DIABETES RESEARCH AND CLINICAL PRACTICE 172 (2021) 108646

ELSEVIER

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Prevalence of diabetes and pre-diabetes in Greece. Results of the First National Survey of Morbidity and Risk Factors (EMENO) study

Konstantinos Makrilakis[a,b,], Natasa Kalpourtzi[c], Ioannis Ioannidis[a,d], Stella Iraklianou[a,e], Athanasios Raptis[a,f], Alexis Sotiropoulos[a,g], Magda Gavana[h], Apostolos Vantarakis[i], Maria Kantzanou[c], Christos Hadjichristodoulou[j], Grigoris Chlouverakis[k], Grigoris Trypsianis[l], Paraskevi V. Voulgari[m], Yannis Alamanos[n], Giota Touloumi[c,1], Stavros Liatis[a,b,1], on behalf of EMENO Study Group*

[a] *Hellenic Diabetes Association, Athens, Greece*
[b] *First Department of Propaedeutic Internal Medicine, National and Kapodistrian University of Athens Medical School, Athens, Greece*
[c] *Department of Hygiene, Epidemiology & Medical Statistics, National and Kapodistrian University of Athens Medical School, Athens, Greece*
[d] *First Department of Internal Medicine and Diabetes Center, Konstantopoulio Hospital, Nea Ionia, Greece*
[e] *Third Department of Internal Medicine, General Hospital Tzaneio, Piraeus, Greece*
[f] *Second Department of Propaedeutic Internal Medicine, Research Unit and Diabetes Center, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece*
[g] *3rd Internal Medicine Department & Diabetes Center, General Hospital of Nikaia-Piraeus, Greece*
[h] *Dept of Primary Health Care, General Practice and Health Services Research, Medical School of Aristotle University, Thessaloniki, Greece*
[i] *Public Health, Medical School, University of Patras, Patra, Greece*
[j] *Dept of Hygiene and Epidemiology, Medical Faculty, University of Thessaly, Larisa, Greece*
[k] *Laboratory of Biostatistics, School of Medicine, University of Crete, Crete, Greece*
[l] *Laboratory of Medical Statistics, Medical School, Democritus University of Thrace, Thrace, Greece*
[m] *Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece*
[n] *Institute of Epidemiology, Preventive Medicine and Public Health, Corfu, Greece*

ARTICLE INFO

Article history:
Received 17 May 2020
Received in revised form
1 December 2020
Accepted 21 December 2020
Available online 24 December 2020

Keywords:
Diabetes mellitus
Pre-diabetes
Prevalence

ABSTRACT

Aims: To report the results of the first national Health Examination Survey (HES) on the prevalence of diabetes, its pharmacologic treatment and level of control, as well as pre-diabetes in Greece.

Methods: Data were derived from the National Survey of Morbidity and Risk Factors (EMENO), in a randomly selected, representative sample of the adult Greek population. Sampling weights were applied to adjust for study design and post-stratification weights to match sample age/sex distribution to the population. Non-response was adjusted by inverse probability weighting. Weighted prevalence estimates are provided.

Results: A total of 4393 persons with HbA1c and/or fasting plasma glucose measurements were included. Total diabetes prevalence was 11.9% (95% CI: 10.9–12.9), known diabetes 10.4% (9.5–11.4), and unknown 1.5% (1.1–1.9), with considerable increase in older age groups

* Corresponding author at: First Department of Propaedeutic Medicine, National and Kapodistrian University of Athens Medical School, Laiko General Hospital, 17 Ag. Thoma St, 115 27 Athens, Greece.
E-mail address: kmakrila@med.uoa.gr (K. Makrilakis).
[1] Equal contribution.
https://doi.org/10.1016/j.diabres.2020.108646

Health examination survey
Greece

and no difference between genders. Pre-diabetes prevalence was 12.4% (11.4–13.6). The majority of persons with known diabetes were receiving metformin. Of those with known diabetes (and measured HbA1c), 70.9% were well controlled (HbA1c <7.0%).

Conclusions: This first representative national HES showed high prevalence of diabetes in Greece, with low prevalence of unknown diabetes. Pre-diabetes prevalence is also substantial. These results will hopefully enable national authorities develop tailored and efficient strategies for disease prevention and management.

1. Introduction

The prevalence of diabetes mellitus has increased dramatically in recent decades, most markedly in the world's low-to-middle income countries [1], and this trend is projected to continue as the global population ages and becomes more obese [2]. Furthermore, diabetes usually remains asymptomatic for several months up to years before clinical diagnosis, leading to potential premature micro- or even macrovascular complications during the pre-diabetic [3] or especially the early, still undetected diabetic phase [4]. Thus, it is postulated that its timely diagnosis may yield benefits for controlling and preventing complications [5]. The economic costs of the disease and its consequences are large and will substantially increase in the future [6]. Policymakers need to take urgent action to prepare health and social security systems to mitigate these effects, but to do that, national population-representative data on the prevalence of the disease, its prodromal phases, and its risk factors are necessary.

Methods to estimate diabetes prevalence at the national level may vary substantially. Sources commonly used include lists from general practitioners, family physicians, or other health-care professionals, diabetes registries, and prescription lists [7]. Epidemiologic data regarding diabetes in Greece have been largely based either on regional, small-scale studies [8-14] or on self-reported information [15]. Only recently was a large-scale nation-wide study published, extracting data from the National Organization for Health Care Services Provision (EOPYY) database, the largest health-care provider in Greece, including however only data exclusively based on the pharmacologic treatment of the disease [16] and not on the measurement of the disease existence. Data on pre-diabetes prevalence are also very scarce, again based on small-scale, regional studies [11,14,17].

To capture total diabetes prevalence, however, by including both cases of the known and unknown (screen-detected) disease, representative population-based studies or surveys are needed. Nation-wide Health Examination Surveys (HES) that combine information collected by interviews together with a physical examination of the participants are the gold standard design to provide such data [18]. HES have a long history in the USA [19,20], and since the '90s have been widely introduced in Europe as well [21]. In Greece, no such HES has so far been performed at the national level to record the prevalence of common diseases (such as diabetes) and their risk factors.

Herein, we present the results of the first national HES regarding the prevalence of diabetes (known and unknown), its pharmacologic treatment and level of control, as well as pre-diabetes prevalence in Greece, performed on a representative sample of the population. This study is part of The National Survey of Morbidity and Risk Factors (EMENO) [22], which was set up focusing on cardiovascular and respiratory diseases and risk factors, assessing population well-being and use of health services, medications, and preventive measures.

2. Subjects, materials and methods

2.1. *Study population and data collection*

The study has been previously described in detail [22]. In brief, EMENO is a cross-sectional HES, combining health data collected by trained interviewers (using standardized questionnaires) and medical examinations (conducted by trained physicians), in a randomly selected sample of all adults (≥18 years old) living in Greece, excluding those in supervised care or custody in institutional settings. It was initiated in May 2013 and completed in June 2016. The EMENO study was approved by the Ethics and Deontology Committee of the National and Kapodistrian University of Athens and by the Hellenic Data Protection Authority. All participants were given enough time to read the informed consent form carefully and to ask relevant questions before signing it. The work described has been carried out in accordance with The Declaration of Helsinki for experiments involving humans [23].

Multistage stratified random sampling based on the 2011 national census was applied to select the sample. The target sample size was 6000. The sampling strategy and the sampling flow chart have been previously explained in detail [22]. In brief, based on the ATTICA study results [24], the overall prevalence of hypercholesterolemia, hypertension, and diabetes mellitus was about 40%, 32%, and 7%, respectively. Calculating sampling errors using a corresponding formula for stratified sampling and with a target sample size of 6000 individuals, the above-mentioned prevalence could be estimated with 1.28%, 1.22%, and 0.66% precision, respectively. During home visits, trained interviewers administered a standardized questionnaire to study participants, and trained physicians performed physical examinations, collected blood samples, recorded all medications currently being taken by the participants, including anti-diabetic ones, if any, and made anthropometric measurements using standardized procedures and equipment. Efforts were made blood samples to be collected in a fasting state, and the time elapsed from the last meal was recorded by the examiners. For glucose, serum samples were collected in sodium fluoride tubes. Blood samples were immediately transported to collaborating local laboratories for centrifugation. Centrifugal aliquots were stored in the collaborating laboratories at −80 °C until sent to the central laboratory (National Retrovirus Reference Center, Laboratory of Hygiene, Epidemiology and Medical Statistics of the National and Kapodistrian University of Athens Medical School) for testing. Body mass index (BMI, in kg/m^2) was calculated based on the physicians' weight and height measurements (not the participants' self-report to the interviewers).

2.2. Laboratory analyses

Collected blood samples were analyzed for serum glucose and glycated haemoglobin (HbA1c), by standard methods. HbA1c was measured by turbidimetric inhibition immunoassay (TINIA) (Tina-quant® HbA1c Gen. 3, Roche Diagnostics Ltd, Switzerland).

2.3. Definition of diabetes and pre-diabetes

Diabetes was considered known in persons who were either taking anti-diabetic medications or self-reporting the existence of the disease ("known diabetes"). Among individuals who reported no known diabetes, the following three criteria were used to calculate the prevalence of unknown diabetes: 1) a fasting plasma glucose (FPG) level of ≥ 7.0 mmol/L (126 mg/dl) and/or HbA1c ≥ 6.5% (≥48 mmol/mol); 2) an FPG-only level ≥ 7.0 mmol/L (126 mg/dl); and 3) HbA1c-only level ≥ 6.5% (48 mmol/mol). "Total diabetes" was the sum of known and unknown diabetes, with the latter being dependent upon diagnostic criteria.

"Pre-diabetes" was diagnosed in participants with no known diabetes, who had FPG 5.6–6.9 mmol/L (100–125 mg/dl) (Impaired Fasting Glucose [IFG]) and/or HbA1c 5.7–6.4% (39–46 mmol/mol) [25,26]. Since the World Health Organization (WHO) and numerous other diabetes organizations define the IFG cut-off at 6.1 mmol/L (110 mg/dl) [27], this criterion (i.e. FPG 6.1–6.9 mmol/L [110–125 mg/dl]) was also examined as a secondary analysis of pre-diabetes prevalence.

Among persons with known diabetes, those with an HbA1c level <7.0% (53 mmol/mol) were considered as having good glycaemic control [28].

2.4. Statistical analysis

Sampling weights were applied to adjust for study design and post-stratification weights to match sample age/sex distribution to that of the Greek population based on the 2011 census provided by the National Statistics Agency (www.statistics.gr/en/demographic-data). Since only a sub-sample of the interviewed individuals had available information for fasting plasma glucose or HbA1c, the inverse probability weighting method was applied to adjust for differences between those with and without available information. Weights were the reciprocal of the probabilities of having available information, estimated through weighted multivariable logistic regression. Weighted mean and standard deviations for continuous variables and weighted percentages for categorical variables are provided. To evaluate the differences between diabetic and non-diabetic individuals, a modified Rao-Scot chi-square test [29] and weighted linear regression were used for categorical and continuous variables, respectively. All statistical analyses were performed using the statistical software STATA (version 13.0; Stata Corp, College Station, TX).

3. Results

To achieve the target sample size, 8340 eligible households were reached and 6006 persons accepted to participate in the study (response rate 72%) [22]. Out of these, information about age (necessary for post-stratification weighting) was missing in 13.

Of the remaining 5993 participants, 4393 had HbA1c and/or FPG measurements available and were included in the analysis. The 1600 excluded were more likely to reside in urban areas and be over 70 years of age and less likely to have a chronic health problem (by declaration) or be of Greek nationality. There seemed to be no differences in participation between men and women. A weighted logistic regression model adjusted for all these factors was fitted to estimate the probability of been included in the analysis.

Of the 4393 participants with HbA1c and/or FPG measurements, 4343 had HbA1c data, 2384 had FPG data and 2334 had both. For the calculation of diabetes prevalence, the data from the 4393 participants with relevant blood measurements were used (Fig. 1).

The demographic characteristics of the participants are depicted in Table 1. As shown, there was equal representation of the two genders, similar distribution in the various age categories, the majority were mostly of secondary-level education, of urban inhabitance, and Greek nationality. Their mean (SD) age and BMI (available in all but 45 individuals) were 49.3 (18.6) years and 28.2 (5.8) kg/m^2, respectively.

Based on the FPG-and/or-HbA1c combined criterion, a total of 621 persons (11.9% [95% CI: 10.9, 12.9]), with mean (SD) age 66.3 (14.8) years, and BMI 31.6 (6.9) kg/m^2, were found to have diabetes. The prevalence of diabetes based on self-report only (i.e. known diabetes, 549 persons) was 10.4% (9.5, 11.4). The estimated prevalence of unknown diabetes was 1.5% (1.1, 1.9) (72/4393 persons), yielding the proportion of unknown diabetes among people with total diabetes 12.6%. Based on the FPG-only criterion, the estimated prevalence of unknown diabetes (40/2384 persons) was 1.6% (1.1, 2.3), contributing to 13.0% of total diabetes prevalence (40/347). However, under the HbA1c-only criterion (50/4343 persons), the prevalence of unknown diabetes was 1.0% (0.8, 1.4); yielding 8.8% (50/612) of total prevalence. Thus, total diabetes prevalence was 11.9% (10.9, 12.9), 12.0% (10.4, 13.2), and 11.4% (10.4, 12.4), respectively, according to FPG-and/or-HbA1c, FPG-only, and HbA1c-only criteria.

In a sensitivity analysis on the 2334 persons with both HbA1c and FPG data, the prevalence of total diabetes was 12.0% (10.7, 13.5), of known diabetes 10.1% (8.9, 11.5), and unknown 1.9% (1.4, 2.7).

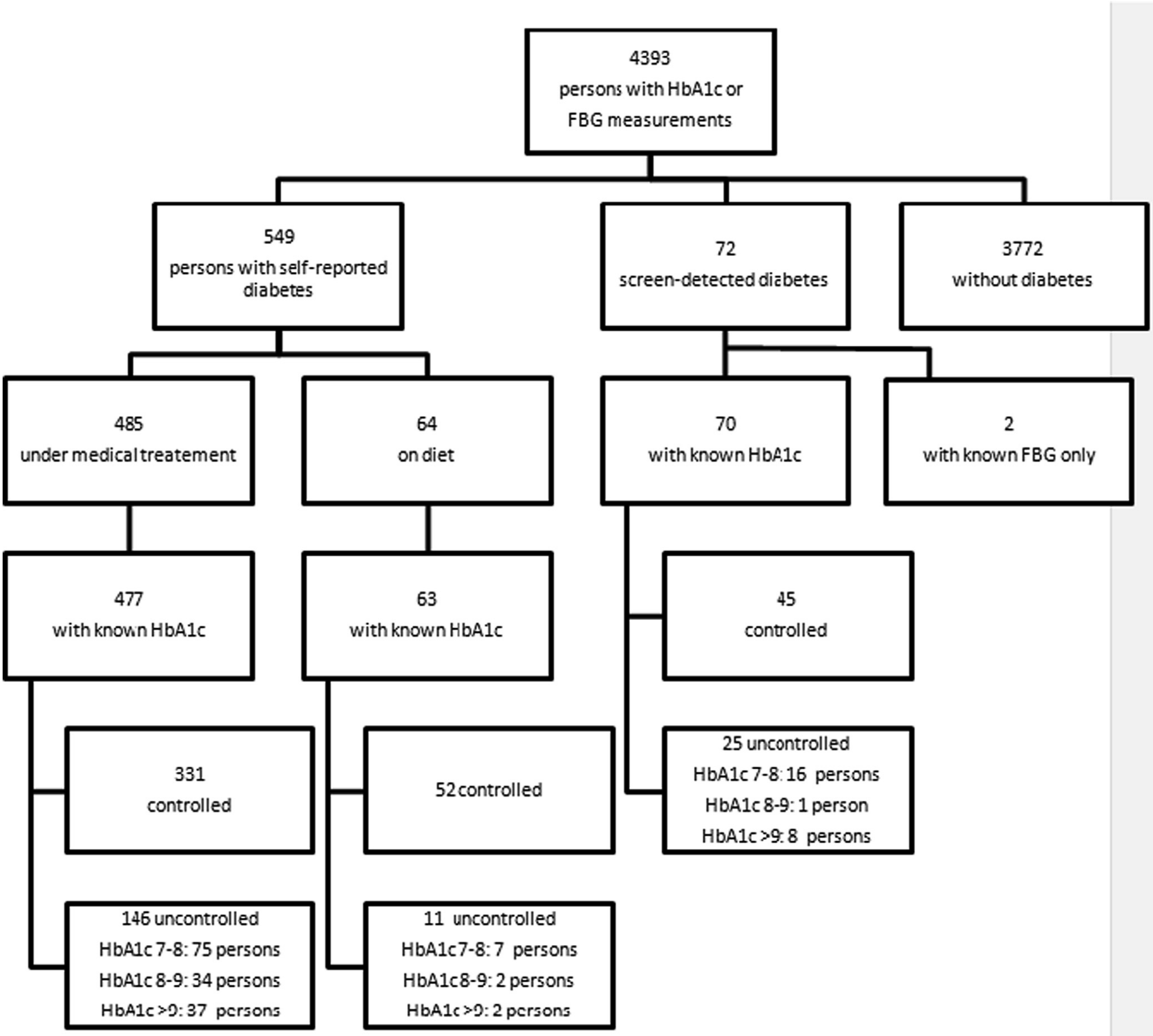

Fig. 1 – Flow chart for the classification of the sample participants regarding diabetes prevalence.

There was significant age variation in diabetes prevalence, ranging from 0.8% in the 18–29 years age-group, to 12.1% in the 50–59 years and to 30.5% in those >70 years old (Table 2). Differentiation between Type 1 and Type 2 diabetes could not be ascertained from the present data. There was no difference in diabetes prevalence between the two genders (12.7% for men, 11.1% for women, $p = 0.127$), whereas it was higher with increasing BMI ($p < 0.001$, Table 2) and lower in people living in urban areas (10.8%) compared to rural and semi-rural ones (13.8% in each). However, after further adjusting for age (as average age was significantly higher in semi-urban, and even more in rural areas, compared to urban ones) the differences in the prevalence by the degree of urbanization were reversed, with the adjusted prevalence being higher in urban than in rural areas.

A total of 658 persons [mean (SD) age 61.8 (16.6) years, BMI 31.1 (6.4) kg/m^2] were found to have pre-diabetes, based on FPG levels of 5.6–6.9 mmol/L (100–125 mg/dl) and/or HbA1c of 5.7–6.4% (39–46 mmol/mol), yielding a prevalence in the whole population of 12.4% (95% CI: 11.4, 13.6) (658/4393) (Table 2). In accordance to diabetes data, there was a similar pattern of increasing prevalence with age (going up to 25% for people >70 years old) and adiposity (19.6% for obese persons), a trend towards male predominance ($p = 0.088$), and lower prevalence in urban areas (10.0%) compared to semi-rural (13.2%) and rural ones (19.8%) ($p < 0.001$). The prevalence based on FPG-only data was 8.2% (253/2673), whereas based on HbA1c-only values, it was 9.0% (495/4343).

In the secondary analysis, using the WHO criterion for IFG (6.1–6.9 mmol/L [110–125 mg/dl]), the prevalence of pre-diabetes (based on FPG and/or HbA1c levels) was 9.6% (95% CI 8.7–10.6) (534/4393 persons).

Of those with known diabetes (549 persons), the majority (weighted percentage: 89.5%, [485 persons]), were receiving anti-diabetic medications (either non-insulin [pills and/or

Table 1 – Demographic characteristics of the study participants (n = 4393).

Variable	N (% [weighted])
Gender (males/females) [n (%)]	1888 (48.5)/2505 (51.5)
BMI [kg/m^2, mean (SD)]	28.2 (5.8)
Age [years, mean (SD)]	49.3 (18.6)
Age distribution (yrs)	
18–29	410 (17.7)
30–39	583 (18.3)
40–49	785 (17.7)
50–59	870 (15.6)
60–69	848 (12.7)
70+	897 (17.9)
Family income (€/month)	
<900	1831 (40.1)
900–1.700	1199 (28.6)
>1.700	459 (12.1)
Unknown	904 (19.2)
Educational level	
Primary	1637 (29.0)
Secondary	1856 (45.7)
Tertiary	829 (23.9)
Unknown	71 (1.5)
Employment status	
Employed	1573 (39.1)
Unemployed	602 (15.3)
Pensioner/Household chores	1903 (35.3)
Other	254 (9.1)
Unknown	61 (1.2)
Urbanization degree	
Urban (>10,000 inhabitants)	2218 (64.1)
Semi-rural (2000–9999 inhabitants)	815 (16.1)
Rural (<2000 inhabitants)	1360 (19.8)
Nationality	
Greek/Western Europe	4165 (93)
Africa	10 (0.4)
Eastern Europe/former Soviet Union	203 (6.1)
Asia	11 (0.4)
America/Canada	4 (0.1)

BMI: Body mass index

injectables, 88.4%] or insulin only [7.9%] or both [3.7%]), whereas the rest (64 persons, 10.6%) were on diet only. The distribution of the various categories of anti-diabetic medications is depicted in Table 3. As expected, based on current guidelines [30], the majority were receiving biguanides (i.e. metformin, 71.5%), whereas DPP-4 inhibitors (26.3%) and sulfonylureas (24.5%) were the next most commonly prescribed medications.

Among those with known diabetes (and HbA1c measurements), 70.9% (383/540) were well controlled (had HbA1c <7.0% [53 mmol/mol]), with this percentage being equal between the two genders (69.9% and 71.9%, for males and females, respectively), and among the age groups ($p = 0.066$) (Table 4). The percentage of good control was 73.5% among those receiving oral drugs, 29.8% for those on insulin, 53.0% for both, and 84.8% for those on diet only ($p < 0.001$).

4. Discussion

The present study is the first nation-wide health survey (that includes both an interview and examination component), based on a representative sample of the Greek adult population, that reports the prevalence of diabetes as well as pre-diabetes, using actual measurements of fasting blood glucose as well as glycated haemoglobin (HbA1c) levels. It showed that diabetes affects a substantial proportion of the general population (11.9%), with known diabetes 10.4% and unknown 1.5% (yielding the proportion of unknown diabetes among people with total diabetes of 12.6%). Significant increases in the older age groups were observed (23% in the 60–69 years, 30.5% in those aged >70 years). Furthermore, the prevalence of pre-diabetes was found to be equally substantial (12.4%).

When comparing the findings of the current survey with other studies, one should be careful when different definitions of diabetes, based on different criteria (especially for unknown or pre-diabetes) are used [31]. When comparing and interpreting measurements, it is important to ensure that all prevalence estimates are based on the same diagnostic criteria.

Previous reports of diabetes prevalence in Greece, using varying diagnostic criteria, have been largely based either on regional, small-scale studies, [8–14], or on self-reported information [15], estimating the prevalence of the disease

Table 2 – Weighted prevalence of diabetes and pre-diabetes stratified by age group, gender, obesity, and urbanization degree of the participants.

	n/N (number of persons with diabetes/total)	Prevalence (FPG- and/or-HbA1c criterion, %, [95% CI])	P*	n/N (number of persons with pre-diabetes/total)	Prevalence (%, [95% CI])	P*
Age group (years)						
18–29	2/410	0.8 (0.2, 3.1)		4/410	0.8 (0.3, 2.3)	
30–39	12/583	1.8 (1.0, 3.5)		28/583	4.9 (3.3, 7.2)	
40–49	43/785	6.3 (4.6, 8.5)		90/785	11.9 (9.4, 14.9)	
50–59	105/870	12.1 (9.8, 14.8)		131/870	14.2 (11.9, 17.0)	
60–69	194/848	23.0 (20.0, 26.2)		175/848	20.4 (17.4, 23.7)	
70+	265/897	30.5 (27.2, 33.9)		230/897	25.0 (22.1, 28.2)	
Total	621/4393	11.9 (10.9, 12.9)	**<0.001**	658/4393	12.4 (11.4, 13.6)	**<0.001**
Gender						
Male	305/1888	12.7 (11.2, 14.3)		311/1888	13.4 (11.7, 15.2)	
Female	316/2505	11.1 (9.8, 12.5)		347/2505	11.5 (10.3, 12.9)	
Total	621/4393	11.9 (10.9, 12.9)	0.127	658/4393	12.4 (11.4, 13.6)	0.088
BMI categories (kg/m^2)						
Normal (18.5–24.9)	51/1121	3.8 (2.8, 5.2)		61/1121	4.3 (3.2, 5.7)	
Overweight (25.0–29.9)	208/1641	10.7 (9.2, 12.4)		242 /1641	12.8 (11.0, 14.7)	
Obese(≥30.0)	354/1586	20.6 (18.5, 22.9)		345/1586	19.6 (17.6, 21.7)	
Total	613/4348	11.8 (10.8, 12.9)	**<0.001**	648/4348	12.4 (11.3, 13.5)	**<0.001**
Urbanization degree						
Urban	290/2218	10.8 (9.6, 12.1)		266/2218	10.0 (8.7, 11.4)	
Semi-rural	127/815	13.8 (11.4, 16.6		117/815	13.2 (10.6, 16.3)	
Rural	204/1360	13.8 (11.7, 16.2)		275/1360	19.7 (17.3, 22.4)	
Total	621/4393	11.9 (10.9, 12.9)	**0.017**	658/4393	12.4 (11.4, 13.6)	**<0.001**

* Comparison among the various categories in each group.

Table 3 – Distribution of anti-diabetic medications' categories.

	N	Weighted % (95% CI)
Anti-diabetic treatment in the total sample of persons with known diabetes (N = 549)	485	89.5 (86.0, 92.1)
Category of medicines (N = 485)		
Non-insulin (pills or injectables)	426	88.4 (84.7, 91.4)
Insulin only	36	7.9 (5.4, 11.3)
Insulin + non-insulin (combination with pills and/or injectables)	23	3.7 (2.4, 5.6)
Category of antidiabetic pills and/or injectables (not mutually exclusive; N = 449)		
Biguanides	313	71.5 (66.4, 76.0)
Sulfonylureas	114	24.5 (20.4, 29.1)
α-glucosidase inhibitors	3	0.5 (0.1, 2.1)
Glitazones	16	3.7 (2.2, 6.2)
DPP-4 inhibitors	121	26.3 (22.3, 30.7)
Meglitinides	9	1.4 (0.7, 3.0)
GLP-1 receptor agonists	5	1.0 (0.4, 2.5)
SGLT2 inhibitors	1	0.3 (0.0, 1.9)
Combinations	88	18.8 (15.4, 22.8)
Unknown category*	66	13.9 (10.6, 18.1)
Number of different non-insulin categories of medicines among those with known category (N = 383)		
1	230	62.3 (57.0, 67.3)
2	55	12.7 (9.5, 16.8)
3	65	16.4 (12.7, 20.9)
4	30	7.9 (5.6, 11.2)
5	3	0.7 (0.2, 2.1)
Insulin users (N = 59)		
Prandial	20	28.9 (18.2, 42.6)
Pre-mixed	7	12.7 (5.3, 27.5)
Basal	31	47.5 (33.3, 62.2)
Unknown type of insulin	16	34.0 (21.3, 49.5)

DPP-4: Dipeptidyl peptidase-4; GLP-1: Glucagon-like peptide-1; SGLT2: sodium glucose co-transporters 2.
* Participants who reported use of anti-diabetic medications, but unable to specify the exact name of them.

Table 4 – A. Level of glycaemic control in individuals with known diabetes who had HbA1c measured (n = 540). B. Percentages of individuals with HbA1c < 7.0% by age subgroups.

A. Level of glycaemic control	N (%)
Controlled (HbA1c < 7.0%)	383 (70.9%)
7% ≤ HbA1c < 8%	82 (14.2%)
8% ≤ HbA1c < 9%	36 (7.4%)
HbA1c ≥ 9%	39 (7.4%)
B. Good control (HbA1c < 7%) by age group (years)	
18–29	0
30–39	10 (89.2)
40–49	20 (63.8)
50–59	55 (60.6)
60–69	117 (69.0)
>70	181 (75.9)

between 3.1% and 11.7%. Specifically, Katsilambros et al. studied the prevalence of diabetes in a small urban area around Athens in 1974 and again 17 years later [8], and based on self-reported information, they found an increase in prevalence from 2.4% to 3.1% during that period. Results from the Attica study [10], based on FPG measurements of a sample of people with no evidence of cardiovascular or any other chronic disease from the area of Athens, conducted in 2001–2002, reported an age-adjusted prevalence of Type 2 diabetes of 7.6% in men and 5.9% in women. A small study in the remote island of Elafonisos, performed in 2012–2013 and based on point-of-care FPG and HbA1c measurements, showed that the prevalence of known diabetes was 7.7%, with unknown diabetes an additional 4.0%, yielding a total prevalence (11.7%) very close to the current study [14]. In the only somewhat representative sample of the Greek population, conducted during the period 1996–1999, and based on self-reported, physician-diagnosed diabetes, the prevalence of known diabetes was 4.29%, with an increasing prevalence by age group (age ≥70 years: 11.8%, P for trend <0.001) [15]. Finally, in a recent large-scale nation-wide study [16], extracting data from the National Organization for Health Care Services Provision (EOPYY) database, based on a real-world data analysis of all medication-prescribed diabetes in 2014–2015, it was shown that the prevalence of the pharmacologically-treated disease was 7.0%, with wide age variation and high figures in older adults. Of note, prevalence for persons aged older than 15 years was 8.2%, close to the findings of known diabetes prevalence (10.4%) in the current study.

Regarding pre-diabetes, in a report from the DE-PLAN (Diabetes in Europe–Prevention using Lifestyle, Physical Activity and Nutritional Intervention) Athens area study, based on the performance of 869 oral glucose tolerance tests (OGTTs) in a non-representative sample of people without known diabetes in 2004–2005, the prevalence of IFG (based on a cut-off value of 6.1 mmol/L [110 mg/dl]) was 9.8% and of IGT 12.6% [17]. In the aforementioned study in Elafonisos [14], pre-diabetes prevalence (based on point-of-care FPG and HbA1c measurements) was found at 23%.

Thus, based on the current study, the prevalence of diabetes over the previous decades has substantially increased in Greece, showing the same trend and reaching comparable numbers to other industrialized countries. In neighboring European countries, for example, Italy, between 1980 and 2013 the number of people with known diabetes more than doubled [32], more steeply so in men (age-standardized prevalence rose from 3.8% in 1980 to 6.8% in 2013, a 79% increase) than in women (age-standardized prevalence from 5.0% in 1980 to 5.8% in 2013, a 14% increase), mostly attributed to the aging of the population and the increase in obesity. In another study, however, based on FPG measurements, the prevalence of total diabetes had remained stable in Italy for 10 years (1998–2002 and 2008–2012), albeit high, at around 12% for men and 8% for women [33]. In Spain, according to a nationwide, population-based, cluster sampling study in 2011 [34], the overall prevalence of diabetes, adjusted for age and sex, was 13.8% (increasing with age), of which about half (6.0%) had unknown disease; the prevalence of known diabetes was 6.8%, while in those aged >75 years it was between 20.7% (men) and 23.2% (women). In France, the prevalence of diabetes is estimated at 6%, including patients treated with oral anti-diabetic medications and/or insulin (4.4%), patients treated with diet alone (0.6%), and individuals with unknown diabetes (1%) [35]. In Germany, current nationwide estimates for diabetes prevalence range between 7.2% (population aged 18 to 79 years) based on health examination surveys of the Robert Koch Institute (RKI), 8.9% (population aged 18 years and over) based on RKI telephone health interview surveys and 9.9% (among all age groups) based on statutory health insurance data [36].

The prevalence of unknown diabetes (1.5%) and its proportion among people with total diabetes in the current study (12.6%) are much lower than those reported in other populations. In Germany, data from nationwide RKI health examination surveys that are based on HbA1c measurements, identified a 3.4% prevalence of unknown diabetes between 1997 and 1999 and a decrease to 2.0% prevalence between 2008 and 2011 among 18- to 79-year-olds [21]. It has been argued that there has been increased awareness of the disease in recent years and more frequent diagnosis in several countries, that have led to a reduction in the number of cases of unknown diabetes [32]. The reason for the lower proportion of unknown diabetes in Greece needs to be investigated further, but this low proportion is encouraging, in that by reducing the lead time between diabetes onset and clinical diagnosis, combined with prompt initiation of treatment for glycaemia and cardiovascular risk factors, it is likely to confer substantial health benefits [37].

A novel finding of the present study is the measurement of pre-diabetes prevalence in the Greek population (12.4%), based on HbA1c and FPG measurements. Since several definitions of pre-diabetes are currently in clinical use, and since, depending on the definition used, prevalence estimates for pre-diabetes identified using a single test can differ by up to 4-fold [38], it is not always possible to compare the prevalence of pre-diabetes between studies with different definitions. Thus, in Spain, the age- and sex-adjusted prevalence rates of isolated IFG, isolated IGT, and combined IFG–IGT were 3.4%, 9.2%, and 2.2%, respectively [34]. In Germany, based on HbA1c measurements of 39–47 mmol/mol (5.7%–6.4%) for the definition of pre-diabetes, between 1997–1999 and 2008–2011 the prevalence decreased from 27.7% to 20.8% [21]. A study in Switzerland found pre-diabetes prevalence in 30.9% of the population; of these 79.9% were identified based on HbA1C, 9.9% based on FPG, and 10.3% based on both [39].

The use of anti-diabetic medications in the current sample of people with diabetes showed, as expected based on the (at the time of study initiation) guidelines [30], a preponderance of metformin use. Also, comparable to the recent pharmacologic study from the EOPYY database [16], DPP-4 inhibitors and sulfonylureas were the second most commonly prescribed medications. Insulin users comprised 11.6% of the participants (compared to 19.4% of Type 2 diabetes in the EOPYY database), with the majority of them (47.5%) using basal insulin.

A high percentage (70.9%) of the treated participants were well controlled (HbA1c <7.0% [53 mmol/mol]), with no difference between genders and among age categories. This compares to a mean of 52.5% in the NHANES 2007–2010 population having HbA1c <7.0% [40]. In that study, the prevalence of good control was significantly higher among those aged $\geq$75 years (63.3%), compared with about 50% among those aged 20–64 years, an age group of great interest given its anticipated longer life expectancy. The prevalence of good control did not differ between the two genders in that study as well.

4.1. *Strengths and limitations*

The main strength of the present study is its design and sampling procedures [22], which make it representative of the current general adult population in Greece, thus enabling accurate estimation of the prevalence of diabetes and pre-diabetes. Also, the fact that it included both self-report as well as blood glycaemic measurements (FPG and HbA1c), enables estimation of the prevalence of unknown diabetes and pre-diabetes for the first time.

However, there are also some limitations to consider. First, measurement of the participants' diabetic state did not include an OGTT, but only FPG and/or HbA1c. It is known that diabetes may be under-diagnosed without the 2-hour post-glucose challenge test [41], but in clinical practice, because of the inconvenience of OGTT testing, the majority of screening for diabetes is currently performed using FPG, HbA1c, or both [42]. Thus, the current study is consistent with how medicine is practiced in routine clinical care. Second, the HbA1c test may be affected by haemoglobin- and red blood cell-related diseases, such as anaemia, not uncommon in Greece. However, a recent study in individuals with heterozygous beta-thalassaemia in Greece has shown only a borderline effect on HbA1c levels [43]. Moreover, while the measurement of FPG is relatively simple and inexpensive to perform, HbA1c measurement is a more convenient diagnostic technique that does not require the patient to fast, it can be performed at any time of the day, displays less day-to-day variability and although it does not detect the same individuals with diabetes as FPG or OGTT, it has been advocated as a way of screening for diabetes, as long as it is performed using a certified method [44,45]. In the current study, HbA1c was measured in a central certified laboratory, using an accredited laboratory method. Third, because the survey was cross-sectional, only one measurement for every participant was taken and therefore, some participants without diabetes may have been misclassified as having diabetes. The American Diabetes Association (ADA) recommends a repeat measurement after a first diabetes-positive test result, to mitigate day-to-day variability [45]. The ADA recommends that the same test be used to make and confirm the diagnosis of diabetes [45], and most clinicians perform only the HbA1c or FPG test. In clinical practice, however, it is not uncommon for both of these tests to be performed simultaneously on the same blood sample. A sensitivity analysis of persons with both FPG and HbA1c measurements in the current study showed a comparable prevalence of diabetes with the main findings (12.1% vs. 11.9%). Fourth, since known diabetes was self-reported, self-reporting bias cannot be excluded, although the fact that the vast majority (around 90%) of those with self-reported diabetes were pharmacologically treated, indicates that this bias, if exists, would be of minimal magnitude. Fifth, a subset of the interviewed participants did not provide blood samples and thus were excluded from current analysis. We applied the inverse probability method to adjust for non-response from the excluded from the analysis participants, using as predictors the factors measured in EMENO, but the existence of other, non-measured, prognostic factors cannot be excluded. Extreme weights could also lead to biased estimates, but, in our case, no extreme weights were seen in the weights' distribution. Furthermore, since the study included only non-institutionalized persons, it may not be representative of certain people in the general population.

5. Conclusions

High rates of diabetes and pre-diabetes (especially in older age groups), but relatively low rates of unknown diabetes were shown in this national health survey of a representative sample of the Greek non-institutionalized adult population. These findings raise the importance of public health and medical efforts to screen and intervene in a coordinated and comprehensive manner to slow the transition of pre-diabetes to Type 2 diabetes. The finding of a high percentage of good control of the treated population is also encouraging. National surveillance of prevalence in diabetes is critical for the allocation of public health resources and planning and evaluation of screening, prevention, and treatment strategies. Longitudinal data should further explore trends and population subgroups' differences in conversion from normal status to pre-diabetes and from pre-diabetes to Type 2 diabetes and most importantly, the risk of long-term complications.

The findings of the present study will undoubtedly inform national and international authorities about the prevalence of diabetes and pre-diabetes in Greece and will hopefully enable the development of tailored and efficient strategies for disease prevention and management.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

EMENO Study Group Steering Committee: Alamanos Yannis, Benos Alexis, Chlouverakis Grigoris, Hajichristodoulou Christos, Karakatsani Anna, Stergiou George, Touloumi Giota (chair), Trypsianis Grigoris, Vantarakis Apostolos, Voulgari Paraskevi.

Coordinating Center: Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens (NKUA): Touloumi Giota, Karakosta Argiro, Pantazis Nikos, Vourli Georgia, Kalpourtzi Natasa.

Participating Centers: Department of Hygiene, Epidemiology and Medical Statistics, Medical School, NKUA: Touloumi Giota, Katsouyanni Klea, Kantzanou Maria, Pantazis Nikos, Karakosta Argiro, Kalpourtzi Natasa; **2nd Pulmonary Department, "Attikon" University Hospital, Medical School, NKUA:** Karakatsani Anna; **Hypertension Center STRIDE-7, Third Department of Medicine, Medical School, NKUA, "Sotiria" Hospital:** Stergiou George; **Department of Psychology, Panteion University of Political and Social Sciences:** Chrysochoou Xenia; **Department of Primary Health Care, General Practice and Health Services Research and Department of Hygiene, Medical School, Aristotle University of Thessaloniki:** Benos Alexis, Gavana Magda, Haidich Bettina; **Department of Hygiene and Epidemiology, Medical Faculty, University of Thessaly, Larissa:** Hadjichristodoulou Christos, Rachiotis George; **Environmental Microbiology Unit, Department of Public Health, Medical School, University of Patras:** Vantarakis Apostolos; **Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina:** Voulgari V Paraskevi; **Institute of Epidemiology, Preventive Medicine and Public Health:** Alamanos Yannis; **Department of Medical Statistics, Faculty of Medicine, Democritus University of Thrace:** Trypsianis Grigoris; **Division of Biostatistics, Department of Social Medicine, Medical School, University of Crete:** Chlouverakis Grigoris; **Department of Political Science and Public Administration, NKUA:** Nikolakopoulos Ilias, Panagiotis Koustenis; and **Hellenic Diabetes Association:** Makrilakis Konstantinos, Liatis Stavros, Ioannidis Ioannis, Iraklianou Stella, Raptis Athanasios, Sotiropoulos Alexis.

Funding

The EMENO survey was implemented under the Operational Program "Education and Lifelong Learning" and was co-funded by the European Union (European Social Fund) and national resources [grant number: MIS 376659]. Additional funding was obtained from the Hellenic Diabetes Association to measure glycated haemoglobin [grant number: K.E. 12008]. Microlife AG, Widnau, Switzerland offered 20 validated electronic (oscillometric) devices for blood pressure measurement. The funders had no involvement in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Author contribution

KM: wrote the original draft, reviewed and edited the final manuscript, NK: data curation, formal analysis; II: reviewed and edited the final manuscript; SI: reviewed and edited the final manuscript; AR: reviewed and edited the final manuscript; AS: reviewed and edited the final manuscript; MG: reviewed and edited the final manuscript; AP: reviewed and edited the final manuscript; MK: reviewed and edited the final manuscript; CH: reviewed and edited the final manuscript; GC: reviewed and edited the final manuscript; GT: reviewed and edited the final manuscript; PVV: reviewed and edited the final manuscript; YA: reviewed and edited the final manuscript; GT: conceptualization, administration of the project, reviewed and edited the final manuscript, SL: conceptualization, administration of the project, reviewed and edited the final manuscript.

REFERENCES

[1] WHO. Global Report on Diabetes. Isbn 2016;978:1–88. doi:ISBN 978 92 4 156525 7.

[2] Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Research and Clinical Practice 2019;157:107843. doi:10.1016/j.diabres.2019.107843.

[3] Hostalek U. Global epidemiology of prediabetes - present and future perspectives. Clin Diabetes Endocrinol 2019;5:5. https://doi.org/10.1186/s40842-019-0080-0.

[4] Koopman RJ, Mainous AG, Liszka HA, Colwell JA, Slate EH, Carnemolla MA, et al. Evidence of nephropathy and peripheral neuropathy in US adults with undiagnosed diabetes. Ann Family Med 2006;4:427–32. https://doi.org/10.1370/afm.577.

[5] Chaturvedi N. The burden of diabetes and its complications: Trends and implications for intervention. Diabetes Res Clin Pract 2007;76:S3–S12. https://doi.org/10.1016/j.diabres.2007.01.019.

[6] Bommer C, Sagalova V, Heesemann E, Manne-Goehler J, Atun R, Bärnighausen T, et al. Global economic burden of diabetes in adults: projections from 2015 to 2030. Diabetes Care 2018;41:963–70. https://doi.org/10.2337/dc17-1962.

[7] Gill GV, Ismail AA, Beeching NJ, Macfarlane SBJ, Bellis MA. Hidden diabetes in the UK: use of capture-recapture methods to estimate total prevalence of diabetes mellitus in an urban population. J Royal Soc Med 2003;96:328–32.
[8] Katsilambros N, Aliferis K, Darviri C, Tsapogas P, Alexiou Z, Tritos N, et al. Evidence for an increase in the prevalence of known diabetes in a sample of an urban population in Greece. Diabetic Med J Br Diabetic Assoc 1993;10:87–90.
[9] Lionis CD, Sasarolis SM, Koutis AD, Antonakis NA, Benos A, Papavasiliou S, et al. Measuring the prevalence of diabetes mellitus in a Greek primary health care district. Family Pract 1996;13:18–21.
[10] Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C. The epidemiology of Type 2 diabetes mellitus in Greek adults: the ATTICA study. Diabetic Med J Br Diabetic Assoc 2005;22:1581–8. https://doi.org/10.1111/j.1464-5491.2005.01731.x.
[11] Melidonis AM, Tournis SM, Kompoti MK, Lentzas IL, Roussou VR, Iraklianou SL, et al. Increased prevalence of diabetes mellitus in a rural Greek population. Rural Remote Health 2006;6:534.
[12] Gikas A, Sotiropoulos A, Panagiotakos D, Pastromas V, Paraskevopoulou E, Skliros E, et al. Rising prevalence of diabetes among Greek adults: findings from two consecutive surveys in the same target population. Diabetes Res Clin Pract 2008;79:325–9. https://doi.org/10.1016/j.diabres.2007.09.002.
[13] Gikas A, Lambadiari V, Sotiropoulos A, Panagiotakos D, Pappas S. Prevalence of major cardiovascular risk factors and coronary heart disease in a sample of greek adults: the saronikos study. Open Cardiovasc Med J 2016;10:69–80. https://doi.org/10.2174/1874192401610010069.
[14] Kapelios CJ, Kyriazis I, Ioannidis I, Dimosthenopoulos C, Hatziagelaki E, Liatis S. Diet, life-style and cardiovascular morbidity in the rural, free living population of Elafonisos island. BMC Public Health 2017;17:147. https://doi.org/10.1186/s12889-017-4053-x.
[15] Tentolouris N, Andrianakos A, Karanikolas G, Karamitsos D, Trontzas P, Krachtis P, et al. Prevalence of diabetes mellitus and obesity in the general adult population of Greece: a door-to-door epidemiological study. Diabetic Med J Br Diabetic Assoc 2009;26:451–2. https://doi.org/10.1111/j.1464-5491.2009.02692.x.
[16] Liatis S, Dafoulas GE, Kani C, Politi A, Litsa P, Sfikakis PP, et al. The prevalence and treatment patterns of diabetes in the Greek population based on real-world data from the nation-wide prescription database. Diabetes Res Clin Pract 2016;118:162–7. https://doi.org/10.1016/j.diabres.2016.06.018.
[17] Makrilakis K, Liatis S, Grammatikou S, Perrea D, Stathi C, Tsiligros P, et al. Validation of the Finnish diabetes risk score (FINDRISC) questionnaire for screening for undiagnosed type 2 diabetes, dysglycaemia and the metabolic syndrome in Greece. Diabetes Metab 2011;37:144–51.
[18] Ward MM. Estimating disease prevalence and incidence using administrative data: Some assembly required. J Rheumat 2013;40:1241–3. https://doi.org/10.3899/jrheum.130675.
[19] Cowie CC, Rust KF, Byrd-Holt DD, Eberhardt MS, Flegal KM, Engelgau MM, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health And Nutrition Examination Survey 1999-2002. Diabetes Care 2006;29:1263–8. https://doi.org/10.2337/dc06-0062.
[20] Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988–2012. JAMA 2015;314:1021–9. https://doi.org/10.1001/jama.2015.10029.
[21] Heidemann C, Du Y, Paprott R, Haftenberger M, Rathmann W, Scheidt-Nave C. Temporal changes in the prevalence of diagnosed diabetes, undiagnosed diabetes and prediabetes: findings from the German health interview and examination surveys in 1997–1999 and 2008–2011. Diabetic Med J Br Diabetic Assoc 2016;33:1406–14. https://doi.org/10.1111/dme.13008.
[22] Touloumi G, Karakatsani A, Karakosta A, Sofianopoulou E, Koustenis P, Gavana M, et al. National Survey of Morbidity and Risk Factors (EMENO): Protocol for a Health Examination Survey Representative of the Adult Greek Population. JMIR Res Protoc 2019;8:e10997. https://doi.org/10.2196/10997.
[23] Williams JR. The declaration of helsinki and public health. Bull World Health Org 2008;86:650–2.
[24] Pitsavos C, Panagiotakos DB, Chrysohoou C, Stefanadis C. Epidemiology of cardiovascular risk factors in Greece: aims, design and baseline characteristics of the ATTICA study. BMC Public Health 2003;3:32. https://doi.org/10.1186/1471-2458-3-32.
[25] The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus*. Follow-up Report on the Diagnosis of Diabetes Mellitus. Diabetes Care 2003;26:3160–7. doi:10.2337/diacare.26.11.3160.
[26] The International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009;32:1327–34. https://doi.org/10.2337/dc09-9033.
[27] Diabetes mellitus. Report of a WHO Study Group. World Health Organization - Technical Report Series 1985:Tech. Rep. Ser., no. 727. doi:10.7326/0003-4819-104-4-597_2.
[28] American Diabetes Association. 6. Glycemic Targets: Standards of Medical Care in Diabetes—2020. Diabetes Care 2020;43:S66–76. doi:10.2337/dc20-S006.
[29] Rao JNK, Scott AJ. The analysis of categorical data from complex sample surveys: chi-squared tests for goodness of fit and independence in two-way tables. J Am Stat Assoc 1981;76:221–30. https://doi.org/10.1080/01621459.1981.10477633.
[30] American Diabetes Association. Standards of medical care in diabetes - 2013. Diabetes Care 2013;36:S11–66. https://doi.org/10.2337/dc13-S011.
[31] Geiss LS, Bullard KM, Brinks R, Gregg EW. Considerations in epidemiologic definitions of undiagnosed diabetes. Diabetes Care 2018;41:1835–8. https://doi.org/10.2337/dc17-1838.
[32] Gnavi R, Migliardi A, Maggini M, Costa G. Prevalence of and secular trends in diagnosed diabetes in Italy: 1980–2013. Nutr Metab Cardiovasc Dis 2018;28:219–25. https://doi.org/10.1016/j.numecd.2017.12.004.
[33] Giampaoli S, Palmieri L, Donfrancesco C, Noce C lo, Pilotto L, Vanuzzo D. Cardiovascular health in Italy. Ten-year surveillance of cardiovascular diseases and risk factors: Osservatorio Epidemiologico Cardiovascolare/Health Examination Survey 1998–2012. European Journal of Preventive Cardiology 2015;22:9–37. doi:10.1177/2047487315589011.
[34] Soriguer F, Goday A, Bosch-Comas A, Bordiú E, Calle-Pascual A, Carmena R, et al. Prevalence of diabetes mellitus and impaired glucose regulation in Spain: the Di@bet.es study. Diabetologia 2012;55:88–93. https://doi.org/10.1007/s00125-011-2336-9.
[35] Chevreul K, Berg Brigham K, Bouché C. The burden and treatment of diabetes in France. Globalization Health 2014;10:6. https://doi.org/10.1186/1744-8603-10-6.
[36] Koch-Institut R. Incidence and mortality of diabetes mellitus in adults in Germany FOCUS Journal of Health Monitoring FOCUS Prevalence, incidence and mortality of diabetes mellitus in adults in Germany-A review in the framework of

the Diabetes Surveillance 2017;2:DOI 10.17886/RKI-GBE-2017-062. doi:10.17886/RKI-GBE-2017-062.

[37] Herman WH, Ye W, Griffin SJ, Simmons RK, Davies MJ, Khunti K, et al. Early detection and treatment of type 2 diabetes reduce cardiovascular morbidity and mortality: a simulation of the results of the anglo-danish-dutch study of intensive treatment in people with screen-detected diabetes in primary care (ADDITION-Europe). Diabetes Care 2015;38:1449–55. https://doi.org/10.2337/dc14-2459.

[38] Warren B, Pankow JS, Matsushita K, Punjabi NM, Daya NR, Grams M, et al. Comparative prognostic performance of definitions of prediabetes: a prospective cohort analysis of the atherosclerosis risk in communities (ARIC) study. Lancet Diabetes Endoc 2017;5:34–42. https://doi.org/10.1016/S2213-8587(16)30321-7.

[39] Blum J, Aeschbacher S, Schoen T, Bossard M, Pumpol K, Brasier N, et al. Prevalence of prediabetes according to hemoglobin A1c versus fasting plasma glucose criteria in healthy adults. Acta Diabetol 2015;52:631–2. https://doi.org/10.1007/s00592-014-0659-y.

[40] Stark Casagrande S, Fradkin JE, Saydah SH, Rust KF, Cowie CC. The prevalence of meeting A1C, blood pressure, and LDL goals among people with diabetes, 1988–2010. Diabetes Care 2013;36:2271–9. https://doi.org/10.2337/dc12-2258.

[41] Meijnikman AS, De Block CEM, Dirinck E, Verrijken A, Mertens I, Corthouts B, et al. Not performing an OGTT results in significant underdiagnosis of (pre)diabetes in a high risk adult Caucasian population. Int J Obesity 2005;2017(41):1615–20. https://doi.org/10.1038/ijo.2017.165.

[42] Matsushita K, Tang O, Selvin E. Addressing challenges and implications of national surveillance for racial/ethnic disparities in diabetes. JAMA 2019;322:2387–8. https://doi.org/10.1001/jama.2019.19428.

[43] Tsilingiris D, Makrilakis K, Voskaridou E, Pagkrati S, Dalamaga M, Liatis S. Effect of heterozygous beta thalassemia on HbA1c levels in individuals without diabetes mellitus: a cross sectional study. Clin Chim Acta 2019;494:132–7. https://doi.org/10.1016/j.cca.2019.03.1611.

[44] Olson DE, Rhee MK, Herrick K, Ziemer DC, Twombly JG, Phillips LS. Screening for diabetes and pre-diabetes with proposed A1C-based diagnostic criteria. Diabetes Care 2010;33:2184–9. https://doi.org/10.2337/dc10-0433.

[45] American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care 2020;43:S14–31. doi:10.2337/dc20-S002.