

Prevalence of known diabetes mellitus in a central region of Italy

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ABSTRACT. A survey on the prevalence of known diabetes mellitus has been conducted in the Foligno area, in the region of Umbria in central Italy, using the capture-recapture method. Three independent sources of information were used to obtain the most reliable and complete data. In 1990, the number of people registered with the National Health Services in the Foligno area was 92,196. A total of 2908 subjects with known diabetes were identified (crude prevalence of diabetes was 3.15%). The diabetic population was distributed between 0.08% for Type I and 3.1% for Type II diabetes. Out of 2908 patients identified by the 3 sources of information utilized, 1092 were traced in general practitioners' and paediatricians' registries, 1653 in diabetic clinic registries and 2101 from prescriptions for hypoglycaemic agents, insulin syringes or reagent strips. The applications of the capture-recapture methodology led to an estimated prevalence of diabetes mellitus in the Foligno Health Care District of 3.18% (95% CI:3.17%-3.19%). This survey allowed the identification of about 99% of the diabetic population. Knowledge of the data referring to other areas in Italy and in European countries could help to evaluate the possible differences between the various Italian regions and other European countries. The next step should be a survey to obtain data on the prevalence of chronic diabetic complications on which life expectancy depends.

INTRODUCTION

Knowledge of epidemiological data on diabetes mellitus (DM) is particularly important for several reasons. First of all, it is useful for a better definition and classification of this complex and heterogeneous disease. Secondly, it can contribute to the understanding of the mechanisms involved in the pathogenesis of both genetic and environmental DM. Thirdly, it can offer valuable information for programming health care services in diabetes, particularly through correction of the risk factors for diabetes and its complications.

It is not easy to collect epidemiological data on diabetes, since surveys cannot usually be applied to large populations. Different methods of case identification have often been used in the various studies conducted in different countries. Furthermore, new diagnostic criteria for diabetes have been introduced and widely accepted since 1979. For these reasons, it is often difficult to compare the data obtained from different epidemiological studies.

Therefore, some years ago the Italian Health Minister proposed and strongly urged that an epidemiological study on DM be carried out by several groups in different geographical areas (northern, central and southern Italy). The study used a similar innovative

methodology based on the collection of data from several independent sources, known as the capture-recapture methodology. This method, already successfully applied in other fields of biology and human epidemiology, guarantees a more accurate and reliable estimation of diabetes prevalence (1, 2).

This paper presents the data obtained by this methodology in the population of Foligno, which is a municipality located in Umbria, a region in central Italy.

SUBJECTS AND METHODS

The survey was conducted in 1990 in the Foligno area, which is partly urban and partly rural with a total population of 92,196, who, by law, are all reg-

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istered with the National Health Services (NHS). Only patients previously diagnosed as having diabetes, alive until 31 December 1990 and resident in the area of the NHS of Foligno, were considered. Three independent sources of information were used to obtain the most reliable and complete data.

Criteria used to confirm the diagnosis of diabetes were those established by the NDDG (3). The patients were classified as having Type I DM if the diagnosis had been made before 30 years of age and insulin treatment had begun within the first two years, and Type II DM if the diagnosis had been made after 30 years of age, irrespective of treatment. These criteria are arbitrary, but in an epidemiological study they are realistic.

The first and primary source of information was obtained from the list of patients attending the Diabetic Clinic and the Day-Hospital in Foligno. The health care system of our Region foresees that all diabetic patients attend the NHS. The other sources were considered secondary.

The second source consisted of data obtained from family practitioners and paediatricians. Several meetings had been previously organised with these colleagues to explain the reasons for the survey and to carefully instruct them on their participation. They were requested to report the essential clinical data of their diabetic patients on a preprepared form.

The third source was derived from the data collected from the prescriptions for insulin and oral hypoglycaemic agents during 1990. This information is important, although it excludes patients treated by diet alone, since the NHS in Italy allows all citizens with diabetes to receive prescriptions of insulin and hypoglycaemic agents free of charge.

Prescription forms, collected during a 3-month period in the pharmacies located in this area, include the NHS identification number for both the prescription holder and the family physician, and, they were manually checked by one of the team. The third source also included data gathered from the list of all residents of the Foligno area who received insulin syringes and reagent strips through the NHS. For subjects who had died in the meantime, the exact date of death was obtained from the public registries.

STATISTICAL ANALYSIS

The prevalence of diabetes in the area of Foligno was estimated by employing the capture-recapture

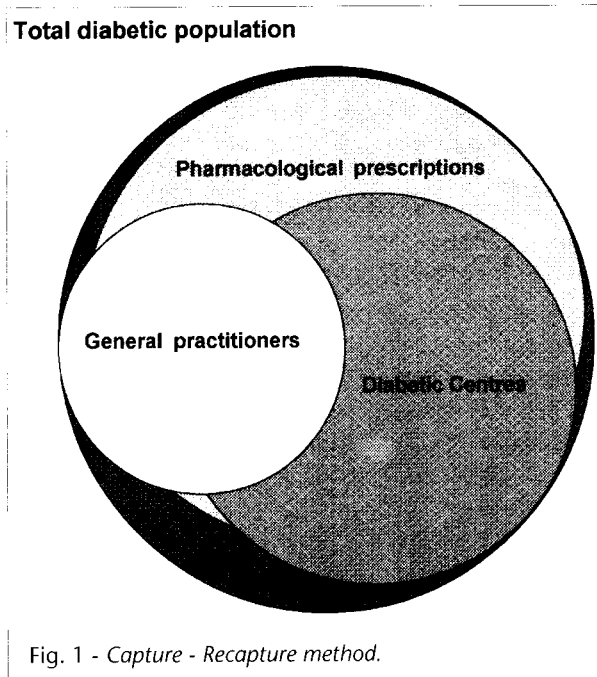


Fig. 1 - Capture - Recapture method.

technique. A graph of the contribution by each information source is presented in Figure 1.

Briefly, this method requires at least two different sources of information, both including less than 100% of the cases. For the purpose of our study, 3 sources were considered: a) general practitioners' and paediatricians' registries; b) diabetic clinic registries and c) prescriptions for drugs, insulin syringes or reagent strips. The incomplete 2^3 table of counts for the triple system model has been divided into one complete 2×2 subtable and one incomplete 2×2 subtable as follows (4-6):

		Third sample			
		1		0	
Second sample		1		0	
		1	0	1	0
First sample					
1	X_{111}	X_{101}	X_{110}	X_{100}	
0	X_{011}	X_{001}	X_{010}	$X_{000}=?$	

In order to take into account the possible dependencies among different sources, loglinear analysis was employed (7), using SAS GENMOD procedure (8). Applying this package module in a GLIM fashion, parameterization (5) allowed the estimation of

study. Their collaboration led to the identification of 1092 diabetic patients.

Through the sale of syringes and processing of prescriptions for reagent strips, 189 subjects with DM were identified. The prevalence of total diabetes mellitus according to age (yr) and sex is reported in Table 2. The combination of data from the different sources lead to the prevalence of diabetes of 3.15%.

According to the therapeutic regimen, we noted that 14.6% were treated with diet alone; 17.6% with insulin; 67.0% with oral hypoglycaemic agents and 0.8% with a combination of insulin and oral hypoglycaemic drugs. This information was drawn from General Practitioners (G) and from Day Hospital and Diabetes Centres (C) sources. As shown in Table 1 the source G and C cover 2130 patients (ie 73% of the total).

The age distribution of subjects with Type II DM is characterized by a marked increment of prevalence after 50 years, with a slight excess of men under 60 years of age.

The application of log-linear models (Table 3) leads to the selection of a model allowing the presence of sources single effects as well as the interaction between P and C.

This model leads to an estimate of 2930 patients (95% CI : 2921 - 2946) with DM in the Foligno area, corresponding to a prevalence of 3.18% (95% CI : 3.17% - 3.19%). The same model shows a strong negative correlation between sources P and C. In fact, the parameter estimate of the interaction term was equal to -0.85 (SE = 0.07), which leads to an estimate of the association odds-ratio equal to 0.033.

DISCUSSION

The prevalence of diabetes mellitus in the Foligno Health Care District has been estimated in our study as 3.18% (95 CI : 3.17% - 3.19%). The source of information derived from drug prescriptions led to the identification of about 60% of the entire diabetic population. This depends on the National Health Services in Italy, which potentially allows all the diabetic population to attend Diabetic Clinics. A negative association was found between sources P and C (prescriptions and centres), ie, an important proportion of patients were traced by source P but not by source C and *viceversa*. It is reasonable to suppose that patients identified in source C only are

Table 1 - Distribution of the data collected by each information source.

Patients	Patients			TOTAL
	P	G	C	
n =				
341	X	X	X	464
464	X	X		518
778	X			13
13		X		274
274		X	X	520
520			X	1653
2908				
2101				
1092				

P = Pharmacological prescriptions, reagent strips and syringes.
G = General Practitioners' forms.
C = Centres (Day Hospitals, Diabetes Centres).

the logarithm of the number of patients in the missing cell through the intercept term estimate as well as 95% confidence intervals (95% CI) calculated as $\exp(\text{intercept} \pm 1.96 * SE(\text{intercept}))$. Parameter estimates and the odds-ratio of association can be derived for each interaction term. A strong deviation from the unit indicates the existence of an association (and its direction) between the sources. The analysis proceeded from fitting the saturated model including all sources and first-order interaction terms to the simplest models including each case of two independent sources. Interaction terms were dropped when the action did not result in a significant lack of fit expressed by the probability of the difference in deviance between nested models.

RESULTS

In the Foligno area, in the period 1 January-31 December 1990, 2908 subjects with known diabetes were identified from amongst 92,196 people. An analysis of more than 40,000 prescriptions, collected over a 3-month period, was made. Of these, about 5,000 referred to prescriptions for insulin and oral hypoglycaemic agents and allowed the identification of 2101 subjects with DM (Table 1). Through the Diabetic Clinic and Day Hospital in Foligno, 1653 subjects with DM were identified in the prevalence data; of these, 520 (17.9%) were not identified through the other sources. The third source of data was through the general practitioners. Of the 93 physicians, only 54 (60%) participated in the

Table 2 - Prevalence of diabetes mellitus (DM) according to age groups (yr).

Age (yr)	Males			Females			Total DM		
	Cases (n)	Population (n)	Prevalence (%)	Cases (n)	Population (n)	Prevalence (%)	Cases (n)	Population (n)	Prevalence (%)
0-9	3	4245	0.07	1	3935	0.03	4	8180	0.05
10-19	7	5732	0.12	2	5388	0.04	9	11120	0.08
20-29	10	6475	0.16	13	6362	0.21	23	12837	0.18
30-39	21	6024	0.35	14	5806	0.24	35	11830	0.30
40-49	89	6017	1.48	76	6039	1.25	165	12056	1.37
50-59	206	5557	3.70	212	6065	3.50	418	11622	3.59
60-69	468	6022	7.77	506	6893	7.34	974	12915	7.54
70-79	382	3444	11.08	507	4482	11.32	889	7926	11.21
80-89	114	1182	9.68	272	2152	12.64	386	3334	11.59
>=90	1	104	0.97	4	272	1.50	5	376	1.35
Total	1301	44802	2.90	1607	47394	3.39	2908	92196	3.15

Table 3 - Log linear model fitting results.

Sources	N	(95%CI)	Deviance	DF	P
P-G	3315	3284-3348	454.36	4	<0.001
G-C	3576	3533-3621	622.05	4	<0.001
P-C	3161	3140-3183	798.08	4	<0.001
P-G-C	3317	3278-3361	454.33	3	<0.001
P-G-C-PC	2930	2921-2946	4.77	2	0.092
P-G-C-PG	3484	3420-3556	357.15	2	<0.001
P-G-C-GC	3383	3332-3439	423.02	2	<0.001
P-G-C-PG PC	2933	2922-2951	1.17	1	0.278
P-G-C-GC PC	2930	2921-2946	4.76	1	0.029
P-G-C-PG-GC	3689	3587-3807	293.39	1	<0.001
P-G-C-PG-PC-GC	2935	2923-2957			

those on diet alone or those who had no drug prescriptions during the 3-month period of collection of the prescription forms. On the other hand, patients traced exclusively by prescriptions could be those not attending diabetes clinics and under the care of GPs who did not participate in the study (accounting for 40% of the total number of GPs). Prescriptions could also have identified patients who chose to be cared for by private specialists and thus very unlikely to be traced in other locations.

The prevalence observed in the Foligno area is close to that reported some years ago in Gubbio, located about 50 km from Foligno. In Gubbio, all residents of the ancient urban area of the town, *ie* about 3,000

people, were examined for a survey on hypertension, "Gubbio Hypertension Project". In this survey, it was only possible to identify with certainty subjects with physician-diagnosed diabetes. The diagnosis was confirmed through plasma glucose analysis according to NDDG criteria (3). The overall prevalence of DM was 2.8% (Laurenzi M., Hypertension Gubbio Study, 1993, personal communication).

Comparing the data of our study with that obtained through the same methodology in other Italian areas, the prevalence of DM in Foligno (Umbria) appears to be similar to the one in Lombardia (9), but somewhat higher than it is in Piedmont (10), Tus-

cany (11), Campania (12) and Veneto (13). This difference, while not relevant, may reflect some local environmental factors, including the mean age of the examined population. Other population studies on diabetes were conducted in Italy many years ago (14). Because of the different diagnostic criteria and methods used, however, the data cannot be compared with those obtained by the more recent studies. For the same reason, it is hard to compare our data with other epidemiological studies conducted abroad, in Europe and in North America, where the methods of survey were often quite different and heterogeneous (15-21).

However, in the large NHNES II survey, conducted in the USA between 1976 and 1980, in the population aged 20-74 years, the prevalence of physician-diagnosed diabetes was estimated to be 3.4% (20) which is comparable to the data obtained recently in the Italian studies, although it refers to the adult population.

The distribution of the diabetic population by age and sex is similar to that usually described. It is well known that ageing increases the risk of Type II DM and the increase in mean life span certainly exposes elderly people to a higher risk of developing this disease. Indeed, the sharp increase in the prevalence of diabetes after 50 years of age was also noted in this study.

Type I DM was present in 0.085% of the population. A similar rate has recently been reported in other Italian surveys (9-12). This indicates that, except for Sardinia (22), in the other Italian regions the risk for Type I DM is similar, even though some difference has been described in the past (23).

The remaining 3.1% was represented by subjects with Type II DM. The criteria used for the diagnosis of either Type I or Type II DM, were based on the age of onset of diabetes, before and after the age of 30. Although these criteria are usually accepted and apparently realistic, they should be considered arbitrary. Indeed, those patients with Type I DM appearing in adult age are not identified. This subgroup of diabetics should be better characterized on the basis of the immunological tests and HLA gene identification, and such a possibility should be taken into account for future epidemiological surveys.

The type of treatment received by our diabetic population should be considered. It can be noted that the percentage of patients with DM in diet therapy alone is rather high, while it is low for patients on

combined regimen (insulin plus hypoglycaemic drugs). In the Umbria region, a teaching programme has been conducted in the past to emphasize the role of diet and physical exercise in the treatment of Type II DM. Furthermore, therapeutical standards consider combined use of insulin and hypoglycaemic agents only under very rare conditions.

Some conclusions can be drawn from this survey carried out in Umbria. The study confirms the validity of the methodological approach employed, which is made possible by the Italian NHS. The method of capture-recapture has been proposed to monitor the prevalence and incidence of DM. It is used on case ascertainment with several data sources (1, 10, 24), that allow assessment of the prevalence and incidence of diabetes adjusted for the degree of undercount.

This model of survey, already applied successfully in several areas of Italy, allowed the identification of 99% of the diabetic population and may be considered simple, cost effective, accurate and reproducible. It would be of interest to extend this methodology to other European countries. This may allow a realistic evaluation of the prevalence of known diabetes in the various regions of Italy, in comparison with other European countries, both in the northern and Mediterranean areas. Due to its simplicity and reproducibility the survey could be repeated at regular intervals to give information on the trend of the prevalence and incidence of DM.

REFERENCES

1. La Porte R.E., McCarty D., Bruno G., Tajima N., Baba S.: Counting diabetes in the next millenium. *Diabetes Care* 16: 528-534, 1993.
2. Darroch J.N., Fienberg S.E., Glonek G.F.V., Junker B.W.: A three-sample multiple-recapture approach to census population estimation with heterogeneous catchability. *J. Am. Stat. Ass.* 88: 1137-1148, 1993.
3. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28: 1039-1057, 1979.
4. Hook E.B., Regal R.R.: The value of capture-recapture methods even for apparent exhaustive surveys. *Am. J. Epidemiol.* 135: 1060-1067, 1992.
5. Agresti A.: Simple capture recapture models permitting unequal catchability and variable sampling effort. *Biometrics* 50: 494-500, 1994.
6. Fineberg S.E.: The Multiple Recapture Census for closed populations and incomplete 2^k contingency tables. *Biometrika* 59: 591-603, 1972.

7. Agresti A.: *Categorical Data Analysis*, John Wiley & Sons, Inc., 1990.
8. SAS Institute Inc. Version 6 Edition, SAS Institute Inc., Cary, NC, 1990.
9. Garancini M.P., Calori G., Manara E. Izzo A., Ebbli E., Galli L., Boari L., Gallus C.: An Italian population-based study of the prevalence of diabetes: some methodological aspects. *Diabete Metab.* 19: 116-120, 1993.
10. Bruno G., Bargerò G., Vuolo A., Pisu E., Pagano G.: A population based prevalence survey of known diabetes mellitus in northern Italy based upon multiple independent sources of ascertainment. *Diabetologia* 35: 851-56, 1992.
11. Di Cianni G., Bonzi L., Giannarelli R., Orsini P., Villani G., Ciccarone A.M., Cecchetti P., Fedele O., Navalesi R.: A prevalence study of known diabetes mellitus in Tuscany assessed from pharmaceutical prescriptions and other independent sources. *Acta Diabetol.* 31: 87-90, 1994.
12. Vaccaro O., Imperatore G., Ferrara A., Palombino R., Riccardi G.: Epidemiology of diabetes mellitus in southern Italy: a case-finding method based on drug prescriptions. *J. Clin. Epidemiol.* 45: 835-839, 1992.
13. Muggeo M., Verlato G., Bonora E., Bressan F., Girotto S., Corbellini M., Gemma M.L., Moghetti P., Zenere M., Cacciatori V., Zoppini G., De Marco R.: The Verona diabetes study: a population-based survey on known diabetes mellitus prevalence and 5-year all-cause mortality*. *Diabetologia* 38: 318-325, 1995.
14. Gallus G., Garancini P.: Il diabete mellito in Italia. *G. Ital. Diabetol.* 13: 389-396, 1993.
15. Papoz L.: Recent trends in the epidemiology of diabetes mellitus in European and Mediterranean countries. *Acta Diabetol.* 28: 140-142, 1991.
16. Croxson S.C.M., Burden A.C., Bedington M., Botha J.L.: The prevalence of diabetes in elderly people. *Diabetic Med.* 8: 28-31, 1991.
17. Wong J.S.K., Pearson D.W.M., Murchison L., Williany M.J.: The prevalence of diabetes mellitus in north east Scotland. *Diabetic Med.* 8 (Suppl. 11): 28, 1991.
18. Tuomilehto J., Korhonen H., Kartoaara L., Salomaa V., Stengard J.H., Pitkanen M., Aro A., Javela K., Unsutupa M., Pitkanemi M.: Prevalence of diabetes mellitus and impaired glucose tolerance in the middle-aged population of three areas in Finland. *Int. J. Epid.* 20: 1010-1017, 1991.
19. Anderson D.K.G., Svardsudal K., Tibblin G.: Prevalence and incidence of diabetes in a Swedish community 1972-1987. *Diabetic Med.* 8: 428-434, 1991.
20. Harris M.I., Hadden W.C., Knowler W.C., Bennett P.N.: Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20-74 yr. *Diabetes* 36: 523-534, 1987.
21. Warram J.H., Rich S.S., Krolewski A.S.: Epidemiology and genetics of diabetes mellitus. In: Kahn C.R., Weir G.G. (Eds), *Joslin's diabetes mellitus*. Lea and Febiger: 1994, pp. 201-215.
22. Muntoni S., Songini M.: Sardinian collaborative group for epidemiology of IDDM: High incidence ratio of IDDM in Sardinia. *Diabetes Care* 15: 1317-1322, 1992.
23. Karvonen M., Tuomilehto J., Libman I., Laporte R., for the WHO Diamond Project Group: A review of the recent epidemiological data on the worldwide incidence of type I diabetes Mellitus. *Diabetologia* 30: 883-892, 1993.
24. Bruno G., La Porta R.E., Merlett F., Biggeri A., McCarty D., Pagano G.: National Diabetes Program - Application of capture-recapture to count diabetes? *Diabetes Care* 17: 548-556, 1994.