Arrhythmia	295	7.7	91** (5.8)	204 (9.0)	21 (2.6)	48 (4.6)	25 (5.4)	71 (9.3)	45 (17.4)	78 (20.6)
Don't know	42	1.1								
Stroke	41	1.1	18 (1.1)	23 (1.0)	1 (0.1)	2 (0.2)	3 (0.7)	4 (0.5)	14 (5.4)	17 (4.5)
Don't know	11	0.3								
Cancer	53	1.2	14** (0.7)	39 (1.5)	3 (0.4)	1 (0.1)	3** (0.6)	28 (3.7)	8 (3.1)	10 (2.6)
Don't know	8	0.2								
Diabetes (Type I & II)[d]	162	3.6	73 (3.8)	89 (3.4)	3 (0.4)	4 (0.4)	27** (5.9)	21 (2.7)	42 (16.3)	64 (16.9)
Don't know	24	0.5								
Thyroid (any type of condition)[e]	629	13.8	93*** (4.8)	536 (20.4)	36*** (4.5)	160 (15.4)	26*** (5.6)	248 (32.4)	24*** (9.3)	113 (29.8)
Don't know	102	2.2								
Asthma	184	4.0	69 (3.6)	115 (4.4)	40 (5.0)	48 (4.6)	8* (1.7)	37 (4.8)	6 (2.3)	20 (5.3)
Don't know	16	0.4								
Chronic Obstructive Pulmonary Disease (COPD)	63	1.6	25 (1.6)	38 (1.7)	5 (0.6)	8 (0.8)	9 (2.0)	15 (2.0)	11 (4.3)	15 (4.0)
Don't know	77	0.6								
Chronic kidney disease	27	0.6	13 (0.7)	14 (0.5)	3 (0.4)	1 (0.1)	2 (0.4)	4 (0.5)	8 (3.1)	9 (2.4)
Don't know	3	0.1								
Osteoporosis[f]	206	5.4	13*** (0.8)	193 (8.3)	1 (0.1)	3 (0.3)	4*** (0.9)	95 (12.3)	8*** (3.1)	95 (25.8)
Don't know	79	2.1								
Arthritis/ Rheumatoid disease	324	7.1	65*** (3.3)	259 (9.9)	9* (1.1)	23 (2.2)	28*** (6.1)	106 (13.9)	28*** (10.8)	128 (33.8)
Don't know	83	1.8								
Crohn's disease or Ulcerative colitis	16	0.4	6 (0.3)	10 (0.4)	2 (0.2)	3 (0.3)	1 (0.2)	6 (0.8)	3 (1.2)	1 (0.3)
Don't know	6	0.1								
Irritable Bowel Syndrome (IBS)	317	6.9	53*** (2.7)	264 (10.1)	25*** (3.1)	105 (10.1)	18*** (3.9)	121 (15.8)	9* (3.5)	35 (9.2)

Table 7 Prevalence of chronic disease in adult population sampled, in total, by gender and by gender and age group *(Continued)*

Presence of disease/condition	Total				By gender and age group[a]					
	Total sample		By Gender[b] N (%)		20–39 N (%)		40–64 N (%)		65+ N (%)	
	N	%	M	F	M	F	M	F	M	F
Don't know	46	1.0								
Depression	180	4.2	42*** (2.3)	138 (5.6)	15 (1.9)	33 (3.2)	12*** (2.6)	62 (8.1)	15 (5.8)	42 (11.1)
Don't know	63	1.5								
Chronic Stress	495	11.6	128*** (7.1)	367 (14.9)	56*** (7.0)	143 (13.8)	42*** (9.1)	134 (17.5)	25** (9.7)	78 (20.6)
Don't know	39	0.9								

By gender: % of males or females who reported as having the outcome in question compared to total number of males or females, respectively
By age-group: Number of outcomes reported per gender in each age-group (%)
[a]Tested via chi square test for gender differences by age group
[b]tested via chi square test for gender differences in total sample; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$
[c]3.5% of the sample replied that they do not know for cholesterol; < 1% for hypertension, coronary heart disease, angina, myocardial infarction (0.3), stroke (0.3), heart failure,; arrhythmia (1.1%), diabetes (0.53), 2.2% for any thyroid disease, asthma (0.35%), chronic obstructive pulmonary disorder (0.63%). Kidney failure (0.1%), 2.1% for osteoporosis, 1.8% for arthritis, 0.1% for Crohn's disease, 1.0% for irritable bowel syndrome, 1.5% for depression, 0.91% for chronic stress
[d]Prevalence for type I diabetes: 3/4754
[e]0–19 age group: for thyroid disease: Males (1.6%) and females (3.4%); For asthma: Males (3.5%), Females (2.3%); For chronic stress: Males 1.55%, females 4.3%
[f]Out of which 13 osteopenia

conditions (hypothyroidism, hyperthyroidism, Hashimoto thyroiditis), especially among women, underlies the value of HNNHS and stresses the need to further investigate risk factors linked to this outcome, such as iodine and vitamin D status, as well as nutritional intake and search for deficiencies. The prevalence of cardiovascular disease, the leading cause of mortality worldwide, found in the study population was 13.9%, in total. This included 7.7% of the total sample that reported having arrhythmia, 1.8% coronary heart disease, 1.3% myocardial infarction, 0.9% angina, 1.1 heart failure, and 1.1% had suffered a stroke.

Furthermore, an increased level of stress-associated disorders including chronic perceived stress (11.6%), depression (4.2%), Crohn's disease (0.4%) or ulcerative colitis (0,4%), and irritable bowel syndrome (6.9%) were found. These outcomes may be associated with the economic crisis seen in Greece over the past years but can also be linked to various nutritional and behavioral factors, that need to be examined. Interestingly, data with regards to perceived change in household budget show that most volunteers perceived change being more severe in 2012 (23.2%) than 2011 (18.3%) and 2013 (12.6%). Details that may have affected these stress-associated disorders, remain to be investigated.

Limitations

Due to the cross-sectional nature of the study, no causal relationships can be formulated. Also, the data presented and analyzed in this first report are from reported data. However, experienced field investigators checked the data and recorded clinical outcomes based on ICD-10th version codes. Furthermore, sensitive personal questions, were self-completed to decrease reporting bias. All clinical outcome data were further cross-checked with other related questions, ie, medications, in order to accurately code the participants and decrease misclassification. Reporting of data in more depth and comparison with other past small, non-nationally representative surveys in Greece are beyond the scope of this first methodological publication and will be described elsewhere.

Strengths

Health surveys as HNNHS can reveal target groups in need for prevention strategies according to educational level, employment and marital status, area of residence in a subnational level, and health behavior [40, 44]. HNNHS, is the first national representative study performed in Greece to assess nutrition and health status of the population including all age groups. Questionnaires used were constructed after performing an extensive literature review and based on other validated questionnaires that have been used in other large national studies and in the Greek population. Another strength is the synergistic action of multiple health care specialists in study design, filed work and data analysis. Furthermore, the use of the especially designed computer software, CAPI, increases reliability of collected data, since it reduces response bias, misclassification and volunteer burden. Measurements, clinical assessment and blood tests performed in a subsample of the population will be used to further validate the preliminary results presented here.

Conclusions

The HNNHS study aims to evaluate the health of the Greek population. The data presented provide a preliminary overview of demographic and lifestyle data of the population. We envision that this study will provide valuable information regarding the health of the Greek population and that it will become a rolling program that will facilitate the development and evaluation of public health policies addressing key risk factors that impact on the health of the Greek population.

Additional files

Additional file 1: Table S1. List of questionnaires applied to volunteers according to age during the initial interview. **Table S2.** List of questionnaires to be self-completed at home, according to age. **Table S3.** List of exams and questionnaires applied to volunteers, according to age, during their visit to the mobile unit. (DOCX 38 kb)

Additional file 2: 3 worksheets (All, Males, Females) for age adjusted chronic disease calculations, standardized by Hellenic population distribution (2011 Census). (XLSX 35 kb)

Abbreviations

ARCHES: Arkansas Cardiovascular Health Examination Survey; BRFSS: Behavioral Risk Factor Surveillance System; CAPI: Computer Assisted Personal Interview; CDC: Centre for Disease Control; CHD: Coronary Heart Disease; COPD: Chronic Obstructive Pulmonary Disease; CVD: Cardiovascular disease; DM: Diabetes Mellitus; EFSA: European Food Safety Authority; EPIC: European Prospective Investigation into Cancer and Nutrition; FGID: Functional Gastrointestinal Disorders; FPQ: Food Propensity Questionnaire; GS–S: Global School-based Student Health Survey; HDPA: Hellenic Data Protection Authority; HNNHS: Hellenic National Nutrition and Health Survey; IPAQ: International Physical Activity Questionnaire; ISAAC: International Study of Asthma and Allergies in Childhood; MI: Myocardial Infarction; MRC: Medical Research Council; NatCen: NatCen Social Research; NDNS: National Diet and Nutrition Survey; NDSR: Nutrition Data System for Research; NHANES: National Health and Nutrition Examination Survey; NIAAA: National Institute on Alcohol Abuse and Alcoholism; OR: Odds ratio; QoL: Quality of Life; USA: United States of America

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

AZ conceptualized, designed and was the Principal Investigator of the study. AZ and RM coordinated the design of the data collection instruments, coordinated and supervised data collection. GM supervised medical data collection. ID, DK, AVM and IB were involved in every step of the study and made substantial contributions to the design and methodology of data collection as well as the acquisition of data and training of field workers. TN coordinated mobile unit data collection. SMT and KA contributed to the mobile unit data collection and analysis. DBP coordinated sample collection methodology. ID drafted the manuscript equally with EM. EM also supervised the design and the preparation of the data base and carried out the statistical analyses and revised the manuscript. GD, CG, EF, EMT, ET, TES, AV, ES, MC, AK, GK, SZ and AP contributed to parts of methodology. All the authors approved the final manuscript as submitted. Contributors: EF, ET, TS, AV, ES, MC, AT, GK, SZ, AP contributed to the writing of the protocols and the data collection on the field. All contributors approved the final manuscript as submitted. Advisory Committee: GC, GD, GD, IM and ER acted as external advisory committee. All the Advisory Committee members approved the final manuscript as submitted. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Department of Food Science and Human Nutrition of the Agricultural University of Athens. It was also approved by Hellenic Data Protection Authority. All members of staff signed confidentiality agreements and all participants, as well as the parent/ guardian when required, were asked to sign a consent form.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.
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4. General discussion

To our knowledge this is the first study that aims to examine and identify the factors associated with 25(OH)D concentration <20 ng/ml in Greek adults. Based on a literature review, performed at the time when the research protocol was developed, probable factors that could influence serum 25(OH)D levels were identified. Consequently, questionnaires were developed in order to assess those factors and later used the acquired data to identify which and to what extent can influence serum 25(OH)D levels.

Based on the IoM cut-offs (IOM 2011), 28.8% is characterized deficient, 36% has insufficient concentration, 35.1% sufficient concentration and 0.1% high concentration. These are comparable with studies from Greece (Katrinaki et al. 2016, Papadakis et al. 2015), Europe (Cashman et al. 2016) and the rest of the world (Palacios and Gonzalez 2014, Schleicher et al. 2016). There were no significant differences in serum 25(OH)D concentration observed between males and females as in other reports (Verdoia et al. 2015).

An additional finding of this study was that less than 1% of the Greek population enrolled in the study met the EAR for vitamin D intake across all ages and gender groups, whereas none met the RDA, highlighting the need for prevention policies. In this section of the PhD thesis the prevalence of low serum 25(OH)D concentration as well as the factors that can have an impact on that prevalence in comparison with other studies will be discussed in detail. Vitamin D food intake and major food contributors will also be discussed as well as an example of a food fortification and its effect on increased intake at population level.

Vitamin D deficiency and insufficiency have been of concern recently with a worldwide review reporting that 37.3% of studies found mean values of 25(OH)D concentration <20 ng/ml with the subtotal for males being 22.3 ng/ml and for females 21.3 ng/ml (Hilger et al. 2014). In accordance to our results, high prevalence of deficiency has been reported in previous studies (Cashman et al. 2016, Grigoriou et al. 2018, Hilger et al. 2014, Katrinaki et al. 2016, Livingstone et al. 2017, Papadakis et al. 2015, Spiro and Buttriss 2014) with a review reporting 35-75% of adults from Mediterranean countries having serum 25(OH)D concentration <20ng/ml (54% of Greek adults) (Manios et al. 2017).

These studies have taken place in more than 40 countries worldwide many of which in Europe (Hilger et al. 2014, Spiro and Buttriss 2014). Included studies were cross-sectional or cohort where vitamin D status was measured, whereas studies where status was estimated, rather than measured, were excluded. Most studies included a random sample. Therefore, the prevalence of low serum 25(OH)D reported in other studies is very similar to the one reported from our study.

With regards to which factors could potentially influence prevalence of low serum 25(OH)D, in our study and considering the total sample (both males and females), associated with lower odds of serum 25(OH)D concentration <20 ng/ml were being very active, supplement intake, increased sun exposure and darker skin colour. Spring season of blood sample collection was associated with higher odds of deficiency.

Concerning season of blood sample collection, reports from Greece (Katrinaki et al. 2016, Papadakis et al. 2015), Europe (Manios et al. 2017) as well as non-European counties (Bolland et al. 2008, Grigoriou et al. 2018, Kasahara et al. 2013, Levis et al. 2005) showed that the highest prevalence of serum 25(OH)D concentration <20 ng/ml was during March. In our study no blood samples were collected during August and September compared to others (Manios et al. 2017) which reported lowest prevalence during July-September. Lowest prevalence was observed in October after which it increases and peaks in March. This is explained by higher sun exposure during summer and spring where 24% & 13% have sun exposure >3 h/d compared to 7% during fall and winter.

Another important factor that can influence serum 25(OH)D levels exposure to sun/ ultraviolet radiation. In our study, sun exposure was associated with lower odds of low serum 25(OH)D concentration. However, even though 0-1 or 1-3 hours/day might seem adequate for vitamin D skin synthesis and Greece has adequate UVB availability all year round (O'Neill et al. 2016), we have to consider that data is self-reported, that the majority of the skin might be covered by clothing, especially during the winter months, and that little might be exposed to the sun rays. Also, participants might have included time exposed in the sun when behind a glass (e.g. inside a building or a car) that acts as a barrier of UVB rays' submission (Duarte et al. 2009). These factors probably explain why, although significantly associated with serum 25(OH)D levels, the hours of sun exposure reported in our sample were not enough to prevent levels below 20 ng/ml. Furthermore, for cultural or

health reasons people might be avoiding sun exposure. Similar trends have been reported in sunny countries in the past (Gannage-Yared et al. 2000, Lips 2010, Mishal 2001).

Furthermore, in our study, darker skin was associated with lower odds, which is contradictory to other findings; this cannot be explained by longer sun exposure as it is the same across all skin colour categories (Pearson's chi-square test P=0.064). This controversy might be because almost all subjects are of Caucasian origin in contrast with other countries where a higher proportion is of non-Caucasian origin who differ physiologically and culturally (SACN 2016). Only 7% of the sample has dark or very dark skin compared to 60% that has light or medium light and therefore associations could be influenced by sample size.

With regards to supplements, in the total sample intake was associated with lower odds of low serum 25(OH)D concentration. Approximately 6% of males and 8% of females reported consuming supplements, and <1% of males & 3.9% of females receiving ≥10 mcg/ day and 3.7% receiving <10 mcg/day. The significant sex difference can be explained by the higher prevalence of osteoporosis in women compared to men as reported in previous findings (8.3% vs. 0.8% in adults) (Magriplis et al. 2019). Regarding other European countries a gradient between countries in the south and those in the north has been reported with regards to use of dietary supplements (Skeie et al. 2009). In more detail, the highest consumption was observed in Norway (61.7% in females) and the lowest in Greece (6.7% in females and 0.5% in males).

Other studies reported a positive effect of physical activity on 25(OH)D concentration adequacy which is hypothesized to be due to increased sun exposure (SACN 2016) however there seems to be an effect irrespective of sun exposure as the same has been observed for indoor activity (Wanner et al. 2015). The main factors that influenced the odds of having 25(OH)D levels <20ng/ml were sun exposure and season of blood collection.

In males, with increasing sun exposure, the odds of low serum 25(OH)D were lower. Spring season of blood sample collection was associated with higher odds of serum 25(OH)D deficiency/insufficiency, probably because of the low levels of sun exposure during preceding months. As previously suggested (Manios et al. 2011), this seasonal difference in 25(OH)D concentrations could possibly be improved with the consumption of fortified products. Supplement use might not have been significantly associated with lower

odds of deficiency, in males, due to the small sample size of male individuals that were receiving vitamin D containing supplements.

The latter, as previously mentioned, could probably be explained by the lower prevalence of osteoporosis in males and/or lower degree of actively checking for osteoporosis in comparison to females, and hence reduced supplemental intake. Smoking, as per other reports, was associated with higher odds of serum 25(OH)D concentration <20 ng/ml, in males, and it is hypothesized that smoking impairs conversion of 25(OH)D to 1,25(OH)D (Mulligan et al. 2014).

In females, obesity was associated with higher odds of low serum 25(OH)D concentration. The lipophilic nature of adipose tissue is hypothesized to act as sequester of vitamin D, rather than storage, and studies have reported increases in 25(OH)D concentration with weight reduction in obese individuals (SACN 2016). The exact mechanisms remain unclear (IOM 2011).

Supplement use and sun exposure were associated with lower odds as was darker skin. The association of supplement use, in females, with lower odds of serum 25(OH)D <20 ng/ml, in contrast with males, could probably be explained by higher supplemental intake in females. Season of blood sample collection was not significantly correlated with 25(OH)D concentration however a seasonal difference in supplement intake was observed. Women taking ≥10 μg/day via supplements were more likely to be taking it during Spring (43.2%) and Winter (25%) than during the Summer (18.2%) and Fall (13.6%). This could be the result of their perception that during Summer sunlight exposure is adequate for synthesis. In accordance with other studies, our biochemical data also show a negative correlation between serum PTH concentration and 25(OH)D concentration (Chapuy et al. 1997, Looker et al. 2008, Sai et al. 2011) but it was not significant in the model.

Concerning both genders and with regards to vitamin D food intake our results our similar to those that have been reported from other studies in Greece as well as internationally where intakes were well below the EAR of 10 mcg/ day (Au et al. 2013, Bailey et al. 2010, Freisling et al. 2010, Manios et al. 2014, Moore et al. 2004, Ross et al. 2011, Spiro and Buttriss 2014). It is noteworthy that in an EFSA report, including intakes from 14 European countries, a mean dietary intake ranging from 1.1 to 8.2 mcg/day was observed (EFSA 2012).

In the United States, were milk and cereals are fortified, intakes are higher (3.9-7.0 μg/day) (Moore et al. 2004). Higher intakes are also observed in European countries except Spain where there is also no fortification law and intake is 1.6-1.7 μg/day (Hilger et al. 2014). Although, dietary assessment methodologies vary between European countries, a notable discrepancy between intakes and recommendations exists (Hilger et al. 2014).

In our study and in both genders, probably due to the very low intakes observed, vitamin D intake from food did not significantly influence the odds of low serum 25(OH)D concentration probably because most individuals had extremely low intakes. In another recent study, it was showed that European participants with higher intakes of vitamin D from food had higher 25(OH)D concentrations (Livingstone et al. 2017).

The low vitamin D intake can be explained as very few foods naturally contain vitamin D (IOM 2011), and include fish, especially fatty fish; other sources are milk, meat, eggs and fortified products, such as cereals (Spiro and Buttriss 2014). Requirements, however, were developed to cover population's needs for health, hence other means to cover these requirements, through food and or supplements are potentially needed.

As many factors associated with vitamin D status are modifiable, including dietary intake, sunlight exposure and supplement use this study aimed at identifying strategies in order to reduce deficiency levels. This was demonstrated with an example of milk fortification, a food consumed regularly by most individuals in all age and gender groups, where a moderate fortification (about 7 mcg/ 100g of milk) would cover EAR recommendations for over half of the population, in respect to their current estimated vitamin D intakes.

Major contributors to dietary vitamin D intake in our study were fish, meat and cereals, with these varying between gender. Compared to other European countries fish contributes 70% of vitamin D from food intake in Spain (18-64 years old) (AESAN 2011), 38% in France (ANSES 2013), 25% in the UK (19-64 years old) (Bates et al. 2015), 12-16% (12% for those 18-64 years, 16% for those ≥65 years) in Ireland (Spiro and Buttriss 2014) and only 8-11% in the Netherlands (8% in 7-69 years old and 11% in ≥70 years old) (DNFCS 2011, Ocke et al. 2013), compared to 46% in HNNHS.

In our study, the dietary contribution of meat was 15% whereas in the UK meat contributes to 22% of vitamin D from food intake (19-64 years old) (Bates et al. 2015), in

Ireland 22-30% (30% for 18-64 years old, 22% for ≥65 years old) (Spiro and Buttriss 2014), in Spain 2% (AESAN 2011) and in the Netherlands 12-20% (20% in those 7-69 years old and 12% in those aged ≥70 years old) (DNFCS 2011, Ocke et al. 2013).

Finally, cereals contributed 12% to the vitamin D intake in our study, as in the UK (12% in males and 13% in females) (Spiro and Buttriss 2014), compared to 4% in Spain 4% (AESAN 2011) and to 2-5% in Irish adults (Spiro and Buttriss 2014).

Vitamin D can also be obtained via exposure to sunlight; however, many avoid sun exposure or use sunscreens to reduce the risk of melanoma. Supplements are also an option, especially during the winter months or for people with minimal sunlight exposure (Cashman and Kiely 2014). The latter were accounted for in the study, and intake remained extremely low, demonstrating again the need for preventive programs.

Milk was chosen as the most appropriate and practical example for Greece, as it can be consumed daily by all age groups and is also a very good source of calcium, and phosphorus, nutrients with a vital role in bone health. Fish and meat cannot be fortified. Cereals could be fortified, however, as most of the cereal products consumed in Greece are imported, this would complicate the implementation of such a policy.

In addition, cereals, in general, contain high amounts of sugar and any public health policy to increase their intake could provoke controversial results. Another potential food for fortification, which does not contribute vitamin D, could be flour. Nevertheless, most consumers in Greece buy bread from many different local bakeries and producers rather than from a few companies as is the case in other countries and implementation would be much more difficult and impractical.

According to our estimations, even a low level (7-10 mcg per 100g of milk, which is approximately 100ml) of milk fortification could improve vitamin D intake of the population without increasing the risk of toxicity (UL of vitamin D is 100 mcg/day). A higher level of fortification (e.g. 20 mcg/ 100g of milk) could increase the risk of toxicity in some age and gender groups, especially in female individuals ≥71 years old, who regularly consume vitamin D supplements for osteoporosis at a level of 25-75 mcg/day.

Our study examined other fortification scenarios for the adult (≥19 years) population where the UL is set at 100 mcg/ day (for those ≥9 years). However, milk is a food product that is consumed regularly by children as well, where the UL is 63 mcg/ day for children 1-

3 years old and 75 mcg/ day for children 4-8 years old. Therefore, when considering the implementation of fortification scenarios, safe consumption data also referring to children must be taken into consideration not to exceed the UL in any population group. Likewise, one should consider the presence of subjects with lactose intolerance and milk protein allergies, in whom food vitamin D should be taken via other foods or as a supplement.

Due to the nature of the study, some limitations should be considered. Firstly, no causal relationships can be drawn, since it is a cross-sectional study. Most participants lived in urban areas and therefore we were unable to explore differences between urban vs. semi-urban regions (0.37% from non-urban regions). However, in Greece, most of the population reside in metropolitan areas. In addition, we did not explore ethnic differences as <1% of the sample were of non-Caucasian race.

Although this study is cross-sectional in nature, the results are strengthened by its design. It included a representative sample of the Greek population, in all age groups, and dietary intake was assessed using the most advanced research tools and standardized procedures following European and International guidelines (e.g. AMPM, food atlases).

In addition, assessment of intake included all days of the week, as well as all twelve months and, therefore, effects due to seasonal variation in consumption of foods is minimized, and the NRC method was used in determining final intake to account for within and between individual variation. Moreover, fortification scenarios were performed based on actual consumption data, to provide specific results that public health officials can use as primary information.

Also, sunlight exposure and complete vitamin D status need to be accounted for before implementation. The geographical latitude of Greece, despite the amount of sunlight, require those residing in Greece to have a larger amount of sunlight exposure for synthesis, an area of contradiction with skin health. In addition, although extreme intakes and misreporters were excluded this could have created a biased sample as some misreporters could have been reporting true intake.

5. Conclusions

Vitamin D deficiency is the most common nutritional deficiency in the world. Its link with skeletal health and probably with other health outcomes increases the importance of reducing the prevalence of low serum 25(OH)D concentration at population level. Although it is influenced by many factors there are factors, like for example food and supplement intake, a change in which can bring a significant improvement.

In our study, prevalence of low serum 25(OH)D deficiency is high in Greek adults of both genders. More than two thirds of our study population have insufficient levels. Dietary intake among the Greek population, is also extremely low, below the EAR levels, placing the population at multiple risks.

In our study, the odds of having serum 25(OH)D concentration <20 ng/ml significantly decreased with being very active, having increased duration of sun exposure and having lighter skin colour, but increased with obesity and spring season of blood sample collection.

According to the IoM cut-off levels for vitamin D deficiency, one third of the adult Greek population is deficient, 36.0% has insufficient levels and just 35.1% sufficient. There were no significant differences in serum 25(OH)D levels between males and females nor between different age groups. The highest prevalence of 25(OH)D levels <20 ng/ml during March (end of Winter, beginning of Spring season).

In addition, there were significant differences in serum 25(OH)D concentration for the total sample (P=0.03) as well as for males (P=0.002) and females (P=0.03) per season of blood sample collection with higher prevalence of 25(OH)D concentration <20 ng/ml during Spring, as per total sample.

The results from the present thesis can offer a valuable tool towards the development of relevant policies that could probably revert this epidemic. Given vitamin D's possible link to several diseases, relevant actions and policies to correct deficiency and reduce prevalence, need to be taken.

Food fortification and vitamin D supplements are two options towards that goal. Longer but safe sun exposure could offer an additional effective and low-cost strategy for 25(OH)D

deficiency prevention. Food fortification policies have not yet been formulated, potentially because of insufficient data. This study increases public health awareness on the need for preventive public health strategies, even in areas where sunlight is found in abundance. In addition, it can be used by health care professionals in order to better assess and treat low serum 25(OH)D levels.

6. Future work

This PhD thesis adds to the growing literature regarding low serum 25(OH)D levels. Further research that could deepen our understanding on how to improve vitamin D intake and status includes the following:

i) Actual measurement of how much of an impact can food fortification have on serum 25(OH)D concentration and therefore status in the Greek population.

ii) Identify other, presently unknown, factors that could possibly influence serum vitamin D levels.

iii) Estimate the prevalence of low serum vitamin D and level of food intake in individuals <18 years old in the Greek population.

iv) Explore associations that serum vitamin D levels might have with health outcomes in the Greek population.

v) Develop an optimal algorithm at individual level, if there can possibly be one, in order to estimate an ideal combination of sun exposure and vitamin D intake (from food and supplements) that could reduce the percentage of the population with low serum 25(OH)D concentration without increasing the risk of melanoma.

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8. Appendix (Questionnaires used for this study)

Έντυπο Συγκατάθεσης Συμμετέχοντα

Πανελλαδική **Με**λέτη **Δ**ιατροφής και **Υ**γείας

	Για ηλικίες ≥18 ετών	
	ΝΑΙ (Σημειώστε με ✓)	**ΟΧΙ (Σημειώστε με ✓)**
➢ **Βεβαιώνω ότι έχω διαβάσει και κατανοήσει το ενημερωτικό φυλλάδιο σχετικά με την ανωτέρω μελέτη και ότι μου δόθηκε η δυνατότητα να κάνω διευκρινιστικές ερωτήσεις, οι οποίες και απαντήθηκαν πλήρως.**	☐	☐
➢ **Κατανοώ ότι η συμμετοχή μου στη μελέτη είναι εθελοντική και ότι μπορώ να την ανακαλέσω οποτεδήποτε, καθώς και ότι τα προσωπικά μου δεδομένα είναι ανώνυμα και απόρρητα και ότι θα χρησιμοποιηθούν αποκλειστικά για τους σκοπούς της μελέτης.**	☐	☐
➢ **Συναινώ στη συμπλήρωση όλων των ερωτηματολογίων που περιλαμβάνονται στη μελέτη.**	☐	☐
➢ Συναινώ στην πραγματοποίηση των εξετάσεων και των μετρήσεων σχετικών με διατροφή και υγεία που περιλαμβάνονται στη μελέτη.	☐	☐
➢ Συναινώ στην αποθήκευση των βιολογικών δειγμάτων που συλλέχθηκαν για μελλοντική τους χρήση για περαιτέρω αναλύσεις/ εξετάσεις σχετικές με διατροφή και υγεία.	☐	☐
➢ Συναινώ στην αποθήκευση των βιολογικών δειγμάτων που συλλέχθηκαν για μελλοντική τους χρήση για γενετικές αναλύσεις/ εξετάσεις.	☐	☐
➢ Επιθυμώ την επαναπροσέγγισή μου έως 31 Δεκέμβρη 2020 για να εξεταστεί το ενδεχόμενο συμμετοχής μου σε μελλοντική μελέτη διατροφής και υγείας.	☐	☐

Για τον συμμετέχοντα/ τη συμμετέχουσα

_____/_____/_____ _____

Όνομα, Επίθετο *(κεφαλαία)* Πατρώνυμο Υπογραφή Ημερομηνία *(ΗΗ/ΜΜ/ΕΕΕΕ)*

Για το/ τη νόμιμο εκπρόσωπο του συμμετέχοντα/ της συμμετέχουσας

_____/_____/_____ _____

Όνομα, Επίθετο *(κεφαλαία)* Πατρώνυμο Υπογραφή Ημερομηνία *(ΗΗ/ΜΜ/ΕΕΕΕ)*

Για τον ερευνητή/ την ερευνήτρια της μελέτης

_____/_____/_____ _____

Όνομα, Επίθετο *(κεφαλαία)* Πατρώνυμο Υπογραφή Ημερομηνία *(ΗΗ/ΜΜ/ΕΕΕΕ)*

Ελάχιστη προϋπόθεση για τη συμμετοχή στην ΠΑ.ΜΕ.Δ.Υ. είναι η συμπλήρωση των ερωτηματολογίων που περιλαμβάνει.

«Δημογραφικά/ Κοινωνικο-Οικονομικά Χαρακτηριστικά»
Ημερομηνία: _ _ /_ _/ _ _ _ _
Ηλικία ΕΣ: _ _ Φύλο ΕΣ: _____

ΚΩΔΙΚΟΣ ΕΘΕΛΟΝΤΗ	**3**

≥6 μηνών

ΤΜΗΜΑ 1. ΟΙΚΟΓΕΝΕΙΑΚΗ ΚΑΤΑΣΤΑΣΗ

ΔΚΧ 1. Ποια είναι η οικογενειακή σας κατάσταση; {Στην περίπτωση που ο συμμετέχοντας είναι κάτω των 18 ετών η ερώτηση αφορά στην οικογενειακή κατάσταση του γονέα ή του κηδεμόνα.}

1. Άγαμος/η 2. Έγγαμος/η 3. Με σύμφωνο συμβίωσης 4. Χήρος/α 5. Διαζευγμένος/η
6. Σε διάσταση 777. ΔΞ 999. ΔΑ

Μου είπατε ότι στο σπίτι σας κατοικούν, μαζί με εσάς, Χ άτομα. {Επιβεβαίωση απάντησης από την ερώτηση ΕΕ1 του ερωτηματολογίου επιλεξιμότητας.}

ΔΚΧ 2. Πόσα άτομα συνολικά, μαζί με εσάς, συντηρούνται από τον προϋπολογισμό του νοικοκυριού, είτε συνεισφέρουν σε αυτόν είτε όχι, και ανεξάρτητα από το αν διαμένουν ή όχι στο σπίτι σας;

1. ☐☐ (αριθμός ατόμων 0-20) 777. ΔΞ 999. ΔΑ

ΤΜΗΜΑ 2. ΕΚΠΑΙΔΕΥΣΗ

≥18 ετών

ΔΚΧ 3. Ποιο είναι το ανώτερο επίπεδο σπουδών που έχετε ολοκληρώσει; {Καταγράφεται η εκπαιδευτική βαθμίδα που ο συμμετέχοντας έχει ολοκληρώσει κατά την ημέρα διενέργειας της συνέντευξης. Για όσους παρακολουθούν κάποια βαθμίδα εκπαίδευσης, θα καταχωρηθεί το επίπεδο εκπαίδευσης το οποίο έχει ήδη ολοκληρωθεί π.χ. αν ο συμμετέχοντας παρακολουθεί μαθήματα σε κάποιο ανώτατο εκπαιδευτικό ίδρυμα, θα απαντήσει ότι έχει ολοκληρώσει το Λύκειο.} **ΔΕΙΞΤΕ ΚΑΡΤΑ 1**

Ανώτατο επίπεδο σπουδών
1. Δεν παρακολούθησα ποτέ καμία βαθμίδα εκπαίδευσης/ Μερικές τάξεις του Δημοτικού
2. Απολυτήριο Δημοτικού Σχολείου
3. Απολυτήριο Γυμνασίου
4. Απολυτήριο Λυκείου ή Εξατάξιου Γυμνασίου
5. Απολυτήριο Τεχνικού Λυκείου, Σχολής Μαθητείας ΟΑΕΔ
6. Πτυχίο ΙΕΚ, Ιδιωτικού Κολλεγίου, Κέντρου ελευθέρων Σπουδών
7. Πτυχίο ΑΕΙ
8. Πτυχίο ΤΕΙ, ΑΤΕΙ
9. Κάτοχος Μεταπτυχιακού Τίτλου Σπουδών
10. Κάτοχος Διδακτορικού
11. Άλλο, προσδιορίστε:
777. ΔΞ
999. ΔΑ

ΤΜΗΜΑ 3. ΑΣΦΑΛΕΙΑ ΥΓΕΙΑΣ ΚΑΙ ΧΡΗΣΗ ΥΠΗΡΕΣΙΩΝ ΥΓΕΙΑΣ

≥ 6 μηνών

ΔΚΧ 4. Διαθέτετε ασφάλεια υγείας;

1. Ναι → 1. Ιδιωτική
→ 2. Δημόσια
→ 3. Ιδιωτική και Δημόσια
→ 777. ΔΞ
→ 999. ΔΑ

0. Όχι 777. ΔΞ 999. ΔΑ

ΔΚΧ 5. Συνολικά τον τελευταίο χρόνο αντιμετωπίσατε κάποιο θέμα υγείας ώστε να χρειάστηκε να απευθυνθείτε σε κάποια από τις υπηρεσίες υγείας; {Ναι ή Όχι} {Αν ναι:} **ΔΕΙΞΤΕ ΚΑΡΤΑ 2 Για ποιο λόγο; Επιλέξτε έναν ή περισσότερους λόγους.**

1.Ναι
- 1. Προληπτικές εξετάσεις
- 2. Συμπτώματα ή προσωρινή ασθένεια όπως κρύωμα ή τραυματισμός
- 3. Αντιμετώπιση χρόνιας ασθένειας ή χρόνιου προβλήματος υγείας
- 4. Συνταγογράφηση
- 5. Οδοντίατρος
- 6.Άλλη αιτία, προσδιορίστε_____
- 777. ΔΞ
- 999. ΔΑ

0. Όχι 777. ΔΞ 999. ΔΑ

ΤΜΗΜΑ 4. ΑΠΑΣΧΟΛΗΣΗ

≥ 2 ετών

{Για συμμετέχοντες ≥12 ετών} ΔΚΧ 6α. Με τι ασχολείσθε σήμερα; Επιλέξτε μία ή περισσότερες απαντήσεις. Για παράδειγμα, αν είστε φοιτητής και εργάζεστε επιλέξτε 1 και 7.
{Για συμμετέχοντες ≥2- <5 ετών} ΔΚΧ 6β. Πηγαίνει το παιδί σας παιδικό σταθμό ή νηπιαγωγείο;
{Για συμμετέχοντες ≥5- <12 ετών} ΔΚΧ 6γ. Πηγαίνει το παιδί σας σχολείο; {Αν ναι: **Σε ποια τάξη;**}
ΔΕΙΞΤΕ ΚΑΡΤΑ 3

Απασχόληση	**Αν 4 ή 5**
1. Εργαζόμενος/η (Περιλαμβάνονται και άμισθοι βοηθοί στην οικογενειακή επιχείρηση, οι μαθητευόμενοι με αμοιβή, καθώς και όσοι προσωρινά απουσιάζουν από την εργασία τους λόγω άδειας μητρότητας, γονικής άδειας, ασθένειας ή είναι σε διακοπές)	1. Παιδικός σταθμός 2. Νηπιαγωγείο 3. Δημοτικό. Σε ποια τάξη 1. Α' Δημοτικού 2. Β' Δημοτικού 3. Γ' Δημοτικού 4. Δ' Δημοτικού 5. Ε' Δημοτικού 6. Στ' Δημοτικού 4. Γυμνάσιο. Σε ποια τάξη; 1. Α' Γυμνασίου 2. Β' Γυμνασίου 3. Γ' Γυμνασίου 5. Λύκειο. Σε ποια τάξη; Α' Λυκείου Β' Λυκείου Γ' Λυκείου
2. Σε καθεστώς διαθεσιμότητας	
3. Άνεργος/η	
4. Μαθητής	
5. Παρακολουθεί κατ' οίκον διδασκαλία	
6. Δεν πηγαίνει σχολείο	
7. Φοιτητής, μετεκπαιδευόμενος, μαθητευόμενος χωρίς αμοιβή για απόκτηση εμπειρίας	
8. Συνταξιούχος, σε κανονική ή πρόωρη συνταξιοδότηση ή έχετε διακόψει τις εργασίες της επιχείρησής σας	
9. Μόνιμη αναπηρία (Περιλαμβάνονται και όσοι έχουν μακροχρόνια προβλήματα υγείας ή ασθένεια) Συνταξιούχοι λόγω αναπηρίας	
10. Στρατιώτης {όχι στρατιωτικός που είναι το 1.}	
11. Οικιακά	
12. Άλλο, προσδιορίστε:	
777. ΔΞ	
999. ΔΑ	

! {Αν η απάντηση στην ερώτηση ΔΚΧ 6 είναι:
1. Εργαζόμενος συνεχίστε στην 7
2. Σε καθεστώς διαθεσιμότητας συνεχίστε στην 8α
3. Άνεργος συνεχίστε στην 8β
8. Συνταξιούχος συνεχίστε στην 8γ
Σε κάθε άλλη περίπτωση προχωρήστε στην 14}

! Αν στην ερώτηση 6 έχουν επιλεγεί περισσότερες από μία απαντήσεις, τότε ισχύουν οι συνθήκες για όλες τις επιλογές.

3

≥ 16 ετών

ΔΚΧ 7. Ως τυπική εβδομάδα θεωρείται μία συνηθισμένη εβδομάδα κατά τη διάρκεια της χρονιάς και όχι απαραίτητα η τελευταία εβδομάδα. Σε μία τυπική εβδομάδα, συμπεριλαμβανομένου του σαββατοκύριακου, πόσες ημέρες και πόσες ώρες εργάζεστε, συνολικά για όλες τις δουλειές σε περίπτωση που εργάζεστε σε περισσότερες από μία;

1. ☐ (αριθμός ημερών) ή Εύρος ☐-☐
Και ☐☐☐ (αριθμός ωρών) ή Εύρος ☐☐☐- ☐☐☐ 777. ΔΞ 999. ΔΑ

Πόσες από τις ώρες αυτές είναι από υπερωριακή απασχόληση;

☐☐☐ (αριθμός ωρών) 777. ΔΞ 999. ΔΑ

{Προχωρήστε στην ερώτηση ΔΚΧ 9α.}

{ΜΟΝΟ ΣΕ ΚΑΘΕΣΤΩΣ ΔΙΑΘΕΣΙΜΟΤΗΤΑΣ} ΔΚΧ 8α. Πόσο καιρό είστε σε διαθεσιμότητα;

1. Εισάγετε χρονικό διάστημα ☐☐ και κυκλώστε μονάδα χρόνου: Ημέρες, Εβδομάδες, Μήνες Χρόνια
777. ΔΞ 999. ΔΑ

{Προχωρήστε στην ερώτηση ΔΚΧ 9β.}

{ΜΟΝΟ ΣΕ ΑΝΕΡΓΟΥΣ} ΔΚΧ 8β. Πόσο καιρό είστε άνεργος;

1. Εισάγετε χρονικό διάστημα ☐☐ και κυκλώστε μονάδα χρόνου: Ημέρες, Εβδομάδες, Μήνες Χρόνια
777. ΔΞ 999. ΔΑ

{Προχωρήστε στην ερώτηση ΔΚΧ 9β.}

{ΜΟΝΟ ΣΕ ΣΥΝΤΑΞΙΟΥΧΟΥΣ ή ΔΙΑΚΟΠΗ ΕΡΓΑΣΙΑΣ} ΔΚΧ 8γ. Πόσο καιρό είστε συνταξιούχος ή έχετε διακόψει την εργασία σας;

1. Εισάγετε χρονικό διάστημα ☐☐ και κυκλώστε μονάδα χρόνου: Ημέρες, Εβδομάδες, Μήνες Χρόνια ή
Έτος συνταξιοδότησης ☐☐☐☐ 777. ΔΞ 999. ΔΑ

{Προχωρήστε στην ερώτηση ΔΚΧ 9β.}

ΔΚΧ 9α. Ποια είναι η <u>κύρια</u> απασχόλησή σας; {π.χ. υπάλληλος ΔΕΗ- γραμματέας, υπάλληλος ΔΕΗ- διευθυντής, υπάλληλος ΔΕΗ- τεχνικός} {Στην περίπτωση που ο συμμετέχοντας έχει παραπάνω από μία εργασίες, ως κύρια εργασία θεωρείται αυτή που ο συμμετέχοντας θα υποδείξει ή σε περίπτωση που ο συμμετέχοντας αδυνατεί, αυτή στην οποία εργάζεται τις περισσότερες ώρες.}

1. _____(περιγραφή/ τίτλος εργασίας)
777. ΔΞ 999. ΔΑ

{Αν απαντήθηκε η 9α προχωρήστε στη 10.}

ΔΚΧ 9β. Ποια ήταν η <u>κύρια</u> απασχόλησή σας {πριν μείνετε άνεργος, πριν τεθείτε σε διαθεσιμότητα, πριν από τη συνταξιοδότησή σας ή πριν από τη διακοπή της εργασίας σας;} {π.χ. υπάλληλος ΔΕΗ- γραμματέας, υπάλληλος ΔΕΗ- διευθυντής, υπάλληλος ΔΕΗ- τεχνικός}. {Στην περίπτωση που ο συμμετέχοντας έχει παραπάνω από μία εργασίες, ως κύρια εργασία θεωρείται αυτή που ο συμμετέχοντας θα υποδείξει ή σε περίπτωση που ο συμμετέχοντας αδυνατεί, αυτή στην οποία εργάζεται τις περισσότερες ώρες.}

1. _____(περιγραφή/ τίτλος εργασίας)
2. Δεν έχω εργαστεί ποτέ 777. ΔΞ 999. ΔΑ

{Αν στην ΔΚΧ 9β δόθηκε η απάντηση 2 "Δεν έχω εργαστεί ποτέ", προχωρήστε στην ΔΚΧ 11.}

ΔΚΧ 10. Για πόσο διάστημα {κάνετε/ κάνατε} τη συγκεκριμένη εργασία;

1. Εισάγετε χρονικό διάστημα ☐☐ και κυκλώστε μονάδα χρόνου: Ημέρες, Εβδομάδες, Μήνες Χρόνια
777. ΔΞ 999. ΔΑ

<u>! Αν στην ερώτηση 8γ η απάντηση είναι έτος πριν από το 2008 ή διάστημα ≥6 ετών προχωρήστε στην ερώτηση ΔΚΧ 13.</u>

ΔΚΧ 11. Έχει αλλάξει η επαγγελματική σας κατάσταση εξαιτίας της οικονομικής κρίσης; {Αν ναι: **Με ποιον τρόπο;**} **ΔΕΙΞΤΕ ΚΑΡΤΑ 4**

1. Ναι-----> Με ποιόν τρόπο;
   - 1. Απόλυση από την εργασία
   - 2. Πρόωρη συνταξιοδότηση λόγω οικονομικής κρίσης
   - 3. Μετάβαση σε καθεστώς διαθεσιμότητας
   - 4. Μετάβαση σε καθεστώς μερικής απασχόλησης
   - 5. Αλλαγή επαγγέλματος
   - 6. Απασχόληση σε επιπρόσθετη θέση εργασίας
   - 7. Άλλο, προσδιορίστε _____
   - 777. ΔΞ
   - 999. ΔΑ

0. Όχι 777. ΔΞ 999. ΔΑ

{Αν η απάντηση στην ερώτηση ΔΚΧ 11 είναι «Όχι», «ΔΞ», «ΔΑ» προχωρήστε στην ερώτηση ΔΚΧ 13.}

ΔΚΧ 12. Ποια χρονιά συνέβη αυτή η αλλαγή στην επαγγελματική σας κατάσταση εξαιτίας της οικονομικής κρίσης;

1. ☐☐☐☐ (ΕΕΕΕ) 777. ΔΞ 999.ΔΑ

ΔΚΧ 13. Ως καθαρές αποδοχές θεωρούνται οι αποδοχές που λαμβάνετε αφού αφαιρεθούν από αυτές ο φόρος που παρακρατήθηκε και οι εισφορές για την κοινωνική ασφάλιση. Έχουν αλλάξει οι καθαρές μηνιαίες αποδοχές από όλες τις πηγές, εξαιτίας της οικονομικής κρίσης;

1. Ναι-----> Με ποιόν τρόπο;
   - 1. Μειώθηκαν
     - 1. Λίγο
     - 2. Αρκετά
     - 3. Πολύ
   - 2. Αυξήθηκαν
     - 1. Λίγο
     - 2. Αρκετά
     - 3. Πολύ
   - 777. ΔΞ
     - 777. ΔΞ
     - 999. ΔΑ
   - 999. ΔΑ

0. Όχι, παρέμειναν ίδιες 777. ΔΞ 999. ΔΑ

≥6 μηνών

ΔΚΧ 14. Ποια χρονιά αντιληφθήκατε σημαντική αλλαγή στον προϋπολογισμό του νοικοκυριού σας, έσοδα από όλες τις πηγές και έξοδα, εξαιτίας της οικονομικής κρίσης;

1. ☐☐☐☐ (ΕΕΕΕ) 2. Δεν εχει αλλάξει 777. ΔΞ 999. ΔΑ

ΤΜΗΜΑ 5. ΕΙΣΟΔΗΜΑ

≥6 μηνών

(Θα ήθελα εδώ να σας υπενθυμίσω ότι όλα τα δεδομένα που συλλέγονται είναι εμπιστευτικά. Κανείς άλλος δεν θα λάβει γνώση των στοιχείων αυτών. Τα στοιχεία αυτά θα χρησιμοποιηθούν ανώνυμα για την ανάλυση δεικτών και τη εξαγωγή συμπερασμάτων σημαντικών για την υγεία του ελληνικού πληθυσμού.)

ΔΚΧ 15. Ποιο είναι το συνολικό καθαρό μηνιαίο εισόδημα του νοικοκυριού σας από {όλα τα μέλη} <u>και όλες τις πηγές</u>; Στην κάρτα αυτή, <u>ΔΕΙΞΤΕ ΚΑΡΤΑ 5</u>, υπάρχουν κάποια παραδείγματα πηγών εισοδήματος. Στην κάρτα αυτή, <u>ΔΕΙΞΤΕ ΚΑΡΤΑ 6</u> βλέπετε μία σειρά από εισοδήματα που συνοδεύονται από έναν αριθμό. Θα ήθελα να επιλέξετε την απάντηση που ταιριάζει καλύτερα στο καθαρό μηνιαίο εισόδημα του νοικοκυριού σας και να μου πείτε τον αριθμό που της αντιστοιχεί.

ΕΙΣΟΔΗΜΑ ΝΟΙΚΟΚΥΡΙΟΥ {Αριθμός απάντησης ή 777. ΔΞ, 999. ΔΑ}

- Πόσο χρόνο σας πήρε η συμπλήρωση του ερωτηματολογίου;☐☐ Λεπτά
- Ποιος απάντησε το ερωτηματολόγιο;
  ☐Ο ίδιος/ Η ίδια ☐Η μητέρα ☐Ο πατέρας ☐Άλλος, προσδιορίστε_____
- Βοηθός συνέντευξης _____
- Λόγος διακοπής συνέντευξης:_____

Σχόλια
Για συγκεκριμένες ερωτήσεις του ερωτηματολογίου:

Για το σύνολο του ερωτηματολογίου:

«Ερωτηματολόγιο Πρόσληψης Βιταμίνης D»
Κωδ. ΕΣ: _ _ _ _ _ _ _ _ _ _ _ _ _ _ **Ημερομηνία:** _ _ /_ _/ _ _ _ _ **Ηλικία ΕΣ:** _ _

≥ 6 μηνών

ΤΜΗΜΑ 1. ΕΚΘΕΣΗ ΣΤΟΝ ΗΛΙΟ

VitD1. Τους τελευταίους 12 μήνες, κατά μέσο όρο, πόσες ώρες ανά ημέρα εκτεθήκατε στον ήλιο τις καθημερινές; Σκεφτείτε τις ώρες που περάσατε στον ήλιο στην εργασίας σας, στις δραστηριότητες του ελεύθερου χρόνου σας όπως αθλήματα, κηπουρική, καθώς και στις διακοπές σας.

	Καλοκαίρι	**Φθινόπωρο**	**Άνοιξη**	**Χειμώνας**
Ώρες/ημέρα	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ

VitD2. Τους τελευταίους 12 μήνες, κατά μέσο όρο, πόσες ώρες ανά ημέρα εκτεθήκατε στον ήλιο το σαββατοκύριακο; Σκεφτείτε τις ώρες που περάσατε στον ήλιο στην εργασίας σας, στις δραστηριότητες του ελεύθερου χρόνου σας όπως αθλήματα, κηπουρική, καθώς και στις διακοπές σας.

	Καλοκαίρι	**Φθινόπωρο**	**Άνοιξη**	**Χειμώνας**
Ώρες/ημέρα	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ	1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες 6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ

VitD3. Τις τελευταίες 30 ημέρες , κατά μέσο όρο, πόσες ώρες ανά ημέρα εκτεθήκατε στον ήλιο μεταξύ 10 το πρωί και 5 το απόγευμα;
1. 30 λεπτά ή και λιγότερο 2. 31 λεπτά-1 ώρα 3. 1-2 ώρες 4. 2-3 ώρες 5. 3-4 ώρες
6. 4-5 ώρες 7. 5-6 ώρες 8. 6 ώρες 777. ΔΞ 999. ΔΑ

VitD4. Χρησιμοποιείτε κάποια μέθοδο τεχνητού μαυρίσματος που να περιλαμβάνει έκθεση σε ακτινοβολία όπως π.χ. solarium;
1. Ναι 0. Όχι 777.ΔΞ 999.ΔΑ

VitD5. Πώς θα περιγράφατε το χρώμα του δέρματός σας;

1. Πολύ ανοιχτόχρωμο 2. Ανοιχτόχρωμο 3. Μέτρια ανοιχτόχρωμο
4. Ελαφρώς σκουρόχρωμο 5. Σκουρόχρωμο 6. Πολύ σκούρο 777. ΔΞ 999. ΔΑ

VitD6. Χρησιμοποιείτε αντηλιακό στο σώμα σας, όχι στο πρόσωπο ή το λαιμό, όταν είστε σε εξωτερικό χώρο στον ήλιο μεταξύ 10 το πρωί και 5 το απόγευμα				
Το Καλοκαίρι;	1. Ναι	1. Ναι	1. Ναι	1. Ναι
Το Φθινόπωρο;	0. Όχι	0. Όχι	0. Όχι	0. Όχι
Την Άνοιξη;	777. ΔΞ	777. ΔΞ	777. ΔΞ	777. ΔΞ
Το Χειμώνα;	999. ΔΑ	999. ΔΑ	999. ΔΑ	999. ΔΑ

VitD7. Το αντηλιακό που χρησιμοποιείτε στο σώμα σας, όχι στο πρόσωπο ή το λαιμό, τί δείκτη προστασίας έχει;

1. 4 2. 8 3. 10 4. 15 5. 20 6. 30 7. 40 8. 50+ 777. ΔΞ 999. ΔΑ

- Πόσο χρόνο σας πήρε η συμπλήρωση του ερωτηματολογίου; ☐☐ Λεπτά
- Ποιος απάντησε το ερωτηματολόγιο; ☐Η μητέρα ☐Ο πατέρας ☐Άλλος, _____
- Λόγος διακοπής συνέντευξης:_____ _____

Σχόλια

Για συγκεκριμένες ερωτήσεις του ερωτηματολογίου:

Για το σύνολο του ερωτηματολογίου:

«Φάρμακα και Συμπληρώματα Διατροφής»
Ημερομηνία: _ _ /_ _/ _ _ _ _
Ηλικία ΕΣ: _ _ Φύλο ΕΣ: _____

ΚΩΔΙΚΟΣ	8
ΕΘΕΛΟΝΤΗ	

≥6 μηνών

ΦΑ 1. Τις τελευταίες 30 ημέρες, πήρατε φάρμακα ή συμπληρώματα διατροφής;
(Αναφερόμαστε σε όλα τα φάρμακα, δηλαδή: χάπια, κάψουλες, σιρόπι, υπόθετα, ενέσεις, σταγόνες, σπρέι, σκόνη, αλοιφές και αυτοκόλλητα, και στα συμπληρώματα διατροφής. Τα Συμπληρώματα Διατροφής αποτελούν συμπυκνωμένες πηγές θρεπτικών συστατικών ή άλλων ουσιών και χρησιμοποιούνται με σκοπό τη συμπλήρωση της συνήθους δίαιτας. Διατίθενται σε κάψουλες, παστίλιες, δισκία, σταγόνες και οι κύριες κατηγορίες τους περιλαμβάνουν, βιταμίνες, μέταλλα/ ανόργανα συστατικά, βότανα, φυτικά προϊόντα, υδατάνθρακες, πρωτεΐνες και αμινοξέα.)

1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

{Αν «Όχι», προχωρήστε στην ερώτηση ΦΑ 3- αν έχει καταγραφεί στο ιατρικό ιστορικό η λήψη φαρμάκων για κάποιο πρόβλημα υγείας (ερώτηση ΧΡΝ.3)- και στην ΦΑ.4-αν δεν έχει καταγραφεί η λήψη φαρμάκων στην ΧΡΝ.3. Αν «ΔΞ», ρωτήστε: **Υπάρχει κάποιος που θα μπορούσε να μας βοηθήσει;.** Αν υπάρχει κάποιος διαθέσιμος, ρωτάτε εκείνον. Αλλιώς, ακολουθείτε την παραπάνω οδηγία. Αν "ΔΑ", τότε προχωρήστε στην ερώτηση ΦΑ.5}

ΦΑ 2. Τι φάρμακα/ συμπληρώματα πήρατε; Θα μπορούσατε να μου φέρετε τις συσκευασίες τους για να τα καταγράψω;
{Εάν δεν είναι διαθέσιμες οι συσκευασίες, συνεχίζετε: **Θα μπορούσατε να μου πείτε ποια φάρμακα/ συμπληρώματα πήρατε;**}

1. Καταγραφή τμημάτων Α,Β- πίνακας 1 777. ΔΞ 999. ΔΑ

{Αν «ΔΞ», ρωτήστε: **Υπάρχει κάποιος που θα μπορούσε να μας βοηθήσει;.** Αν υπάρχει κάποιος διαθέσιμος, ρωτάτε εκείνον. Αλλιώς, προχωρήστε στην ΦΑ3 –αν έχει καταγραφεί λήψη φαρμάκων στην ΧΡΝ.3- και στην ΦΑ4 –αν δεν έχει καταγραφεί λήψη φαρμάκων στην ΧΡΝ.3. Αν «ΔΑ», προχωρήστε στην ερώτηση ΦΑ 5. ΠΡΟΣΟΧΗ!!: Αν δεν αναφέρει όλες τις πληροφορίες του τμήματος Α, δεν τον διακόπτετε. Τον αφήνετε να σας πει ότι θυμάται και αφού ολοκληρώσετε και την αναφορά των βοηθητικών ερωτήσεων ΦΑ.3 και ΦΑ.4, τότε τον ρωτάτε για ότι λείπει στην καταγραφή του τμήματος Α.}

{Ρωτήστε την ΦΑ3 μόνο αν χρειαστεί. Αν έχει ήδη πει τα φάρμακα που παίρνει για τα προβλήματα υγείας του, μην ρωτήσετε.}
ΦΑ.3 Νωρίτερα, μου είπατε ότι έχετε _____{αναφέρετε τα προβλήματα υγείας, για τα οποία παίρνει φάρμακα, σύμφωνα με την ερώτηση ΧΡΝ.3 στο ιατρικό ιστορικό}**. Μήπως πήρατε κάποιο φάρμακο ή συμπλήρωμα διατροφής για την αντιμετώπιση αυτού/ αυτών των προβλημάτων υγείας (εκτός από αυτά που μου έχετε πει μέχρι τώρα);**

1. Ναι --> Καταγραφή τμημάτων Α,Β- πίνακας 1 0. Όχι 777. ΔΞ 999. ΔΑ

{Αν απάντηση «1», μετά την καταγραφή όσων σας πει, προχωρήστε στην ερώτηση ΦΑ 4}

ΦΑ.4α Μήπως πήρατε κάποιο φάρμακο για κρύωμα, αλλεργία, αϋπνία, πονοκέφαλο ή αντιβίωση;
{Σε γυναίκες ηλικίας ≥16 και <50 ετών, προσθέστε: **τα αντισυλληπτικά.**}

1. Ναι --> Καταγραφή τμημάτων Α,Β- πίνακας 1 0. Όχι 777. ΔΞ 999. ΔΑ

ΦΑ.4β Μήπως πήρατε κάποιο συμπλήρωμα διατροφής, όπως για παράδειγμα πολυβιταμίνη, σίδηρο, ω-3 ιχθυέλαια, βιταμίνη C, βιταμίνη D, ασβέστιο, σπιρουλίνα, καρνιτίνη, κτλ.;

1. Ναι --> Καταγραφή τμημάτων Α,Β- πίνακας 1 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
1	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
2	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
3	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
4	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
5	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
6	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
7	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
8	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
9	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
10	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
11	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
12	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
13	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
14	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
15	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
16	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
17	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
18	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
19	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
20	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
21	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. ☐☐☐,☐ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
22	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
23	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
24	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
25	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
26	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
27	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

	ΠΙΝΑΚΑΣ 1: ΚΑΤΑΓΡΑΦΗ ΦΑΡΜΑΚΩΝ/ ΣΥΜΠΛΗΡΩΜΑΤΩΝ						
	Α. {Είδατε τη συσκευ-ασία;} 1. Ναι 0. Όχι	Β. **Ποιο φάρμακο/ συμπλήρωμα;** {Συμπληρώνετε το **εμπορικό όνομα**, τη **μορφή** του και τη **συγκέντρωση** του με τη **μονάδα μέτρησης** της (π.χ. Lipitor tab 20 mg). Όπου άγνωστο-> ΔΞ, όπου δεν απαντά-> ΔΑ}	Γ. **Πόσο συχνά το παίρνετε και πόσο τη φορά;** {Συνολική ποσότητα στη μονάδα χρόνου.} {Αν αναφέρει «Το παίρνω όταν χρειαστεί» ρωτήστε τον **«Τις τελευταίες 30 ημέρες πόσες φορές το πήρατε;»** και στη συνέχεια **«Πόσο παίρνετε τη φορά;»**}	Δ. **Πόσο χρονικό διάστημα το παίρνετε;** {Αριθμός και μονάδα χρόνου.}	Ε. **Για ποιο λόγο το παίρνετε;** {Καταγράφετε όσους λόγους σας αναφέρει- Δεν ρωτάτε, αν σας το έχει ήδη πει.}	ΣΤα. **Το αγοράσατε με συνταγή/ συμβουλή ιατρού;** (Συνταγή είναι η γραπτή εντολή για τη χορήγηση φαρμάκου) {Αν Όχι, τότε ρωτάτε το ΣΤβ.}	Ζ. **Μήπως το πήρατε το τελευταίο 24ώρο;**
28	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ
29	1. Ναι 0. Όχι	1._____ _____ Σχόλιο: _____ _____	1._____ _____ 777. ΔΞ 999. ΔΑ Σχόλιο: _____ _____	1. □□□,□ Χρόνια, Μήνες, Εβδομάδες, Ημέρες. 777. ΔΞ 999. ΔΑ	1._____ _____ 777. ΔΞ 999. ΔΑ	1.Ναι 0. Όχι (-> ερ. ΣΤβ) 777. ΔΞ 999. ΔΑ	1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

ΣΤβ. Ποιος σας πρότεινε να χρησιμοποιήσετε το συγκεκριμένο φάρμακο ή συμπλήρωμα διατροφής;
ΔΕΙΞΕ ΚΑΡΤΑ 16 {πολλαπλή επιλογή}

1. Διαιτολόγος 2. Φαρμακοποιός 3. Γυμναστής 4. Φυσικοθεραπευτής
5. Κατάστημα με υγιεινές τροφές/ βότανα 6. Οικογένεια 7. Φίλοι/ Γνωστοί
8. Ίντερνετ 9. Τηλεόραση 10. Περιοδικά/ Εφημερίδες 11. Από προηγούμενη χρήση του
12. Άλλο, _____(προσδιορίστε) 777. ΔΞ 999. ΔΑ

Απάντηση ανά αριθμό φαρμάκου/ συμπληρώματος. {Γράφετε τον αριθμό από κάρτα ή καταγραφή άλλου ή 777.ΔΞ, 999.ΔΑ}	
1.	2.
3.	4.
5.	6.
7.	8.
9.	10.
11.	12.
13.	14.
15.	16.
17.	18.
19.	20.
21.	22.
23.	24.
25.	26.
27.	28.
29.	

ΦΑ 5. Έχετε πάρει καθημερινά γλυκοκορτικοειδή, δηλαδή χάπια που περιέχουν κορτιζόνη, όπως prezolon, medrol για χρονικό διάστημα μεγαλύτερο ή ίσο των τριών μηνών;

1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

ΦΑ 6. Τους τελευταίους 12 μήνες, σας είχε συσταθεί από ιατρό η λήψη κάποιου φαρμάκου/ κάποιων φαρμάκων, που δεν μπορέσατε να βρείτε ή να αγοράσετε;

1. Ναι 0. Όχι 777. ΔΞ 999. ΔΑ

{Εάν η απάντηση είναι «Όχι» ή «ΔΞ» ή «ΔΑ», τέλος ερωτηματολογίου.}

ΦΑ 7. Για ποιο λόγο δεν μπορέσατε να βρείτε ή να αγοράσετε αυτό το φάρμακο/ αυτά τα φάρμακα;

Ήταν επειδή..	Ναι	Όχι	ΔΞ	ΔΑ
Α. Δεν είχατε χρόνο να το/ τα αγοράσετε;	☐	☐	☐	☐
Β. Δεν είχατε αρκετά χρήματα για να το/ τα αγοράσετε;	☐	☐	☐	☐
Γ. Δεν θέλατε να το/ τα αγοράσετε;	☐	☐	☐	☐
Δ. Δεν μπορούσατε να το/ τα αγοράσετε και δεν υπήρχε κάποιο άτομο να σας βοηθήσει; (δηλαδή, δεν μπορούσατε να πάτε στο φαρμακείο επειδή δεν αισθανόσασταν καλά ή είχατε κάποιο κινητικό πρόβλημα που δυσκόλευε τη μετακίνηση σας ή η απόσταση ήταν μεγάλη και δεν είχατε μεταφορικό μέσο)	☐	☐	☐	☐
Ε. Δεν καλύπτεται η αγορά του/ τους από το ασφαλιστικό σας ταμείο;	☐	☐	☐	☐
ΣΤ. Δεν υπήρχε/ υπήρχαν διαθέσιμο/διαθέσιμα στην αγορά;	☐	☐	☐	☐

- Πόσο χρόνο σας πήρε η συμπλήρωση του ερωτηματολογίου;
  ☐☐ Λεπτά
- Ποιος απάντησε το ερωτηματολόγιο;
  ☐Ο ίδιος/ Η ίδια ☐Η μητέρα ☐Ο πατέρας
  ☐Άλλος, προσδιορίστε_____
- Βοηθός συνέντευξης_____
- Λόγος διακοπής συνέντευξης:_____

Σχόλια
Για συγκεκριμένες ερωτήσεις του ερωτηματολογίου:

Για το σύνολο του ερωτηματολογίου:

«Σωματική δραστηριότητα Ενηλίκων ≥18 ετών - <65 ετών»
Ημερομηνία: _ _ /_ _/ _ _ _ _
Ηλικία ΕΣ: _ _ Φύλο ΕΣ: _____

ΚΩΔΙΚΟΣ
ΕΘΕΛΟΝΤΗ

14Γ

≥ 18 - <65 ετών

ΤΜΗΜΑ 1. ΣΩΜΑΤΙΚΗ ΔΡΑΣΤΗΡΙΟΤΗΤΑ ΤΕΛΕΥΤΑΙΩΝ 7 ΗΜΕΡΩΝ

ΕΣΔΕ 1. Πόσο σωματικά δραστήριος/α θα λέγατε ότι είστε{αυθόρμητη απάντηση}**;**

0. Καθόλου {ακολουθώ καθιστικό τρόπο ζωής}
1. Λίγο
2. Μέτρια
3. Πολύ

777. ΔΞ 999. ΔΑ

ΕΣΔΕ 2. Τις τελευταίες 7 ημέρες άλλαξε η σωματική σας δραστηριότητα; {Αν ναι: **Αυξήθηκε ή μειώθηκε η σωματική σας δραστηριότητα;**}

1. Ναι → 1. Αυξήθηκε
→ 2. Μειώθηκε
→ 3. Δεν ασκήθηκα καθόλου
→ 777. ΔΞ
→ 999. ΔΑ

0. Όχι 777. ΔΞ 999. ΔΑ

{Αν η απάντηση είναι «Όχι», «ΔΞ», «ΔΑ» προχωρήστε στην ερώτηση ΕΣΔΕ 4}

ΕΣΔΕ 3. Για ποιο λόγο {ΚΑΡΤΑ 20};

1. Ασθένεια 2.Ταξίδι 3. Καιρικές συνθήκες
4. Διακοπές 5. Αυξημένες υποχρεώσεις στη δουλειά
6.Ξεκίνησε κάποια σωματική δραστηριότητα 7.Αυξημένος ελεύθερος χρόνος
8.Άλλος λόγος, προσδιορίστε _____

777. ΔΞ 999. ΔΑ

{Αν στην ερώτηση ΕΣΔΕ 2 η απάντηση είναι «Δεν ασκήθηκα καθόλου» προχωρήστε στην ερώτηση ΕΣΔΕ 11}

Οι παρακάτω ερωτήσεις αφορούν στο χρόνο που έχετε αφιερώσει για κάποια σωματική δραστηριότητα κατά τις τελευταίες 7 ημέρες. Σκεφτείτε <u>όλες</u> τις δραστηριότητες που κάνατε στην εργασία σας, στο σπίτι ή στον κήπο σας, τις μετακινήσεις σας, τις δραστηριότητες του ελεύθερου χρόνου σας για ψυχαγωγία και την άσκηση ή τη συμμετοχή σε αθλήματα.
Αρχικά θα ήθελα να σκεφτείτε <u>όλες</u> τις <u>έντονες</u> σωματικές δραστηριότητες που κάνατε κατά τις τελευταίες 7 ημέρες και είχαν διάρκεια <u>μεγαλύτερη από 10 λεπτά κάθε φορά</u>. Μια έντονη σωματική δραστηριότητα αναφέρεται σε δραστηριότητες που απαιτούν <u>έντονη</u> σωματική προσπάθεια και σας κάνουν να αναπνέετε <u>σημαντικά δυσκολότερα</u> απ' ότι συνήθως.
ΕΣΔΕ 4. Τις τελευταίες 7 ημέρες, πόσες <u>ημέρες</u> κάνατε κάποια <u>έντονη</u> σωματική δραστηριότητα, όπως σκάψιμο, έντονη άσκηση με βάρη, τρέξιμο σε διάδρομο με κλίση, γρήγορο τρέξιμο, αερόμπικ, γρήγορη ποδηλασία, γρήγορη κολύμβηση, τένις μονό, αγώνα σε γήπεδο όπως ποδόσφαιρο, μπάσκετ, βόλεϊ; <u>Παρακαλώ να μη συμπεριλάβετε το περπάτημα.</u>

1. ☐ (1-7) ημέρες ανά εβδομάδα 0. Δεν έκανα έντονη σωματική δραστηριότητα 777. ΔΞ 999. ΔΑ

{Αν η απάντηση είναι «Δεν έκανα έντονη σωματική δραστηριότητα», «ΔΞ», «ΔΑ», προχωρήστε στην ερώτηση 6.}

ΕΣΔΕ 5. Τις ημέρες που κάνατε κάποια έντονη σωματική δραστηριότητα, πόσο χρόνο αφιερώνατε ανά ημέρα;
{Αν η διάρκεια δοθεί σε ακέραιο αριθμό ωρών σημειώνετε στην απάντηση 1 και στην απάντηση 2 σημειώνετε **00.** π.χ. 2 ώρες και 00 λεπτά, αν η απάντηση δοθεί στη μορφή 1 ώρα και 10 λεπτά, σημειώνετε στην απάντηση 1. 01 ώρες και στην απάντηση 2. 10 λεπτά}

1. ☐☐ (0-24) ώρες ανά ημέρα και 2. ☐☐ (0-59) λεπτά ανά ημέρα 777.ΔΞ 999. ΔΑ

{Ζητείται μία μέση διάρκεια για μία από τις ημέρες που ο ερωτώμενος έκανε έντονη σωματική δραστηριότητα. Αν ο ερωτώμενος δεν μπορεί να απαντήσει επειδή η διάρκεια διαφέρει αρκετά από μέρα σε μέρα ρωτήστε: **«Συνολικά, πόσο χρόνο περάσατε κατά τη διάρκεια των τελευταίων 7 ημερών κάνοντας έντονη σωματική δραστηριότητα;»** και συμπληρώστε το ακόλουθο:}

1. ☐☐ (0-168) ώρες ανά εβδομάδα και 2. ☐☐ (0-59)λεπτά ανά εβδομάδα 777. ΔΞ 999. ΔΑ

Τώρα σκεφτείτε όλες τις μέτριας έντασης σωματικές δραστηριότητες που κάνατε τις τελευταίες 7 ημέρες και είχαν διάρκεια μεγαλύτερη από 10 λεπτά κάθε φορά. Μια μέτριας έντασης σωματική δραστηριότητα αναφέρεται σε δραστηριότητες που απαιτούν μέτρια σωματική προσπάθεια και σας κάνουν να αναπνέετε κάπως δυσκολότερα απ' ότι συνήθως.

ΕΣΔΕ 6. Τις τελευταίες 7 ημέρες, πόσες ημέρες κάνατε κάποια μέτριας έντασης σωματική δραστηριότητα, όπως το να σηκώσετε και να μεταφέρετε ελαφριά βάρη, συνολική καθαριότητα του σπιτιού, ήπιες ρυθμικές ασκήσεις σώματος, ποδηλασία αναψυχής με χαμηλή ταχύτητα, χαλαρή κολύμβηση; Παρακαλώ να μη συμπεριλάβετε το περπάτημα.

1. ☐(1-7)ημέρες ανά εβδομάδα 0. Δεν έκανα μέτριας έντασης σωματική δραστηριότητα
777. ΔΞ 999. ΔΑ

{Αν η απάντηση είναι «Δεν έκανα μέτριας έντασης σωματική δραστηριότητα», «ΔΞ», «ΔΑ», προχωρήστε στην ερώτηση 8.}

ΕΣΔΕ 7. Τις ημέρες που κάνατε κάποια μέτρια σωματική δραστηριότητα, πόσο χρόνο αφιερώνατε ανά ημέρα;

1. ☐☐ (0-24) ώρες ανά ημέρα και 2. ☐☐ (0-59) λεπτά ανά ημέρα 777.ΔΞ 999. ΔΑ

{Ζητείται μία μέση διάρκεια για μία από τις ημέρες που ο ερωτώμενος έκανε μέτριας έντασης σωματική δραστηριότητα. Αν ο ερωτώμενος δεν μπορεί να απαντήσει επειδή η διάρκεια διαφέρει αρκετά από μέρα σε μέρα ρωτήστε: **«Συνολικά, πόσο χρόνο περάσατε κατά τη διάρκεια των τελευταίων 7 ημερών σε μέτριας έντασης σωματική δραστηριότητα;»** και συμπληρώστε το ακόλουθο:}

1. ☐☐ (0-168) ώρες ανά εβδομάδα και 2. ☐☐ (0-59) λεπτά ανά εβδομάδα 777. ΔΞ 999. ΔΑ

Στη συνέχεια θα ήθελα να σκεφτείτε το χρόνο που περπατήσατε κατά τις τελευταίες 7 ημέρες. Να συμπεριλάβετε το περπάτημα στο χώρο της εργασίας σας, στο σπίτι, στις μετακινήσεις σας και στον ελεύθερο χρόνο σας για ψυχαγωγία, άσκηση ή άθληση.

ΕΣΔΕ 8. Κατά τις τελευταίες 7 ημέρες, πόσες ημέρες περπατήσατε για περισσότερο από 10 συνεχόμενα λεπτά;

1. ☐ (1-7) ημέρες ανά εβδομάδα 0. Δεν περπάτησα κατά τις τελευταίες 7 ημέρες
777. ΔΞ 999. ΔΑ

{Αν η απάντηση είναι «Δεν περπάτησα τις τελευταίες 7 ημέρες», «ΔΞ», «ΔΑ», προχωρήστε στην ερώτηση ΕΣΔΕ 10.}

ΕΣΔΕ 9. Τις ημέρες που περπατήσατε, για περισσότερο από 10 συνεχόμενα λεπτά, πόσο χρόνο περάσατε περπατώντας ανά ημέρα;

1. ☐☐ (0-24) ώρες ανά ημέρα και 2. ☐☐ (0-59) λεπτά ανά ημέρα 777. ΔΞ 999. ΔΑ

{Ζητείται μία μέση διάρκεια για μία από τις ημέρες που περπάτησε ο ερωτώμενος. Αν ο ερωτώμενος δεν μπορεί να απαντήσει επειδή η διάρκεια διαφέρει αρκετά από μέρα σε μέρα ρωτήστε: **«Συνολικά, πόσο χρόνο περάσατε κατά τη διάρκεια των τελευταίων 7 ημερών περπατώντας;»** και συμπληρώστε το ακόλουθο:}

1. ☐☐ (0-168) ώρες ανά εβδομάδα και 2. ☐☐ (0-59) λεπτά ανά εβδομάδα 777. ΔΞ 999. ΔΑ

ΕΣΔΕ 10. Κατά τις τελευταίες 7 ημέρες, πόσο χρόνο περάσατε καθισμένος/η σε μια ημέρα της εβδομάδας; Ο χρόνος αυτός μπορεί να περιλαμβάνει το χρόνο που περνάτε καθισμένος/η στο σπίτι, στο γραφείο, στο αυτοκίνητο, όταν διαβάζετε, όταν είστε με φίλους, ξεκουράζεστε σε πολυθρόνα ή βλέπετε τηλεόραση, αλλά <u>δεν περιλαμβάνει τον ύπνο</u>.

1. ☐☐ (0-24) ώρες ανά ημέρα 2. ☐☐ (0-59)λεπτά ανά ημέρα 777. ΔΞ 999. ΔΑ

{Ζητείται μία μέση διάρκεια για το χρόνο που πέρασε ο ερωτώμενος καθισμένος σε μία από τις ημέρες. Αν ο ερωτώμενος δεν μπορεί να απαντήσει επειδή η διάρκεια διαφέρει αρκετά από μέρα σε μέρα ρωτήστε: «**Συνολικά, πόσο χρόνο αφιερώσατε καθισμένος την προηγούμενη** {Τετάρτη}**;»** και συμπληρώστε το ακόλουθο: }

1. ☐☐ (0-24)ώρες την {Τετάρτη} 2. ☐☐ (0-59)λεπτά ανά ημέρα 777. ΔΞ 999. ΔΑ

ΤΜΗΜΑ 2. ΔΙΑΘΕΣΙΜΟΤΗΤΑ ΚΑΙ ΧΡΗΣΗ ΗΛΕΚΤΡΟΝΙΚΩΝ ΣΥΣΚΕΥΩΝ

Τις τελευταίες 7 ημέρες	**Πόσες ημέρες...**	**Πόση ώρα την κάθε ημέρα;**
ΕΣΔΕ 11. ...παρακολουθήσατε τηλεόραση, βίντεο, ή DVD; Συμπεριλάβετε την παρακολούθηση σε οποιοδήποτε μέσο όπως τηλεόραση, υπολογιστής. Μη συμπεριλάβετε τα ηλεκτρονικά παιχνίδια.	0. Καμία 1. Αριθμός ημερών ☐ (1-7) 2. Εύρος ημερών ☐ - ☐ (1-7) 777. ΔΞ 999. ΔΑ {Αν η απάντηση είναι 0 Καμία, «ΔΞ», «ΔΑ» προχωρήστε στην ΕΣΔΕ12}	1. Αριθμός ωρών ☐☐ (0-24) ή/και ☐☐ λεπτών (0-59) 2. Εύρος ωρών ☐☐ - ☐☐ (0-24) ή/και λεπτών ☐☐ - ☐☐ (0-59) 777. ΔΞ 999. ΔΑ
ΕΣΔΕ 12. ...χρησιμοποιήσατε ηλεκτρονικές συσκευές όπως υπολογιστή, tablet, Smartphone για παιχνίδι ή σερφάρισμα στο ίντερνετ ή παίξατε με ηλεκτρονικά παιχνίδια; Μη συμπεριλάβετε παιχνίδια που απαιτούν την κίνηση του σώματος όπως Wii Sports, Xbox kinect, Just Dance.	0. Καμία 1. Αριθμός ημερών ☐ (1-7) 2. Εύρος ημερών ☐ - ☐ (1-7) 777. ΔΞ 999. ΔΑ {Αν η απάντηση είναι 0 Καμία, «ΔΞ», «ΔΑ» προχωρήστε στην ΕΣΔΕ13}	1. Αριθμός ωρών ☐☐ (0-24) ή/και ☐☐ λεπτών (0-59) 2. Εύρος ωρών ☐☐ - ☐☐ (0-24) ή/και λεπτών ☐☐ - ☐☐ (0-59) 777. ΔΞ 999. ΔΑ
ΕΣΔΕ 13. ...παίξατε με ηλεκτρονικά παιχνίδια που απαιτούν την κίνηση του σώματος, όπως Wii Sports, Wii fit, Xbox 360, Xbox kinect, Playstation 3, Dance, Just Dance;	0. Καμία 1. Αριθμός ημερών ☐ (1-7) 2. Εύρος ημερών ☐ - ☐ (1-7) 777. ΔΞ 999. ΔΑ {Αν η απάντηση είναι 0 Καμία, «ΔΞ», «ΔΑ» προχωρήστε στην ΕΣΔΕ14}	1. Αριθμός ωρών ☐☐ (0-24) ή/και ☐☐ λεπτών (0-59) 2. Εύρος ωρών ☐☐ - ☐☐ (0-24) ή/και λεπτών ☐☐ - ☐☐ (0-59) 777. ΔΞ 999. ΔΑ

Ημερομηνία: _ _ /_ _/ _ _ _ _
Ηλικία ΕΣ: _ _ Φύλο ΕΣ: _____

ΤΜΗΜΑ 3. ΓΕΙΤΟΝΙΑ

ΕΣΔΕ 14. Υπάρχουν στη γειτονιά σας τα ακόλουθα;

	Ναι	Όχι	ΔΞ	ΔΑ
1. Ανοιχτοί χώροι (π.χ. παραλία, άλσος, δάσος, αλάνα)	☐	☐	☐	☐
2. Πάρκο	☐	☐	☐	☐
3. Πισίνα	☐	☐	☐	☐
4. Γυμναστήριο	☐	☐	☐	☐
5. Γήπεδο/ στάδιο	☐	☐	☐	☐
6. Δυνατότητα συμμετοχής σε οργανωμένη σωματική δραστηριότητας (π.χ. ομάδα χορού, ποδοσφαίρου)	☐	☐	☐	☐

ΕΣΔΕ 15. Πόσο συχνά αισθάνεστε ασφαλής στη γειτονιά σας;

0. Ποτέ 1. Σπάνια 2. Μερικές φορές 3. Τις περισσότερες φορές 4. Πάντα
777. ΔΞ 999. ΔΑ

- Πόσο χρόνο σας πήρε η συμπλήρωση του ερωτηματολογίου;☐ ☐ Λεπτά
- Ποιος απάντησε το ερωτηματολόγιο;
- ☐Ο ίδιος/Η ίδια ☐Η μητέρα ☐Ο πατέρας
  ☐Άλλος, προσδιορίστε_____
- Βοηθός συνέντευξης _____
- Λόγος διακοπής συνέντευξης:_____

Σχόλια
Για συγκεκριμένες ερωτήσεις του ερωτηματολογίου:

Για το σύνολο του ερωτηματολογίου:

*Η ανάκληση 24ώρου, εφαρμόστηκε με τη χρήση λογισμικού CAPI (που αναπτύχθηκε ειδικά για την ΠΑΜΕΔΥ) και δεν είναι δυνατή η επικόλληση του ερωτηματολογίου στο Παράρτημα αυτής της διδακτορικής διατριβής.