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Cardiovascular risk and access to primary care: Comparisons among Chinese documented and undocumented immigrants

Alessio Pellegrino [a,b], Maria Calabrese [c], Maria Boddi [a,b], Irene Vacirca [a], Cecilia Baccari [a], Laura Bonvicini [d], Francesco Venturelli [d], Alessio Petrelli [e], Anteo Di Napoli [e], Maria Perticone [f], Paolo Giorgi Rossi [d], Pietro Amedeo Modesti [a,b,*]

[a] Medicina dello Sport e dell'Esercizio Fisico, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
[b] Department of Medicina Sperimentale e Clinica, University of Florence, Florence, Italy
[c] Diabetology Unit, Ospedale Misericordia e Dolce, Prato, Italy
[d] Epidemiology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[e] Epidemiology Unit, National Institute for Health, Migration and Poverty (INMP), Rome, Italy
[f] Department of Medical and Surgical Sciences, University Magna Graecia of Catanzaro, Catanzaro, Italy

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ABSTRACT

Aims: The aim of this study was to examine main risk factors of undocumented Chinese migrants living in Italy when compared with Chinese migrants registered with National Health Service (NHS).
Methods: A cohort of 3435 Chinese first-generation immigrants living in Prato underwent blood pressure (BP) measurement and blood tests. Hypertension was diagnosed for BP $\geq$ 140/90 mmHg at 2 visits, and/or antihypertensive drug use; type 2 diabetes (T2DM) for fasting glucose $\geq$ 126 mg/dL at 2 visits, and/or use of hypoglycemic drugs; hypercholesterolemia (HC) for cholesterol $\geq$ 240 mg/dL and/or statins use. Subjects diagnosed with hypertension, T2DM, or HC unaware of their condition were considered newly diagnosed. Comparisons were performed using multivariable adjusted logistic regression analysis.
Results: A large proportion of Chinese migrants were undocumented (1766, 51 %); newly diagnoses of risk factors were performed especially among undocumented migrants; registration with NHS was associated with higher level of awareness for hypertension and T2DM and with 6 times higher rate of treatment for T2DM. Only a small minority of subjects with high cholesterol were treated with statins.
Conclusions: Undocumented immigrants had high prevalence of risk factors with lower levels of awareness than migrants registered with the NHS. Health policies targeting this hard-to-reach population needs to be improved.

1. Introduction

Preventive strategies have led most European countries to a reduction in cardiovascular events over recent decades although inequalities remain in disadvantaged groups such as low-socioeconomic status and immigrant populations [1,2]. Several studies highlighted that in Europe the age-standardized prevalence of cardio-metabolic diseases is higher among non-native ethnic minority groups than among the native population [3,4]. Systematic reviews and single cohort studies did not include undocumented migrants, defined in the European Union (EU) context as third-country nationals present in the territory of a Schengen State who do not meet, or no longer meet, the conditions of entry as set out in the Regulation (EU) 2016/399 (Schengen Borders Code) or other conditions for entry [5]. For this subgroup of people, it is not possible to carry out epidemiological investigations following conventional recruiting procedure. The conventional sampling procedure adopted in epidemiological studies indeed excludes undocumented migrants because the ability to go back to a list of subjects in some form is lacking. Furthermore, undocumented people do not always agree to share their personal data for fear of being deported; they are highly mobile; and cultural and linguistic problems are often a reason for mistrust. The use of administrative data also bears limitations. In the EU, the organization and delivery of medical services is a national competence and therefore greatly differs from country to country. In Italy, immigrants who are in

* Corresponding author at: Department of Medicina Sperimentale e Clinica, Medicina dello Sport e dell'Esercizio Fisico, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Largo Brambilla 3, 50134 Florence, Italy.
E-mail address: pa.modesti@unifi.it (P.A. Modesti).

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possession of a valid residence permit (documented), must register with the National Health Service (NHS) and can access health services as EU citizens do [6]. Undocumented migrants can receive urgent or essential outpatient and hospital care in most EU Member States via an anonymous code (STP for "temporarily present foreigner") which however does not give access to primary care services [6,7]. In countries where these policies are adopted, the retrieval of data from hospital admission databases led to document more urgent hospital admissions, more preventable complications, and a higher recurrence in terms of access and costs to hospital services rather than pharmaceutical prescriptions for undocumented migrants admitted with the STP code [6–9]. However, this approach does not examine the subgroup of undocumented migrants without an STP code, nor does it give an estimate of their proportion, or allow us to explore the prevalence, awareness and treatment rate of the most common risk factors for cardiovascular diseases (hypertension, type 2 diabetes mellitus or hypercholesterolemia).

The present study contributes to filling this gap by presenting a detailed description of the health needs of a large cohort of undocumented Chinese migrants in Prato, Italy. Chinese communities have a strong social structure that may offer protection and social support to undocumented migrants [10,11] and there are now a large number of Chinese present in Europe [12,13]. We therefore performed an analysis of data collected in a large cohort of first-generation Chinese migrants investigated in the CHinese In Prato study (CHIP) [14–16] to examine main risk factors of undocumented Chinese migrants (with or without the STP code) when compared to Chinese registered with the NHS.

2. Material and methods

2.1. Study design, setting and population

Data were collected in a population-based, cross-sectional study (CHinese In Prato study, CHIP) between July 2014 and November 2019 as previously described [14–18]. Briefly, the CHIP survey is a cardiovascular risk-factor screening program of the Chinese population performed at a community level through a sensitive, culturally appropriate, non-coercive recruitment process that adopted a network sampling procedure. Exclusion criteria included pregnant women, critically ill individuals, and impaired cognitive ability, as judged by clinical staff members during the first evaluation. The study received Ethical approval from the "Comitato Etico Regionale per la Sperimentazione Clinica della Regione Toscana" (Rif. OSS 14.089 and CEAVC_23254). All participants provided written informed consent to participate in this study. Each participant received the results of all performed clinical and biochemical tests, with a clear statement of whether the diagnostic criteria for hypertension, type 2 diabetes (T2DM), or hypercholesterolemia (HC) were met. Participants with screen-detected diseases were asked to return for confirmatory testing. If confirmed they were offered second-level assessments and treatments through the NHS, with clinical practices based on current international guidelines. No other incentives were offered to study participants.

2.2. Data collection

All participants were instructed to fast overnight before the day of survey. In the early morning (between 07.00 and 10.00 a.m.), individuals attended the Research Centre, where trained staff members administered a questionnaire and performed physical (blood pressure and anthropometry) and biochemical blood measurements (glucose and total cholesterol). The gathered information included participant sociodemographic data and health insurance (full registration or not with the NHS), tobacco use, oral health, medical (including risk factor awareness and treatment), and migration history. Subjects not registered with the NHS were considered as "undocumented".

Anthropometric measurements were then measured according to standardized protocols [15–17]. Blood pressure (BP) was measured 3 times [19] using clinically validated digital sphygmomanometers (M6; Omron Matsusaka Co.Ltd., Matsusaka, Japan). The average of the last 2 readings was used for analysis. Fingerprick blood samples were immediately processed with validated Point of Care (POC) diagnostics (AccuChek AVIVA. Roche Diagnostics S.p.A., Mannheim, Germany for glucose and MultiCare-in, HPS, Italy, for total cholesterol) [15–17]. Non-fasting participants were asked to return having fasted, for blood tests. Participants with fasting glucose (FG) $\geq$126 mg/dL, systolic BP $\geq$140 mmHg, or diastolic BP $\geq$90 mmHg were also asked to return for confirmatory testing. All requested participants attended the second visit. Oral health questions investigated status of the periodontal supporting tissues and inflammation of the gingiva [20].

2.3. Diagnostic criteria

Hypertension was diagnosed if systolic BP (SBP) was $\geq$140 mmHg and/or diastolic BP (DBP) was $\geq$90 mmHg at the 2 visits, and/or if antihypertension medication had been taken in the previous 2 weeks [19]. The diagnosis of T2DM was based on FG criteria ($\geq$126 mg/dL confirmed by repeated testing at a second visit) and/or current treatment with glucose-lowering drugs. HC was classified for total cholesterol (TC) levels $\geq$240 mg/dL and/or statins use [19]. Subjects were considered aware of their condition (hypertension, T2DM, or HC) whenever having been told by a health professional, in the previous 12 months, that they had high blood pressure, T2DM, or HC, or whenever reporting specific pharmacological treatment.

Subjects with SBP $\geq$140 mmHg and/or DBP $\geq$90 mmHg at the 2 visits, not aware of their condition were defined as hypertension newly diagnosed. Likewise subjects with FG $\geq$126 mg/dL (confirmed by repeated testing at a second visit) or with TC$\geq$240 mg/dL not aware of their condition were defined as T2DM or HC newly diagnosed respectively.

Participants reporting having used antihypertensive and/or glucose lowering medications and/or taking a statin in the previous 2 weeks were considered treated pharmacologically.

The proportions of participants with the 3 risk factors, who were aware of their condition (among those diagnosed), and receiving specific treatment (among aware), were calculated.

Central obesity was defined for a waist circumference $\geq$85 cm for men or $\geq$80 cm for women according to the Working Group on Obesity in China [21]. Other categorized features were education level (illiterate, primary and secondary school, high school, college or more), current smoking (noncurrent smokers defined as those who had never smoked, and former smokers those who-had stopped smoking), health insurance (full registration or not with the NHS). Time spent in Italy since migration (years of residence in Italy) was stratified in quartiles (0 to 7 years; 8 to 11 years; 12 to 14 years; 15 to 32 years).

2.4. Statistical analysis

Data are expressed as mean and standard deviation for continuous variables. Categorical variables are presented as counts and percentages. Normal distribution of continuous variables was checked using skewness and kurtosis. Group differences were estimated using t-tests for continuous variables or χ^2 tests for categorical variables.

Crude prevalence of overall and new diagnosis of hypertension, T2DM, and HC were estimated by subgroups. For awareness and treatment crude prevalence was estimated on the subpopulation of diagnosed and aware patients respectively.

Comparisons between documented and undocumented cohorts were made using logistic regression analysis adjusted for age (categories), sex, education level (categories), quartiles of years in Italy (categories), central obesity, current smoking, newly diagnosed T2DM, newly diagnosed hypertension, and newly diagnosed hypercholesterolemia.

Determinants of awareness and treatment of T2DM and hypertension (dependent variables) were then studied with logistic regression

analyses adjusted for age (categories), sex, education level (categories), quartiles of years in Italy (categories), central obesity, current smoking, and registration with NHS, restricted to subjects diagnosed for the single risk factor. For this reason, in this sub-analysis the age categories were developed considering age <40 years as the reference category. The Odds ratio with 95 % CL was reported.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS Statistics Ver.28, IBM, Armonk, NY).

3. Results

3.1. Burden of main risk factors in undocumented Chinese

Overall, 3435 Chinese were recruited into the survey, 51 % of whom (n = 1766) were undocumented. Only 302 undocumented migrants had the STP code. Characteristics of undocumented and of documented migrants registered with the NHS are reported in Table 1. Compared to those registered with the NHS, the undocumented Chinese were more frequently men, younger, and had been in Italy for fewer years. They had a lower prevalence of central obesity and smoked slightly more. The undocumented Chinese had a similar crude prevalence of T2DM (13.1 % and 13.2 % for undocumented and documented respectively) and a lower crude prevalence of hypertension (24.7 % and 31.3 %). Registration with the NHS increased awareness among people affected by these two conditions (from 52 % to 78 % and from 59 % to 65 % respectively) as well as the rate of treatment for T2DM among aware, when compared with undocumented subjects (from 90 % to 99 %). Most importantly it must be highlighted that new diagnoses of T2DM or hypertension were 118 % and 18 % higher among undocumented migrants than among those registered with the NHS respectively (Table 1). On the other hand, registration with the NHS did not affect the oral health status of Chinese migrants (Table 1). In particular, over 50 % of subjects in both groups reported signs of gingivitis with frequent bleeding and over 10 % had more advanced signs of periodontitis with attachment loss.

Considering the demographic differences between undocumented and documented subjects (dependent variable), a multivariable adjusted logistic regression analysis was performed (Fig. 1). Undocumented Chinese, in spite of being younger and with less central obesity, had a higher rate of new diagnosis for T2DM (OR 1.8), hypertension (OR 1.4), and HC (OR 1.7) than Chinese subjects registered with the NHS (Fig. 1).

3.2. Determinants of risk factor awareness and specific treatment

Determinants of awareness, and allocation to specific treatments for T2DM or hypertension (dependent variables) were then investigated with separate multivariable logistic regression analysis. Only a small minority of Chinese subjects were aware of HC or treated with statins, therefore analysis was not performed within this subgroup.

T2DM awareness and treatment were positively associated with NHS registration (Fig. 2). Most importantly, more than 6 times the registered migrants were treated for T2DM than the undocumented migrants (Fig. 2). Rate of awareness and treatment for T2DM was also associated with age (older subjects more probable).

Registration with the NHS was associated with increased hypertension awareness for hypertension, the chance for hypertensive subjects to receive pharmacological treatment being not affected (Fig. 2).

4. Discussion

This is the first study exploring health needs and above all prevalence, awareness, and treatment of the most common risk factors (hypertension, T2DM or HC) in a large sample of undocumented Chinese migrants, compared with Chinese registered with the NHS. The data highlighted that 1. undocumented immigrants are highly prevalent in a Chinese community; 2. undocumented Chinese immigrants, in spite of

Table 1
Characteristics of Chinese according to their position in the National Health Service: undocumented, or registered with NHS.

	Undocumented (n = 1776)	%	**Registered** (n = 1669)	%	**P ***
Sex	–	–	–	–	<0.001
Men	767	43.4 %	596	35.7 %	–
Women	999	56.6 %	1073	64.3 %	–
Age (years)	44 ± 10		48 ± 11		<0.05
Age (5-year categories)	–	–	–	–	<0.001
<29	167	9.5 %	103	6.2 %	–
30–34	162	9.2 %	112	6.7 %	–
35–39	247	14.0 %	147	8.8 %	–
40–44	269	15.2 %	213	12.8 %	–
45–49	342	19.4 %	280	16.8 %	–
50–54	332	18.8 %	364	21.8 %	–
55–59	162	9.2 %	249	14.9 %	–
60–64	47	2.7 %	122	7.3 %	–
>65	36	2.0 %	80	4.8 %	–
Education (categories)	–	–	–	–	<0.001
Illiterate	181	10.5 %	121	7.4 %	–
Primary School	782	45.2 %	893	54.3 %	–
Middle School	731	42.2 %	572	34.8 %	–
College or more	37	2.1 %	60	3.6 %	–
Years in Italy (Quartiles)	–	–	–	–	<0.001
0 to 7 years	407	36.6 %	154	10.5 %	–
8 to 11 years	339	30.5 %	391	26.6 %	–
12 to 14 years	188	16.9 %	356	24.3 %	–
15 to 32 years	177	15.9 %	567	38.6 %	–
Current smokers	323	18.3 %	218	13.1 %	<0.001
Central obesity	989	56.2 %	1107	67.1 %	<0.001
BMI categories	–	–	–	–	0.045
BMI < 18 Kg/m^2	118	6.7 %	77	4.7 %	–
BMI ≥ 18 & BMI < 24 Kg/m^2	865	49.0 %	810	49.0 %	–
BMI ≥ 24 & BMI < 28 Kg/m^2	602	34.1 %	607	36.7 %	–
BMI ≥ 28 Kg/m^2	179	10.1 %	159	9.6 %	–
Fasting glucose	–	–	–	–	<0.001
never measured	521	49.9 %	880	61.5 %	–
measured > 1 year ago	324	31.0 %	339	23.7 %	–
measured < 1 year ago	199	19.1 %	213	14.9 %	–
T2DM (overall diagnosis)	231	13.1 %	220	13.2 %	0.936

(*continued on next page*)

Table 1 (*continued*)

	Undocumented (n = 1776)	%	**Registered** (n = 1669)	%	**P** *
T2DM (new diagnosis)	112	6.3 %	49	2.9 %	<0.001
T2DM aware (% among all diagnosed)	119	51.5 %	171	77.7 %	<0.001
T2DM treated (% among aware)	107	89.9 %	170	99.4 %	<0.001
Blood pressure	–	–	–	–	<0.001
never measured	345	30.1 %	776	53.0 %	–
measured > 1 year ago	343	29.9 %	264	18.0 %	–
measured < 1 year ago	458	40.0 %	424	29.0 %	–
Hypertension (overall diagnosis)	436	24.7 %	522	31.3 %	<0.001
Hypertension (new diagnosis)	180	10.1 %	183	11.0 %	0.461
Hypertension aware (% among all diagnosed)	256	58.7 %	339	64.9 %	0.048
Hypertension treated (% among aware)	206	80.5 %	277	81.7 %	0.701
HC (overall diagnosis)	428	24.4 %	213	13.1 %	<0.001
HC (new diagnosis)	355	20.0 %	180	10.8 %	<0.001
HC aware (% among all diagnosed)	73	17.1 %	33	15.5 %	0.697
HC treated (% among aware)	29	39.7 %	11	33.3 %	0.680
Periodontal destruction	–	–	–	–	0.494
no teeth loose and loss or teeth extraction due to other reasons	735	83.7 %	237	85.3 %	–
loose teeth without loss	74	8.4 %	25	9.0 %	–
loose teeth with loss	69	7.9 %	16	5.8 %	–
Gingival inflammation	–	–	–	–	0.866
normal gingiva	319	36.3 %	102	36.6 %	–
sometimes bleeding during brushing	438	49.8 %	134	48.0 %	–
always bleeding during brushing	118	13.4 %	42	15.1 %	–
artificial teeth	5	0.6 %	1	0.4 %	–

*= χ^2 or Student's *t* test as appropriate.
Variables are presented as n % (categorical variables) or mean ± SD (continuous variables). BMI, Body Mass Index; T2DM = type 2 diabetes mellitus; HC = hypercholesterolemia.

the high prevalence of investigated risk factors, have lower levels of awareness and treatment when compared to Chinese registered with the NHS; 3. it is especially in this group that new diagnoses of risk factors are detected during a survey. The prevalence of risk factors among first-generation Chinese migrants living in Italy had already been found to be higher than in the native Italian population [16], with values similar to those observed in China [22,23]. Regarding HC, the almost complete absence of treatment, as observed in the present study even in the presence of T2DM, should be noted. If we consider the high prevalence of the main risk factors, combined with the low level of awareness and treatment recorded among undocumented immigrants, it is easy to understand the possible consequences of a failure to integrate these subjects into the NHS. The economic cost of pharmacological treatment of these conditions is certainly lower than that of emergency care for future strokes or myocardial infarctions, also due to the fair presence of undocumented subjects.

The CHIP study offers for the first time an estimation of the proportion (around 51 %) of undocumented subjects present in a Chinese community in Europe. This population often falls off the radar of state-funded health care services and thus from the public health surveillance systems. Limited data and knowledge of these population groups challenge evidenced-based public health policy making and intervention. Therefore, several approaches have been attempted to explore the characteristics of this hard-to-reach group of people. A first approach considered women in relation to motherhood [24–26], a condition that can push an undocumented Chinese woman to overcome her mistrust and turn to the NHS facilities [27]. Less use of contraception [28] and more induced abortions [29] were observed among undocumented compared to documented women. In a second approach, patients attending health facilities of non-governmental organizations (NGOs) were examined [10,30]; this approach can provide useful information regarding barriers experienced by patients in the process of care, but cannot provide data on the health needs of a hard-to-reach population because it only addresses sick people.

More recent studies performed by reviewing administrative data, explored the characteristics of patients admitted to NHS healthcare facilities with the STP code. This third approach, which excludes undocumented migrants who do not have STP, showed that undocumented migrants provided with STP have a higher proportion of hospital admissions for preventable conditions than regular migrants [6,9,31]. Specific information on the access to primary care medicine as well as on prevalence, awareness, and treatment of main risk factors among regular migrants and patients admitted with STP were given [6,9,31]. Health differences were mainly attributed to the lack of access to the primary healthcare services [9]. However, also with this third approach mainly symptomatic patients were studied and undocumented migrants not provided with STP code are still excluded. These two points are especially relevant when the aim is to study risk factors because these are generally asymptomatic.

The present study answers the questions regarding health needs of undocumented subjects, and directly shows the different rates of awareness and treatment of the most common risk factors. The study relies on a general population survey carried out directly within the Chinese community and therefore the distrust, fear and lack of knowledge of the language which create a strong selection bias in surveys carried out in the centers of care of the host country are avoided. This approach, despite the absence of random sampling strategies, allows us to estimate prevalence of the main risk factors, which in this study are measured and not self-reported. Differently, in the Health Survey for England only self-reported data were provided for T2DM among Chinese [32]. In addition, in the present study the diagnosis of hypertension and T2DM resulted from 2 medical visits with the value of a confirmed clinical diagnosis, and not a simple screening investigation.

In the present study treatment rates among Chinese people aware of their condition are over >80 % for both T2DM and hypertension among both undocumented and documented groups. On the contrary, HC seems to be a neglected condition in this population because the rate of treatment among subjects aware of their HC is below 40 % independently from registration with NHS.

Awareness for T2DM and hypertension, as well as treatment rate for T2DM increase with registration in the healthcare system. Other health conditions do not change. Oral health, and in particular periodontal damage, offers further data on the health status of the population, hygiene standards, and lifestyles [33,34]. In this study, oral health was

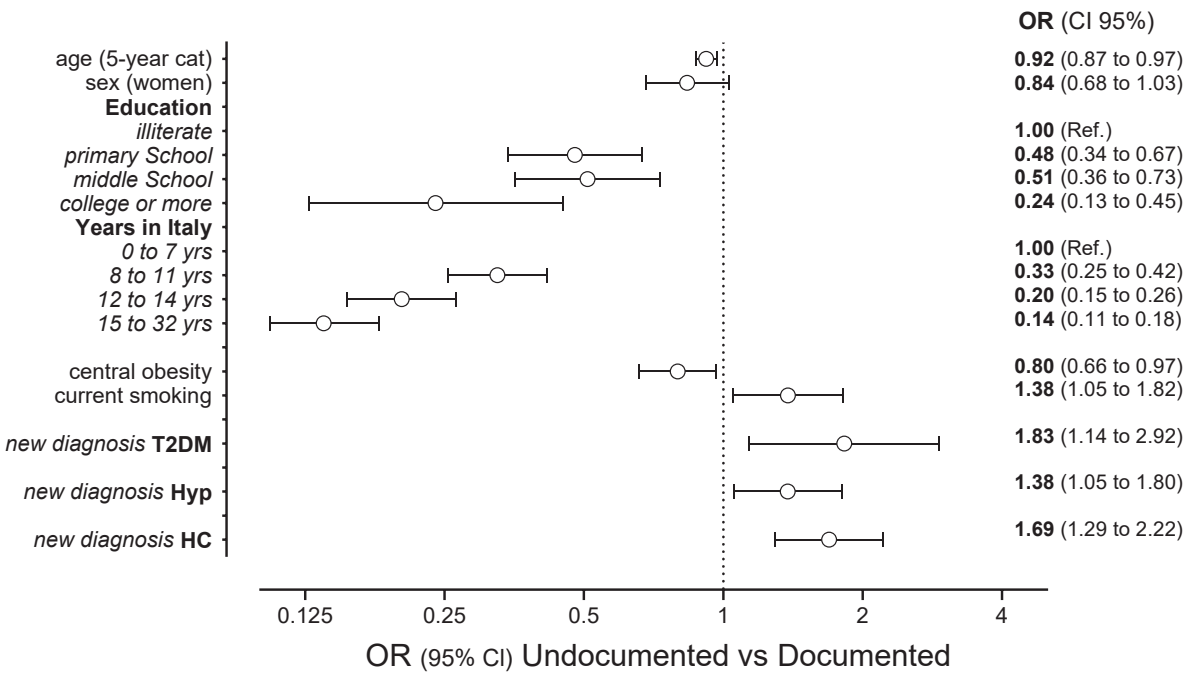

Fig. 1. Characteristics of undocumented Chinese vs subjects registered with the National Health Service (documented) at logistic regression analysis (adjusted for all exposures reported in the figure and including 2472 subjects). Results are expressed as OR with 95 % CI. (T2DM, type 2 diabetes mellitus; Hyp, hypertension; HC, hypercholesterolemia).

assessed using a short questionnaire without specific assessments of periodontal damage with pocket measurement. Documented and undocumented immigrants shared similar signs of gingivitis, a similar background with low access to care and few opportunities for self-care.

The present study reveals the true meaning of the opportunity offered by registration with the NHS which appears evident when considering the prevalence of new diagnoses of all the investigated chronic pathologies (T2DM, hypertension and HC) in the two groups. An adjusted multivariable logistic regression analysis indeed shows that the possibility of not receiving the diagnosis of these asymptomatic conditions is twice as high in the group of undocumented than among documented migrants.

In Italy, people with a valid residence permit are entitled to register for free with the Italian public health care system. Furthermore, registration with the NHS is mandatory within an employment contract. However, in this study a relationship between employment and registration with the NHS was not observed. In the survey no questions were asked concerning the employment contract but it is speculated that the Chinese are not always employed using regular contracts.

It is to be considered that not being registered with the NHS is just a proxy of having a valid residence permit, as many documented migrants might fail/avoid registering with the NHS for a number of reasons, including administrative and linguistic barriers. Both aspects are likely to cause a self-selection issue of individuals in the three groups (registered, with STP and without STP) according to their health status and/or health behaviors. However, the enrollment of Chinese people in the NHS does not appear to be driven by personal health needs (T2DM, hypertension, and HC does not appear to push the Chinese to register with the NHS), but rather by cultural education and the length of stay in Italy.

On the other hand, the lower prevalence of chronic pathologies among Chinese registered with the NHS, should not be considered an effect of better access to treatment because diagnosis was made on a clinical basis considering both measured values, and the regular use of specific drugs.

We are aware that the recruitment procedure is the first limitation of the present study. To have the possibility to collect health needs on undocumented migrants, we adopted a network sampling procedure, in which the identified informants served as recruiters between relatives, friends, or neighbors, to produce a sample matching the target population for age groups and gender. In this case the risk of potential selection bias is limited, although not excluded, since the study cohort involves a large number of participants. The high prevalence of T2DM, hypertension, and HC among Chinese immigrants could specially push undocumented subjects to participate in the survey. However, this potential self-selection bias is limited by the low rate of awareness for these conditions among undocumented subjects.

It must be noted that the fact that undocumented people report having had their sugar and BP values checked more frequently does not translate into a greater rate of awareness and treatment. We are not able to clarify who carried out these measurements but it can be speculated that investigated subjects failed to correctly retain the meaning of checked values. We can speculate that communication with the patient within the NHS can be more effective.

The direct participation of the whole Chinese Community in the present shared project following the principles of a participatory research is to be acknowledged. Secondly T2DM prevalence could be underestimated because the data relied on FG rather than on glucose load or hemoglobin A1c [35]. Unfortunately, a limitation of the study is that it does not explore target organ damage. Third, in the European context the STP code is used for administrative purpose for hospital admission. Undocumented immigrants are seldom aware of it. Furthermore, the code expires after six months. It follows that reporting not having a STP code mixes-up undocumented immigrants that never accessed the NHS, those who accessed but that were not aware of the code and those whose code has expired.

The current political debate in Europe is focused on newly-arrived undocumented migrants, associated with the refugee crisis. This hides other types of irregular migrants with a different immigration “history”, who have been residing in a European country for a relatively long period and who have been investigated in the present study. The STP system, which certainly solves some practical problems for migrants, is used by a minority of the undocumented subjects studied. However, it does not appear to change access to effective treatments for cardiometabolic diseases, and in this scenario, it seems to rather represent a

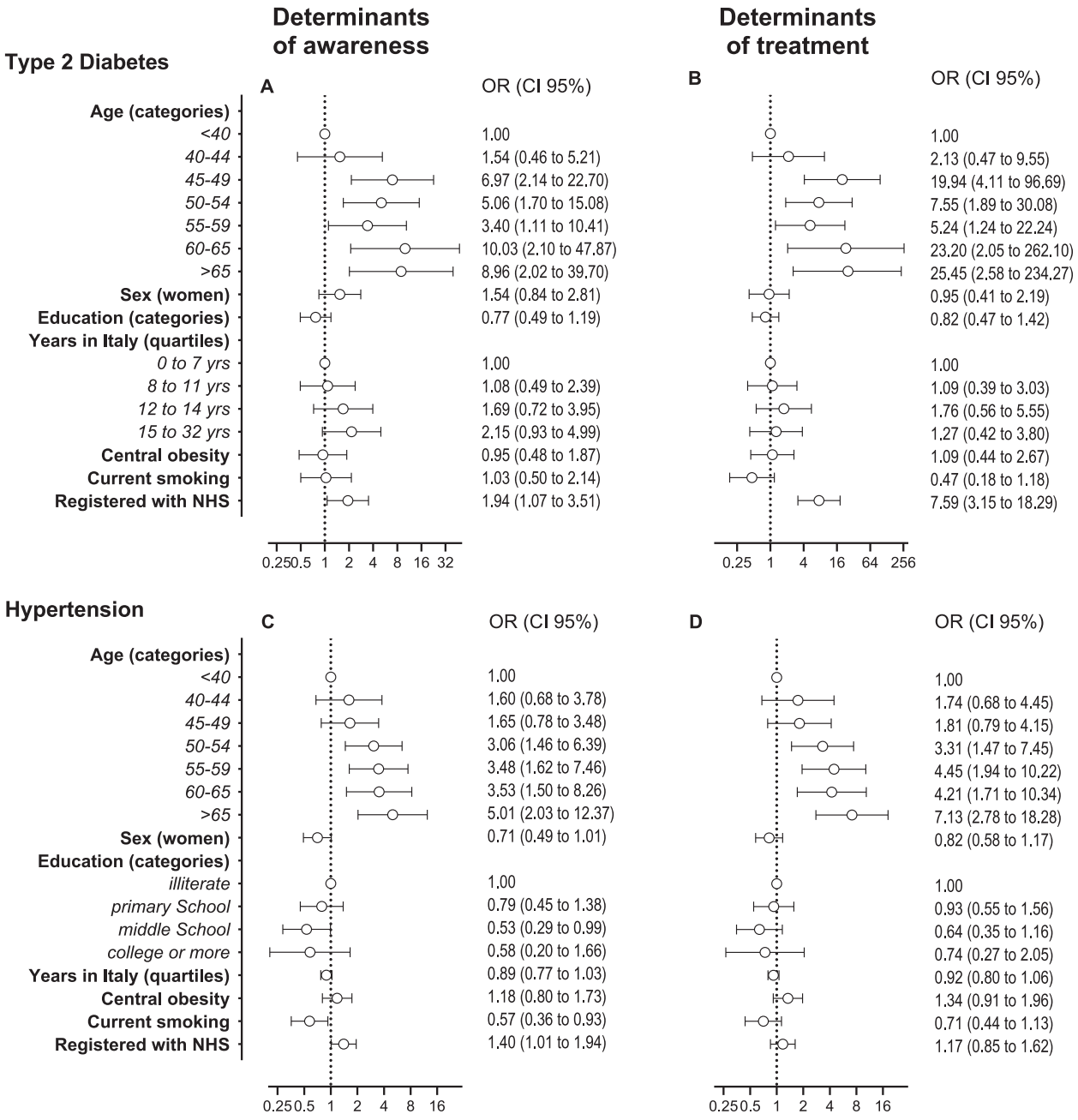

Fig. 2. Determinants of awareness and treatment for type 2 diabetes and hypertension at multivariate logistic regression analyses (adjusted for all exposures reported in the figure and including 304 and 782 subjects with type 2 diabetes or hypertension respectively). Results are expressed as OR with 95 % CI. (NHS, National Health Service).

missed opportunity for prevention.

CRediT authorship contribution statement

Alessio Pellegrino: Investigation. **Maria Calabrese:** Investigation. **Maria Boddi:** Investigation. **Irene Vacirca:** Investigation. **Cecilia Baccari:** Methodology. **Laura Bonvicini:** Investigation. **Francesco Venturelli:** Investigation. **Alessio Petrelli:** Investigation. **Anteo Di Napoli:** Visualization. **Maria Perticone:** Investigation. **Paolo Giorgi Rossi:** Investigation. **Pietro Amedeo Modesti:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization.

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.

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Authors' contributions

P.A.M. conceived and designed the study. P.A.M., M.B. and M.C. contributed to the acquisition of data. A.Pel., P.G.R. and P.A.M. contributed to the analysis and interpretation of data. All authors were involved in writing and revising the manuscript and had final approval of the submitted and published version. P.A.M. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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