Prevalence and determinants of diabetes mellitus in a representative sample of italian adults

ROSARIO ASCIUTTO⁽¹⁾, ALESSANDRA LUGO⁽²⁾, SILVANO GALLUS⁽³⁾, MARIA CARLA RONCAGLIONI⁽⁴⁾, CARLO LA VECCHIA⁽²⁾, CRISTINA BOSETTI⁽³⁾

ABSTRACT

BACKGROUND: There is a dramatic epidemic of diabetes mellitus worldwide. This study provides an updated estimate of its prevalence and determinants among Italian adults.

METHODS: Data were derived from a face-to-face survey conducted in 2013 on 2901 individuals (1391 men, 1510 women) aged 18 years or more, representative of the general adult Italian population. Odds ratios (OR) for diabetes *versus* non diabetes by selected risk factors were derived using multiple logistic regression models.

RESULTS: Overall, 135 out of 2901 adults (4.7%) reported a diagnosis of diabetes, with similar prevalence in men (4.8%) and women (4.5%). Diabetes increased with increasing age (0.6% at age 18-44, 5.1% at age 45-64, and 11.3% at age ≥65 years; p-trend <0.001) and decreased with increasing level of education (12.8% for low, 7.8% for middle, and 1.4% for high education; p-trend <0.001). Prevalence of diabetes was higher among obese subjects (10.8%) compared to normal weight subjects (3.1%; OR=2.46; p-trend=0.001), among individuals reporting less than 30 minutes of walk per day (5.6%) compared to those reporting more than 60 minutes of walk/day (3.8%; OR=1.43), and among ex-smokers (11.6%) compared to never smokers (4.2%; OR=2.51). Moreover, diabetes prevalence was lower among moderate drinkers (3.1%) than among abstainers (6.1%; OR=0.57; p-trend=0.016). Prevalence of diabetes was 16.1% in individuals with a diagnosis of hypertension (OR=4.66), 15.2% in those with high cholesterol (OR=3.84), and 21.6% among aspirin users (OR=4.46).

CONCLUSIONS: Although diabetes prevalence in Italy is still comparatively low on an European and worldwide scale, effective preventive intervention strategies – focused on major risk behaviours – should be implemented to control the diffusion of this condition.

Key words: diabetes; prevalence; risk factors; survey; Italy

- (1) Department of Sciences for the Health Promotion and Mother and Child Care "G. D'Alessandro", Hygiene Section, University of Palermo, Palermo, Italy.
- (2) Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy.
- (3) Department of Epidemiology, IRCCS Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy.
- (4) Department of Cardiovascular Research, IRCCS Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy.

CORRESPONDING AUTHOR: Cristina Bosetti, PhD

Department of Epidemiology. IRCCS - Istituto di Ricerche Farmacologiche "Mario Negri" - Via Giuseppe La Masa 19, 20156 Milano - tel: +390239014526 - fax: +390233200231 e-mail: cristina.bosetti@marionegri.it

DOI: 10.2427/9980

Accepted on 21 May, 2014; Published as Online First on 15 December, 2014



INTRODUCTION

There is a dramatic epidemic of diabetes mellitus – in particular type 2 –worldwide, with more than 380 million adults (8.3%) affected by this condition in 2013 [1]. The number of people with type 2 diabetes has been increasing in most countries over the last few decades [2, 3], alongside social and cultural changes, such as population ageing, dietary changes, increasing obesity, and reduced physical activity [2, 4]. In Europe, the estimated prevalence of diabetes in 2013 was 6.8%, ranging from 4.9% in the UK to 14.9% in Turkey [1].

In Italy, diabetes affects more than 3 million individuals and an almost 30% increase in its prevalence was observed over the last decade (from 3.9% in 2001 to 5% in 2012) [5]. These data are provided by regular annual surveys historically conducted by the National Institute of Statistic [6] and, over the last years, by the PASSI project supported by the National Institute of Health [7]. Data from these surveys constitute a valid mean of monitoring the condition, but they are limited by not being easily available in scientific literature databases. A few surveys available in the international literature are quite outdated or based on selected subgroups, not representative of the Italian population [8-11]. Moreover, those investigations did not analyze the determinants of diabetes in detail, such as socio-demographic factors, lifestyle habits, and concomitant conditions, which play a decisive role in the prevention and control of this chronic disease.

The aim of this study is to provide an updated estimate of diabetes mellitus prevalence and determinants in a representative sample of Italian adults.

METHODS

Data were derived from a survey conducted between March and April 2013 by DOXA – the Italian branch of the Worldwide Independent Network/Gallup International Association – on a sample of 3000 individuals aged 15 years or over, to investigate tobacco smoking habits in the Italian population [12]. The sample was representative of the general Italian population aged 15 years or more in terms of sex, age, geographic area, and socio-economic characteristics. Individuals

were selected through a multistage sampling process from 116 municipalities (the smallest Italian administrative divisions) in the 20 Italian regions (the largest Italian administrative divisions). In the municipalities considered, individuals were randomly sampled from electoral rolls, within strata defined by sex and age. Unavailable individuals were replaced by their neighbours within the same sex and age group. Statistical weights were used to assure the representativeness of the Italian population. For the present analyses, we considered only 2901 individuals aged 18 years or more (1391 men, 1510 women).

Individuals were interviewed by ad hoc trained interviewers using a structured questionnaire in the context of a computerassisted personal in-house interview (CAPI). Besides general information on demographic socio-economic characteristics, the questionnaire included information on tobacco smoking (including smoking status), alcohol drinking (weekly frequency of intake), physical activity (daily minutes of walking), anthropometric measures (height and weight), self-reported diagnosis of hypertension, high cholesterol (>200 mg/dl), and use of aspirin for the prevention of cardiovascular diseases. Moreover, individuals were asked if they ever had a diagnosis of diabetes, and the age at diagnosis. Body mass index (BMI, kg/m2) was calculated from self-reported weight and height.

Data analysis

We computed the percent prevalence, and the corresponding 95% confidence intervals (CI), of diabetes mellitus in the overall population and across strata of selected characteristics. Odds ratios (OR), and the corresponding 95% CIs, for diabetes versus non diabetes by age and selected risk factors were derived using unconditional multiple logistic regression models including terms for sex, age, level of education, geographic area, smoking status, alcohol consumption, BMI, and physical activity [13]. Tests for trend were based on the difference of the likelihood ratio test between models with and without a linear term for the variable considered. All the analyses were performed with SAS version 9.2 (SAS Institute).



RESULTS

Table 1 shows the percent prevalence of diabetes in the Italian adult population by age and selected socio-demographic characteristics. Overall, 135 out of 2901 adults (4.7%, 95% CI 3.9-5.4) reported a diagnosis of diabetes mellitus. Of these, 13% were diagnosed before the age 40 and 87% after that age (data not shown). Prevalence of diabetes was similar in men (4.8%, 95% CI 3.7-6.0) and women (4.5%, 95% CI 3.5-5.6; Table 1). Diabetes prevalence substantially increased with age, being 0.6% in individuals aged 18-44, 5.1% in those aged 45-64, and 11.3% in those aged ≥65 years (OR=6.08 and 8.51, respectively for age 45-64 and ≥65 compared to age 18-44 years; p for trend <0.001). Prevalence of diabetes decreased with increasing level of education, being 12.8% in individuals with no/elementary school, 7.8% in those with middle school, and 1.4% in those with high school or university (OR=3.76 for no/elementary and 3.77 for middle school compared to high school/university; p for trend <0.001). Moreover, a geographic gradient was reported, the prevalence of diabetes being 3.2% in northern and 5.9% in central/southern Italy (OR=1.99). Prevalence of diabetes by sociodemographic characteristics was consistent in the two sexes.

Prevalence of diabetes was higher in overweight (4.9%) and obese (10.8%) individuals compared to underweight/normal weight individuals (3.1%), but the multivariate OR was only significantly increased in obese adults (OR=2.46, Table 2). Diabetes was more frequent among individuals reporting less physical activity (5.6% for <30 and 4.1% for 30-60 minutes of walk/day) than among those reporting a higher physical activity (3.8% for >60 minutes of walk/day), although the corresponding ORs (1.43 and 1.25, respectively) and the trend in risk (p=0.204) were not significant. Prevalence of diabetes was more frequent among ex-smokers (11.6%) than

TABLE 1

SEX-SPECIFIC AND OVERALL PERCENT PREVALENCE OF DIABETES MELLITUS AMONG 2901 ITALIAN ADULTS (1391 MEN, 1510 WOMEN) BY SOCIO-DEMOGRAPHIC CHARACTERISTICS, AND CORRESPONDING ODDS RATIOS (OR) FOR DIABETES VERSUS NON DIABETES. ITALY, 2013

(OI) TOR DIADETES VERSOS NOR DIADETES. TIAET, 2015									
	MEN		WOMEN		TOTAL				
SOCIO-DEMOGRAPHIC CHARACTERISTICS	N.	N. DIABETICS (%)	N.	N. DIABETICS (%)	N.	N. DIABETICS (%)	OR FOR DIABETES VS NON DIABETES (95% CI) ^a		
Total	1391	67 (4.8)	1510	68 (4.5)	2901	135 (4.7)			
AGE GROUP (YEARS)									
18-44	628	4 (0.7)	616	3 (0.5)	1244	7 (0.6)	1 ^b		
45-64	464	26 (5.6)	484	22 (4.6)	948	48 (5.1)	6.08 (2.68-13.79)		
≥65	299	37 (12.4)	410	43 (10.4)	709	80 (11.3)	8.51 (3.66-19.79)		
p for trend							<0.001		
EDUCATION									
No/elementary school	162	21 (13.1)	270	34 (12.6)	432	55 (12.8)	3.76 (2.13-6.64)		
Middle school	351	30 (8.6)	368	26 (7.0)	718	56 (7.8)	3.77 (2.25-6.32)		
High school/university	878	16 (1.8)	872	8 (1.0)	1750	24 (1.4)	1 ^b		
p for trend							<0.001		
GEOGRAPHIC AREA									
Northern Italy	644	20 (3.2)	695	22 (3.2)	1339	43 (3.2)	1 ^b		
Central/southern Italy	747	47 (6.3)	815	46 (5.6)	1562	92 (5.9)	1.99 (1.34-2.96)		

CI. confidence interval.

^aORs were estimated using unconditional multiple logistic regression models including terms for sex, age, education, geographic area, smoking status, alcohol consumption, body mass index, and physical activity. ^bReference category.



in never smokers (4.2%, OR=2.51) and was lower among individuals consuming alcohol (3.1% for <7 and 4.7% for ≥7 drinks/week) than among abstainers (6.1%), the OR being 0.57 for both categories of intake compared to abstainers (p for trend=0.016). The difference in the prevalence of diabetes between ex-smokers and never smokers was evident in men (15.1% and 2.7%, respectively), but not in women (4.9% and 5.2%, respectively), while similar patterns in diabetes prevalence were observed in the two sexes according to other lifestyle habits.

The prevalence of diabetes was 16.1% in individuals with a diagnosis of hypertension and 1.7% in those without hypertension (OR=4.66), 15.2% in those with high cholesterol and 2.1% in those with normal cholesterol levels (OR=3.84), and 21.6% among aspirin users and

2.5% among non aspirin users (OR=4.46, Table 3). Similar diabetes prevalence was found in men and women.

DISCUSSION

In our study, the estimated prevalence of diabetes in the Italian adult population is 4.7%, with similar figures in men (4.8%) and women (4.5%). Our results are consistent with data from the PASSI national survey, conducted in 2009-2012 on Italian adults, reporting a prevalence of diabetes around 4.5% [7]. A few previous Italian studies reported a prevalence of 3.8% (in 2000) in an area of northwestern Italy [8], 4.2% (in 2007) in Lombardy region [9], 4.8% (in 2003) in the population of Turin

-	ч Б	•

SEX-SPECIFIC AND OVERALL PERCENT PREVALENCE OF DIABETES MELLITUS AMONG 2901
ITALIAN ADULTS (1391 MEN, 1510 WOMEN) BY LIFESTYLE HABITS AND CORRESPONDING
ODDS RATIOS (OR) FOR DIABETES VERSUS NON DIABETES. ITALY, 2013

	MEN		WOMEN		TOTAL			
LIFESTYLE HABITS	N.	N. DIABETICS (%)	N.	N. DIABETICS (%)	N.	N. DIABETICS (%)	OR FOR DIABETES VS NON DIABETES (95% CI) ^a	
BODY MASS INDEX								
Under/Normal weight	720	21 (3.0)	923	29 (3.2)	1643	51 (3.1)	1 ^b	
Overweight	485	21 (4.4)	387	22 (5.6)	873	43 (4.9)	0.96 (0.62-1.48)	
Obese	185	25 (13.3)	200	17 (8.5)	386	42 (10.8)	2.46 (1.56-3.90)	
p for trend							0.001	
PHYSICAL ACTIVITY (MINUTES	OF WAL	K/DAY)						
<30	511	29 (5.7)	691	39 (5.6)	1203	68 (5.6)	1.43 (0.82-2.47)	
30-60	594	25 (4.2)	564	22 (4.0)	1157	47 (4.1)	1.25 (0.71-2.20)	
>60	286	14 (4.8)	255	7 (2.6)	541	20 (3.8)	1 ^b	
p for trend							0.204	
SMOKING STATUS								
Never smokers	755	20 (2.7)	1142	59 (5.2)	1897	79 (4.2)	1 ^b	
Ex-smokers	260	39 (15.1)	133	6 (4.9)	392	46 (11.6)	2.51 (1.61-3.93)	
Current smokers	376	8 (2.1)	236	3 (1.2)	612	11 (1.7)	0.53 (0.27-1.05)	
ALCOHOL CONSUMPTION								
Non drinker	284	19 (6.7)	786	46 (5.9)	1070	65 (6.1)	1 ^b	
<7 drinks/week	505	18 (3.5)	508	13 (2.7)	1013	31 (3.1)	0.57 (0.35-0.92)	
≥7 drinks/week	602	30 (5.1)	216	8 (3.8)	818	39 (4.7)	0.57 (0.35-0.92)	
p for trend							0.016	

CI. confidence interval.

^aORs were estimated using unconditional multiple logistic regression models including terms for sex, age, level of education, geographic area, smoking status, alcohol consumption, body mass index, and physical activity. ^bReference category.



[10], and 8.3% (in 2008) in a sample of the population from Rome [11]. Such figures are not directly comparable with ours, since they refer to selected populations not representative of the general Italian population and different calendar years. On a comparative scale, Italy has a prevalence similar to that observed in France (4.6% in 2006-2007) [14], but lower than those reported in Spain (7.8% in 2009-10) [15] and Portugal (6.6% in 2009) [16]. The International Diabetes Federation report on the global prevalence of diabetes confirms that in 2013 Italy had a relatively low rate of diabetes compared to other major European countries [1]. Italy has also been shown to have a relatively low and fairly stable prevalence of obesity over the last decade (around 8-9%) [17]. This may be explained by the relatively favourable dietary and lifestyle habits (including a relatively high adherence to the Mediterranean diet) of the Italian population compared to other European countries [18].

In our survey, we confirm that the prevalence of diabetes significantly increases with age [6, 7, 14-16]. Older adults indeed tend to be more frequently overweight and obese, possibly due to reduced physical activity, and consequently increased insulin resistance and impaired pancreatic isle function [19, 20].

Our findings show that the prevalence of

diabetes is related to the education level, adults with lower education having an almost 4-fold increased risk of diabetes compared to those with higher levels of education. This result is consistent with those from previous studies, including a recent case-cohort study nested within the European Prospective Investigation into Cancer and Nutrition (EPIC) [21], another large European study [22], and two Italian studies [10, 11], which indicated that there are socio-economic inequalities in the prevalence of diabetes. The positive association with education - and socio-economic status in general - is likely mediated by other factors: individuals with a higher level of education generally belong to younger generations and have healthier behaviours, including better dietary habits, more frequent physical activity (with consequently lower BMI), and less frequent tobacco use [23]. Moreover, they may be more receptive to prevention messages and prone to use the health care systems better. However, in our study the association with education was significant even after adjustment for age, obesity, and other selected characteristics. The relation between diabetes and low education/socioeconomic level has important public health implications, because it indicates that any health care program should consider this specific frail population subgroup

TABLE 3

SEX-SPECIFIC AND OVERALL PERCENT PREVALENCE (%) OF DIABETES MELLITUS AMONG 2901
ITALIANS (1391 MEN AND 1510 WOMEN) BY CLINICAL HISTORY, AND CORRESPONDING ODDS RATIOS (OR)
FOR DIABETES VERSUS NON DIABETES. ITALY, 2013

TOR DIABETES VERSUS NON DIABETES. HALF, 2015								
	MEN		WOMEN		TOTAL			
CLINICAL HISTORY	N.	N. DIABETICS (%)	N.	N. DIABETICS (%)	N.	N. DIABETICS (%)	OR FOR DIABETES VS. NON DIABETES (95% CI) ^a	
HYPERTENSION DIAGNOSIS								
No	1113	26 (2.3)	1192	14 (1.2)	2305	39 (1.7)	1 ^b	
Yes	278	42 (15.0)	319	54 (17.0)	596	96 (16.1)	4.66 (3.03-7.16)	
HIGH CHOLESTEROL								
No	1121	29 (2.6)	1217	21 (1.7)	2338	50 (2.1)	1 ^b	
Yes	269	38 (14.2)	294	47 (16.0)	563	85 (15.2)	3.84 (2.56-5.75)	
USE OF ASPIRIN								
No	1229	28 (2.3)	1347	37 (2.7)	2576	65 (2.5)	1 ^b	
Yes	162	39 (24.1)	164	31 (19.1)	325	70 (21.6)	4.46 (2.97-6.70)	

CI, confidence interval.

^aORs were estimated using unconditional multiple logistic regression models including terms for sex, age, level of education, geographic area, smoking status, alcohol consumption, body mass index, and physical activity. ^bReference category.



in order to tackle the diabetes epidemic.

As in previous Italian surveys [6, 7], we report a North to South gradient in the prevalence of diabetes. Such a gradient could be partially explained by the lower education and socioeconomic level in adults from the central/southern regions than those from northern Italy, and the higher prevalence of overweight/obesity [17], although the OR for geographic area remained significantly higher in central/southern compared to northern Italy even after adjusting for education and BMI. The improved prevention programs and management of diabetes in northern Italy could also have had a role in the differences observed in diabetes prevalence across geographic areas.

As expected, a significant trend in diabetes prevalence was reported with BMI, obesity being the major correlate of type 2 diabetes [24]. In our sample, more than 60% of individuals with diabetes were overweight or obese. Major emphasis should be placed by health providers to induce favourable changes in diet. Even a modest weight loss (5-10%) in overweight individuals can have a beneficial impact on glycaemic control [25]. Although we did not find a significant association between physical activity and diabetes prevalence, the fact that in our sample half of the diabetics reported less than 30 minutes of walk per day is a reason of concern. Conversely, moderate physical activity almost daily should be recommended for individuals with diabetes; in addition to its cardiovascular benefits exercise can improve glycaemic control [26, 27].

A significantly higher prevalence of diabetes among ex-smokers than among never smokers was found in our data. Although there is evidence that smoking is a risk factor for diabetes [28], the higher prevalence of diabetes in ex-than in current smokers likely reflects behavioural changes following medical counselling or secondary illnesses in diabetics. Health providers could have played a key role in motivating people with diabetes to quit smoking, but we found that only one out of 42 individuals who quit smoking in correspondence or shortly after the diagnosis of diabetes reported a physician's recommendation as the most important reason to quit. Most diabetic ex-smokers quit because of health reasons. Furthermore, individuals with diabetes who continue to smoke, in fact, have a substantial excess risk of health complications, including cardiovascular diseases [29]. Stronger efforts and commitments to promote smoking cessation among people with diabetes are needed, as seen in countries such as the USA where strategies for smoking cessation have been implemented more effectively than in Italy [30, 31]. Although smoking cessation is associated with weight gain and subsequent risk of diabetes, it has been shown that in the long-term the benefits of smoking cessation outweigh the adverse effect of early weight gain [32].

With reference to alcohol consumption, we found a lower prevalence of diabetes among moderate drinkers compared to abstainers. The cross-sectional design of our study precludes drawing any casual inferences from this association, but it is worth noticing that a large body of evidence suggests that moderate alcohol intake is associated with a 30-50% reduced risk of type 2 diabetes [33, 34]. Moderate alcohol consumption, in fact, has been shown to improve insulin sensitivity and reduce plasma insulin levels [35, 36], probably due to alcohol-induced increases in adiponectin [37].

Diabetes is often associated with other diseases and metabolic disorders, such as the metabolic syndrome. Thus, in our study we found a significantly higher prevalence of diabetes in subjects reporting a diagnosis hypertension or hypercholesterolemia, as observed in other Italian and European surveys [7, 15]. Moreover, we reported a higher prevalence of diabetes among users of aspirin for cardiovascular prevention, diabetics being at a high risk of coronary heart diseases [29, 38]. However, we also found that almost half of the diabetics in our sample (48%) did not use aspirin regularly for primary or secondary prevention, which instead should be considered in individuals with high risk of cardiovascular conditions, once benefits exceed harms [39].

Limitations of the present study include those inherent to the cross-sectional design. Moreover, the diagnosis of diabetes (and other co-morbidities) was based on self-reported information, although the recall of diabetes has been shown to be satisfactorily reproducible [40] and our prevalence estimate is in line with those from national surveys [6, 7]. We also could not distinguish type 1 form type 2 diabetes mellitus, but 87% of subjects with diabetes were diagnosed at 40 years or more, and are thus likely to have type 2 diabetes. Our survey has the strength of being conducted on a representative sample of the general Italian

adult population and included information on various lifestyle habits.

behaviours – should be implemented in order to control the diffusion of this condition.

CONCLUSION

In conclusion, although diabetes prevalence in Italy is still comparatively low on an European and worldwide scale, effective preventive intervention strategies – focused on major risk ACKNOWLEDGEMENTS: The conduction of the survey was supported by the Italian Ministry of Health. This work was partially conducted with the contribution of the Italian Association for Cancer Research (AIRC; grant number: 13203, C. Bosetti).

References

- International Diabetes Federation. IDF Diabetes Atlas,
 6th ed. Available from: http://www.idf.org/diabetesatlas.
 Brussels, Belgium: International Diabetes Federation 2013.
- [2] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27(5):1047-53.
- [3] Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet 2011;378(9785):31-40.
- [4] Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature 2001;414(6865):782-7.
- [5] National Institute of Health. Progetto IGEA. Integrazione, gestione e assistenza per la malattia diabetica. Il diabete: fatti e numeri. Available from: http://www.epicentro.iss. it/igea/diabete/epid.asp [Accessed April 15, 2014].
- [6] Istituto Nazionale di Statistica. Annuario Statistico Italiano 2013. Available from: http://www.istat.it/it/ archivio/107568 [Accessed April 15, 2014].
- [7] Centro Nazionale di Epidemiologia SePdS, National Institute of Health. Rapporto nazionale Passi 2012: diabete. Available from: http://www.epicentro.iss.it/passi/ rapporto2012/diabete.asp [Accessed April 15, 2014].
- [8] Bruno G, Merletti F, Bargero G, et al. Changes over time in the prevalence and quality of care of type 2 diabetes in Italy: the Casale Monferrato surveys, 1988 and 2000. Nutr Metab Cardiovasc Dis 2008;18(1):39-45.
- [9] Monesi L, Baviera M, Marzona I, et al. Prevalence, incidence and mortality of diagnosed diabetes: evidence from an Italian population-based study. Diabet Med 2012;29(3):385-92.
- [10] Gnavi R, Karaghiosoff L, Costa G, Merletti F, Bruno G. Socio-economic differences in the prevalence of diabetes in Italy: the population-based Turin study. Nutr Metab Cardiovasc Dis 2008;18(10):678-82.

- [11] Fano V, Pezzotti P, Gnavi R, et al. The role of socioeconomic factors on prevalence and health outcomes of persons with diabetes in Rome, Italy. Eur J Public Health 2013;23(6):991-7.
- [12] Gallus S, Lugo A, Colombo P, Pacifici R, La Vecchia C. Smoking prevalence in Italy 2011 and 2012, with a focus on hand-rolled cigarettes. Prev Med 2013;56(5):314-8.
- [13] Breslow NE, Day NE. Statistical methods in cancer research. Vol. I. The analysis of case-control studies. IARC Sci Publ No. 32. Lyon, France: IARC 1980.
- [14] Bonaldi C, Vernay M, Roudier C, et al. A first national prevalence estimate of diagnosed and undiagnosed diabetes in France in 18- to 74-year-old individuals: the French Nutrition and Health Survey 2006/2007. Diabet Med 2011;28(5):583-9.
- [15] Soriguer F, Goday A, Bosch-Comas A, et al. Prevalence of diabetes mellitus and impaired glucose regulation in Spain: the Di@bet.es Study. Diabetologia 2012;55(1):88-93.
- [16] Gardete-Correia L, Boavida JM, Raposo JF, et al. First diabetes prevalence study in Portugal: PREVADIAB study. Diabet Med 2010;27(8):879-81.
- [17] Gallus S, Odone A, Lugo A, et al. Overweight and obesity prevalence and determinants in Italy: an update to 2010. Eur J Nutr 2013;52(2):677-85.
- [18] [Rossi M, Turati F, Lagiou P, et al. Mediterranean diet and glycaemic load in relation to incidence of type 2 diabetes: results from the Greek cohort of the populationbased European Prospective Investigation into Cancer and Nutrition (EPIC). Diabetologia 2013;56(11):2405-13.
- [19] Chang AM, Halter JB. Aging and insulin secretion. Am J Physiol Endocrinol Metab 2003;284(1):E7-12.
- [20] Amati F, Dube JJ, Coen PM, Stefanovic-Racic M, Toledo FG, Goodpaster BH. Physical inactivity and obesity underlie the insulin resistance of aging. Diabetes Care 2009;32(8):1547-9.
- [21] Sacerdote C, Ricceri F, Rolandsson O, et al. Lower educational level is a predictor of incident type 2 diabetes in European countries: the EPIC-InterAct study. Int J Epidemiol 2012;41(4):1162-73.



- [22] Espelt A, Borrell C, Roskam AJ, et al. Socioeconomic inequalities in diabetes mellitus across Europe at the beginning of the 21st century. Diabetologia 2008;51(11):1971-9.
- [23] Winkleby MA, Fortmann SP, Barrett DC. Social class disparities in risk factors for disease: eight-year prevalence patterns by level of education. Prev Med 1990;19(1):1-12.
- [24] Astrup A, Finer N. Redefining type 2 diabetes: 'diabesity' or 'obesity dependent diabetes mellitus'? Obes Rev 2000;1(2):57-9.
- [25] Pasanisi F, Contaldo F, de Simone G, Mancini M. Benefits of sustained moderate weight loss in obesity. Nutr Metab Cardiovasc Dis 2001;11(6):401-6.
- [26] Mayer-Davis EJ, D'Agostino R, Jr., Karter AJ, et al. Intensity and amount of physical activity in relation to insulin sensitivity: the Insulin Resistance Atherosclerosis Study. JAMA 1998;279(9):669-74.
- [27] Umpierre D, Ribeiro PA, Kramer CK, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA 2011;305(17):1790-9.
- [28] Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J.

 Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA 2007;298(22):2654-64.
- [29] Tavani A, Bertuzzi M, Gallus S, Negri E, La Vecchia C. Diabetes mellitus as a contributor to the risk of acute myocardial infarction. J Clin Epidemiol 2002;55(11):1082-7.
- [30] Clair C, Meigs JB, Rigotti NA. Smoking behavior among US adults with diabetes or impaired fasting glucose. Am J Med 2013;126(6):541 e15-8.
- [31] Ford ES, Mokdad AH, Gregg EW. Trends in cigarette smoking among US adults with diabetes: findings from the Behavioral Risk Factor Surveillance System. Prev Med 2004;39(6):1238-42.
- [32] Wannamethee SG, Shaper AG, Perry IJ. Smoking as a

- modifiable risk factor for type 2 diabetes in middle-aged men. Diabetes Care 2001;24(9):1590-5.
- [33] Howard AA, Arnsten JH, Gourevitch MN. Effect of alcohol consumption on diabetes mellitus: a systematic review. Ann Intern Med 2004;140(3):211-9.
- [34] Carlsson S, Hammar N, Grill V. Alcohol consumption and type 2 diabetes Meta-analysis of epidemiological studies indicates a U-shaped relationship. Diabetologia 2005;48(6):1051-4.
- [35] Kiechl S, Willeit J, Poewe W, et al. Insulin sensitivity and regular alcohol consumption: large, prospective, cross sectional population study (Bruneck study). BMJ 1996;313(7064):1040-4.
- [36] Mayer EJ, Newman B, Quesenberry CP, Jr., Friedman GD, Selby JV. Alcohol consumption and insulin concentrations. Role of insulin in associations of alcohol intake with high-density lipoprotein cholesterol and triglycerides. Circulation 1993;88(5 Pt 1):2190-7.
- [37] Sierksma A, Patel H, Ouchi N, et al. Effect of moderate alcohol consumption on adiponectin, tumor necrosis factor-alpha, and insulin sensitivity. Diabetes Care 2004;27(1):184-9.
- [38] Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106(25):3143-421.
- [39] Hennekens CH, Dalen JE. Aspirin in the treatment and prevention of cardiovascular disease: past and current perspectives and future directions. Am J Med 2013:126(5):373-8.
- [40] Cricelli C, Mazzaglia G, Samani F, et al. Prevalence estimates for chronic diseases in Italy: exploring the differences between self-report and primary care databases. J Public Health Med 2003;25(3):254-7.

