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**This is the author's manuscript**

*Original Citation:*

*Availability:*

This version is available <http://hdl.handle.net/2318/141563> since

*Published version:*

DOI:10.1016/j.numecd.2013.09.012

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(Article begins on next page)



# UNIVERSITÀ DEGLI STUDI DI TORINO

*This is an author version of the contribution published on:*

**Questa è la versione dell'autore dell'opera:**

*[Nutrition, metabolism, and cardiovascular diseases : NMCD, 24(4), 2014,*

**doi:10.1016/j.numecd.2013.09.012.]**

**The definitive version is available at:**

*La versione definitiva è disponibile alla URL:*

***[<http://www.sciencedirect.com/science/article/pii/S0939475313002603>]***

## **Under-treatment of Migrants with Diabetes in a Universalistic Healthcare System: the ARNO Observatory**

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The analyses of CINECA ARNO Observatory have been supported by a grant from the Italian Diabetes Society (SID), Rome.

**Key words:** Diabetes; Migrants; Treatment; Cost; Healthcare System

**Running Head:** Diabetes in Migrants

Word count: Text, 2 927; Figure legends, 62

Abstract, 245

Tables, 3

Figures, 2

References, 30

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**ABSTRACT**

**AIMS:** To assess whereas prevalence, treatment and direct costs of drug-treated diabetes were similar in migrants and in people of Italian citizenship under the universalistic Italian health care system.

**METHODS:** Drug-treated diabetic individuals were identified in the population-based multiregional ARNO Observatory on the basis of 2010 prescriptions. Migrants were identified by the country-of-birth code on the fiscal identification code. Diabetes prevalence was calculated for Italians (n=7,328,383) and migrants (n=527,965). To assess the odds of migrants of having diabetes compared to Italians, we individually matched all migrants to Italians for major confounders (age, sex and place of residence). Finally, all migrants with diabetes were individually matched for confounders to Italians with diabetes to compare prescriptions, hospitalization rates, services use and direct costs for the National Health System.

**RESULTS:** We identified 368,797 subjects with diabetes among Italians and 10,336 among migrants, giving prevalence of 5.03% and 1.96%, respectively. Migrants with diabetes were younger than Italians ( $52\pm 13$  years vs.  $68\pm 14$  years,  $p<0.001$ ); after matching, their risk of disease was higher (odds ratio, 1.55, 95% confidence interval, 1.50-1.60). The total cost was 27% lower in migrants, due to lower cost of drugs (29%), hospital admission (27%) and health services (22%). The number of packages/treated person-year of all glucose-lowering drugs was also lower in migrants (-15%) ( $P<0.001$ ).

**CONCLUSIONS:** Compared to subjects of Italian ancestry, migrants to Italy show a higher risk of diabetes but less intense treatment. Possible inequalities in health care use are maintained also in a universalistic system.

## Introduction

Integration of the migrant population into the receiving healthcare system is a key issue in the countries receiving a large number of migrants each year. Independently of the healthcare system, there is evidence that migrants remain undertreated compared with the native population [1]. These differences might arise both from lower attendance of migrants to primary care or health services, due to job and time constraints and socio-cultural conditions, and from lack of specific skills of physicians in intercultural communication [2]. Far from being money-saving, the underutilization of drugs, primary care services and diabetes clinics might produce more rapid disease progression, translating into higher costs, as also reported in U.S. [3].

The risk for diabetes in migrant minorities is usually higher than in resident populations, probably fuelled by socioeconomic inequalities and rapid changes in lifestyle; monitoring the prevalence of disease and health care services utilization might be used to identify areas of improvement in health care policies to smoothen inequalities [4]. An extensive literature review in Organization for Economic Co-operation and Development (OECD) countries showed that also the universalistic (Beveridge-type) healthcare systems operating in most European countries were unable to smoothen inequalities and grant equal access to healthcare to all citizens with diabetes [1].

Migrants have long been a negligible number in Italy. From the late '80, their numbers increased rapidly and doubled between 1991 and 2001 (from 1% to 2% of total population) to reach 7.5% (4.57 million migrants) by 2010. Because of this very high immigration rate, Italy is a natural experiment for other countries facing massive migration and recent policy changes shifting healthcare responsibility from the central government to regional authorities might further increase disparities [5].

Systematic data on diabetes care are mandatory for detecting areas of improvement and for planning adequate health care policies. ARNO is an ongoing population-based, multiregional observatory based on administrative data sources, covering 25% of people resident in Italy, independently of their citizenship [6]. We took advantage of this large database to identify the cohorts of migrants and Italian residents with drug-treated diabetes in 2010. Due to differences in the age structure of these populations, we estimated the odds of having diabetes in migrants by comparing them to Italians individually matched for main confounders (age, sex and place of residence). Finally, we examined data on prescriptions, hospitalization rates, services use and related costs in migrants and in Italians with diabetes.

The final aim was to assess whether heterogeneities in access to health care exist under the universalistic coverage of the National Health System (NHS).

## **Materials & Methods**

### *Identification of subjects with drug-treated diabetes*

The population-based multiregional ARNO Observatory is based upon administrative data sources of all Italian residents in 30 Health districts scattered throughout the country [6]. In Italy, all residents receive care through the NHS, irrespective of citizenship, social class and income. Moreover, individuals with diabetes receive free access (without any copayment) to drugs, diagnostic procedures and hospitalization. Drug prescription and hospital admission data are linked to the patients' fiscal code, an identity code generated by name, date and place of birth. Five per cent of prescriptions were excluded from analyses because of incomplete patient identification. All subjects who received at least one prescription of glucose-lowering drugs (Anatomical Therapeutic Chemical Classification System [ATC], code A10A and A10B, respectively) in the course of 2010 were considered as having drug-treated diabetes. A sensitivity analysis using more restrictive criteria (two or more prescriptions/year), obtained similar results (data not reported). Given the study design, both people with undiagnosed diabetes and those treated with diet only could not be traced. The latter group represents nearly 10% of diabetes patients of the ARNO Observatory [7].

### *Identification of migrants*

For people born outside Italy, the city-of-birth code on their fiscal identification code is replaced by the Country-of-birth code, thus permitting univocal identification of foreign-born people. For the purpose of the present report, analysis of data from the ARNO Observatory was limited to health districts providing also individuals' citizenship (n=8,111,660). The Observatory does not include persons who entered Italy without permission (around half a million in 2010), as they have no free access to health treatment [8]. Since the Italian law does not accept *jus soli*, i.e., the automatic acquisition of Italian citizenship by all people born in Italy and very few immigrants receive the Italian citizenship, usually 20 years or more since they entered Italy, we included in the data analyses two groups of residents in Italy in 2010: A) people of Italian citizenship, born in Italy (n=7,328,383 - Italians); B) people of non-Italian citizenship, born in countries characterized by high migratory fluxes (n= 527,965 - Migrants). The 4% subjects remaining in the database are either people of foreign

citizenship, born in Italy (second-generation migrants) or people of non-Italian citizenship, born in countries with low migratory fluxes or the offspring of Italians born abroad. Five countries accounted for over 50% total migrants: Romania (18.4%), Morocco (11.2%), Albania (10.1%), Moldova (5.8%), People's Republic of China (5.8%). Another 10% came from the Indian subcontinent (India, Pakistan, Sri Lanka, Bangladesh, Pakistan) and the remaining from Central Africa and South America. Ninety-two per cent of diabetes subjects among Italians and 82% among migrants had at least one drug prescribed every four months, suggesting a relatively low mobility rate in the areas covered by the ARNO Observatory.

### *Statistical analysis*

The prevalence of drug-treated diabetes and the 95% confidence interval (95% CI) in both Italians and migrants was calculated as the ratio of drug-treated persons to the total resident ARNO population in 2010. The characteristics of the two cohorts were described by mean  $\pm$  standard deviation (SD). Because of a different age structure of the two populations, with a greater distribution of young people among migrants, no direct comparison was allowed. Moreover, other confounders may modify the odds of having diabetes, such as the screening attitude of general practitioners among different Health Districts. Therefore, to calculate the odds of having diabetes in migrants (n=527,965) with respect to Italians, we individually matched all migrants to Italians for major confounders (age, sex and place of residence). Odds ratios (ORs) and 95% CI of drug-treated diabetes were calculated using univariate logistic regression.

Finally, we analyzed prescriptions, hospitalizations, and health care services (consultations, laboratory tests and other diagnostic procedures) in all migrants with diabetes (n=10,336) who were individually matched for confounders (age, sex and residence) to Italians with diabetes (n=10,378). From the database, we derived total drug packages and the cumulative cost of treatment, the number of hospital admissions and consultations/year. The mean cost of drug treatment was calculated by multiplying the number of prescribed packages by their unit cost. Data do not include the drugs supplied during hospital stay and in nursing homes, and the cost of medical equipments and disposable supplies (reactive strips, glucometers, insulin pumps), directly dispensed by the NHS. The mean cost of hospital admissions, consultations and services were derived from the refund paid to hospitals, regulated by government contracts. Differences between migrants and Italians in packages/ treated person-years of prescribed drugs and costs/treated person-year were assessed by non-parametric tests. Two-sided P values <0.05 were considered statistically significant.

## Results

### *Prevalence of drug-treated diabetes*

We identified 10,336 individuals with drug-treated diabetes among migrants and 368,797 individuals among Italians, corresponding to a prevalence of 1.96% (95% confidence interval (CI), 1.92-2.00) and 5.03% (95% CI, 5.01-5.04), respectively. On average, migrants with diabetes were younger than Italians with diabetes ( $50 \pm 13$  years vs.  $68 \pm 14$ ,  $p < 0.001$ ) (Table 1). After matching for age, sex and place of residence, the OR of drug-treated diabetes in migrants was 1.55 (95% CI, 1.50-1.60), ranging between 3.38 (2.83-4.04) in Egyptians and 0.29 (0.23-0.36) in migrants from Ukraine (Figure 1).

### *Drug prescription pattern and cost/person-years*

Among migrants, 72% of subjects with diabetes were treated by oral hypoglycemic agents or DPP-4 inhibitors (DPP-4i) or GLP-1 agonists (GLP-1a), 17% by insulin and 11% by these drugs in combination. Respective figures among Italians were 68%, 22% and 10% ( $p < 0.001$ ). Table 2 shows the prescription data in the migrant population with diabetes ( $n=10,336$ ), individually matched to Italian people with diabetes ( $n=10,378$ ) by age, sex and place of residence. Migrants had 19% lower likelihood of being treated with insulin (OR=0.81, 95% CI 0.76-0.86) and a correlated higher likelihood of being treated with oral glucose-lowering drugs (OR=1.44, 1.35-1.55). Differences in insulin-treatment among migrants and Italians were also found, with lower use of rapid-acting analogues (OR=0.74, 0.69-0.79), whereas the use of basal or mix analogues was similar. Among other antidiabetic drugs, metformin was used in both migrants and Italians (OR=1.01, 0.96-1.07), but the number of package/person/year was lower in migrants (-9.2%,  $P < 0.001$ ) as was the cost/person-year (-13.1%,  $P < 0.001$ ). Data for acarbose showed also lower use in migrants (OR=0.54, 0.41-0.70; package/person/year -31.4%,  $P < 0.01$ ; cost/person-year, -31.5%,  $P < 0.01$ ).

Migrants with diabetes also had a lower likelihood of being treated with other drugs, with the exception of non-steroidal anti-inflammatory drugs (NSAID), which were overprescribed by 17% in migrants (OR=1.17, 1.10-1.24) and conferred a 14.7% higher cost than in Italians with diabetes ( $P < 0.001$ ). Similar level of under-prescriptions was evident for lipid lowering drugs (OR= 0.79, 0.74-0.84) and antithrombotic drugs (OR=0.69-0.78). The drugs for the respiratory system were less frequently prescribed in migrants (OR=0.78, 0.72-0.85) but overused by 10%, which resulted in a 20% increased cost ( $P < 0.001$ ).

The yearly cost of drugs was €515 in migrants and €725 in Italians (-29%;  $P < 0.001$ ) (Figure 2). Glucose lowering drugs accounted for 37.7% (€194/515) and 34.7% (€252/725) of total cost, respectively. The yearly cost of oral drugs/DDP-4i/GLP-1a, insulin and these drugs in combination was €83, €477 and €481 in migrants and €105, €556 and €573 in Italians ( $P < 0.001$ ). The average cost of glucose-lowering drugs was different across migrants from different countries and ranged from €136 (Sri Lanka) to €299 (Egypt). The cost of non-glucose-lowering drugs ranged from €222 (China) to €606 (Egypt).

#### *Hospital admissions and cost/person-year*

Hospital admission rates were similar in migrants and in Italians with diabetes (Table 3). The length-of-stay for all ICD-9 codes were generally longer in migrants, and significantly longer for diabetes (ICD-9 250, +75.0%) and ischemic heart disease (ICD-9 414, +340.0%). The corresponding costs per person-year were also higher (+44.9% and +123.9%, respectively). Whereas pneumonia (ICD-9 486) was not recorded in Italians with diabetes, due to the young age of matched cohorts, in migrants it conferred an average cost per treated patient of €4,600/year. The yearly cost of hospital admission was €657 in migrants and €900 in Italians (-28%;  $P < 0.01$ ) (Figure 2). Differences were also recorded in relation to the country of origin, varying from €222 (China) to €1085 (Philippines).

#### *Services use*

Referral for consultation during 2010 was lower in migrants (82%) than in Italians (OR=0.74, 0.64-0.84). The number of patients who performed at least one laboratory test was similar (91% vs. 92%, respectively), but the overall number of tests and procedures was 10-15% lower in migrants. As to hemoglobin A1c, two or more measurements/year were performed in only 31.1% of migrants and 39.6% of Italians (OR=0.69, 0.61-0.77). The yearly cost of services was €316 in migrants and €437 in Italians (-22%;  $P < 0.01$ ; Figure 2), ranging from €204 in migrants from China to €408 in the Moroccans.

#### *Total costs/patients-year*

Overall, the cost per treated case was 27% lower in migrants compared to Italians (€1,488 (95% CI, 1,485-1,491) vs. €2,062 (2,058-2,066); Figure 2). Migrants had a lower cost of drugs (-29%;  $P < 0.001$ ), hospital admissions (-28%;  $P < 0.01$ ) and services (-22%;  $P < 0.001$ ), with differences in relation to the country of origin. The cost per person with diabetes ranged from a minimum of €891 in people coming from China to €2,148 in those coming from Egypt.

## Discussion

Data from the population-based ARNO Observatory provide a comprehensive analysis of the prevalence of drug-treated diabetes and the amount of care provided to migrants in Italy, under the universalistic coverage of the NHS. The risk of having diabetes was 55% higher in migrants than in Italians of similar age, sex and place of residence, whereas direct costs were 27% lower. The pattern of treatment was different; migrants with diabetes had 40% higher likelihood of being treated with oral drugs and 15-20% lower likelihood of being treated with lipid-lowering and antithrombotic drugs. Although hospitalization rates were similar, length of hospital stay was longer in migrants, particularly for ICD-9 codes of diabetes and ischemic heart disease. Overall, the data suggest lower quality of diabetes care in migrants compared to age, sex and place of residence matched Italians also in a universalistic health care system, in the presence of high migratory fluxes from low-income countries towards the European Community [9]. The alternative hypothesis of less severe disease in migrants cannot be ruled out, as no clinical data are available in the ARNO database, a hypothesis however challenged by similar hospitalization rates. Inequalities in health between ethnic groups living in the same area might be expanded also by genetic and cultural factors, socio-economic level and the prevalence of risk factors (smoking, inactivity, alcohol consumption) [10, 11], as well as access to health services [12].

The risk of drug-treated diabetes in migrants in Italy varied among ethnic groups and was consistent with diabetes prevalence in their countries of origin [13]. The likelihood of being treated with a glucose-lowering drug was halved in migrants from former Eastern socialist countries and four-fold higher in people from Egypt and the Indian subcontinent (Figure 1), as also recorded in the United States [14]. In Italy, a high prevalence of undiagnosed prediabetes/type 2 diabetes was previously recorded in migrants from the Philippines to the city of Rome [15]. However, migrants who had diabetes received a different treatment compared with Italians of similar age, sex and place of residence. The lower insulin use suggests lower implementation of intensified insulin protocols, a finding consistent with other reports [16], whereas the lower package of oral glucose lowering drugs per treated subject with diabetes might be related to lower coverage of or compliance to treatment, also observed in other migrant minorities in other European countries [17].

Underutilization of statins is of particular concern. Scarce adherence and low coverage to statin use has been repeatedly documented in Italy also in high-risk diabetes patients [18, 19];

in individuals attending Italian diabetes clinics, the percent of cases with LDL-cholesterol within target values was very low in 2004 [20] and increased by 10% in 2007 [21]. Statins are provided without copayment to all subjects with diabetes in Italy, therefore underutilization in migrants cannot be ascribed to socioeconomic conditions, but it likely reflects the difficult interaction between general practitioners/diabetologists and migrants, as also reported in the Dutch setting [22]. Notably, only two ATC categories were overprescribed and/or caused increased costs: drugs for the respiratory system and non-steroidal anti-inflammatory agents. The first category fits with the evidence of higher admission rates and hospital costs for pneumonia, and might be favored by a higher prevalence of smokers in minorities and specific ethnic groups [23]. The increased use of non-steroidal anti-inflammatory agents might be related to heavy manual working and lower socioeconomic conditions in migrants compared to Italian blue collars [24].

The risk of hospitalization, the major source of direct costs in diabetes [6, 25], was similar but length of stay was longer in migrants, as already reported for non-Western ethnic cohorts in the Netherlands [26]. Similarly, a cross-sectional analysis of the health service use among elderly immigrants and the native populations of 11 European countries recorded a general overutilization of hospital admission and consultations [27]. No data are available on the attendance of migrants to emergency departments, a procedure not traced by the NHS. We need to investigate whether emergency services, reported to account for less than 1% of total diabetes costs in Italy [28], are overused by migrants to provide immediate care also in the presence of uncomplicated conditions.

This study has limitations. First, data are limited to drug-treated patients, thus excluding those with untreated diabetes, who represents 10% of Italian people with diabetes. Although, no estimate of this subgroup is available for the migrant population, it is likely higher than for Italians, and the final effect on our data would be a bias towards a more reduced health care utilization among migrants. Similarly, no assumption may be made for undiagnosed diabetes, whose number may be higher in migrants [15]. Second, the use of administrative data does not give hints as to the clinical targets attained by migrants. However, we combined the assessment of healthcare consumption with diabetes health outcomes, although based on a quite low number of hospitalized migrants, thus providing clues towards the interpretation of data [9]. Third, we could not retrieve attendance of migrants to diabetes clinics, since there is no specific code for this activity. Compliance to treatment might also differ between Italian and migrants, depending on sociocultural factors [29]. The strengths of the study include the

population-based study design, allowing for internal validity, and the coverage of large Italian areas, allowing for external validity. Finally, the large sample size and the careful matching between migrants and Italian with diabetes provide robust data.

In conclusions, differences exist in the prevalence and treatment of diabetes in migrants to Italy, compared to subjects of Italian ancestry. High-risk migrant minorities may be under-treated also in a universalistic healthcare system. Differences in socioeconomic status and barriers generated by the present culture of biomedicine might make the difference, but inequalities might also stem from physicians' side. Efforts should be made to favor visits to general practitioners/diabetologists and attendance to screening and treatment programs [30], to adapt education programs to specific cultures and to develop community partnerships.

#### **Author Contribution statement**

G.M. planned the study and wrote the draft of manuscript; E.B., G.B., R.M., O.V. contributed to study planning, discussion of results and reviewed the manuscript; D.B., M.D.R., E.R. researched the data, made the analyses and contributed to discussion. All Authors approved the final version.

#### **Conflict of Interest**

The Authors disclose no relevant conflict of interest in relation to the material presented in the article.

#### **Acknowledgments**

The authors are indebted to all participants in the ARNO Working Group (see on-line appendix)

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### **Legend for Figure 1**

Odds ratio (95% confidence interval) of drug-treated diabetes in migrants from different countries compared with Italians, individually matched by age, sex, and place of residence. OR >1 indicates higher risk in migrants.

### **Legend for Figure 2**

Direct cost per treated person with diabetes in 2010. Data are derived by the one-to-one comparison of migrants and Italians with diabetes, matched by age, sex and place of residence.