A Comprehensive Assessment of the Avoidability of Long-Term Complications of Diabetes

A case-control study

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OBJECTIVE — To identify and quantify risk factors for the development of long-term diabetic complications (i.e., critical limb ischemia, amputation, chronic renal failure [creatinine >3 mg/dl], dialysis treatment, proliferative retinopathy, blindness), with particular emphasis on those variables that, being related to quality of care, can be considered avoidable.

RESEARCH DESIGN AND METHODS — We designed a case-control study that enrolled 886 patients with long-term diabetic complications and 1,888 control subjects without complications from 35 diabetic outpatient clinics and 49 general practitioners' offices during a 6-month period. Selected socioeconomic, pathophysiologic, self-care, health care, and lifestyle information were collected for all patients.

RESULTS — A logistic regression analysis showed that several factors are related to the development of major diabetic complications. Among patient characteristics, male sex (odds ratio [OR] = 1.8, 95% CI 1.4–2.3) and age (OR = 1.7, 95% CI 1.2–2.4 for patients between 50 and 69 years of age as opposed to those younger than 50 years of age) were associated with an increased risk of complication. Among clinical variables, the type and the duration of diabetes were the most important predictors of diabetic complications. The presence of hypertension was also associated with the development of diabetic complications, particularly when it was poorly controlled by treatment (OR = 3.1, 95% CI 2.3–4.3). Patients who needed help to reach a health care facility and those who did not regularly attend such a facility were at higher risk of developing complications (OR = 1.5, 95% CI 1.2–1.9; OR = 1.7, 95% CI 1.3–2.2, respectively). Educational aspects were also related to the outcome: patients who did not receive any kind of educational intervention had an increased risk of developing complications (OR = 4.1, 95% CI 1.7–9.7), while self-management of insulin therapy had a protective effect (OR = 0.6, 95% CI 0.5–0.8). The summary attributable risk related to avoidable risk factors (i.e., uncontrolled hypertension, poor compliance with visit scheduling, inadequate diabetes education, no self-management of insulin treatment) was 0.39.

CONCLUSIONS — Our data suggest that, by removing avoidable risk factors, the number of diabetic complications considered could be reduced by more than one-third. The case-control methodology represents an efficient way of monitoring clinical practice and relating it to important outcomes. It can be of help for policy makers in identifying the more effective strategies and in tailoring specific interventions aimed at improving the quality of the care delivered to diabetic patients.

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GP, general practitioner; IDF, International Diabetes Federation; OR, odds ratio; WHO, World Health Organization.

The prevalence of diabetes in industrialized countries is estimated to be ~2–3%, and it increases with age, reaching 5–10% after age 70. This corresponds to more than 1 million cases in Italy and more than 14 million in Europe (1).

Chronic complications are the major cause of diabetic morbidity. Diabetes is the leading cause of blindness in industrialized countries, and it represents the most frequent cause of visual handicap in people under 60 years of age (2). About one-fifth of diabetic patients develop nephropathy that requires dialysis treatment or renal transplantation during their lifetime. Diabetes is currently one of the major causes of renal failure, particularly in young people (3).

Among the more disabling long-term diabetic complications are foot complications, the pathogenesis of which is related to both diabetic neuropathy (sensorimotor and autonomic) and peripheral vasculopathy. Typical manifestations are the loss of sensation in the feet, the development of ulcers and deformations, and finally gangrene, which often requires amputation of various extensions. Amputations are 15 times more frequent in diabetic patients than in the general population, and the risk increases with age, being 7 times greater in patients >65 years of age, compared with those <45 (4–6).

The development of diabetic complications is strictly related to metabolic control (7,8), which can be influenced by a number of factors, including those related to the interaction between patients and the health care system. Problems related to accessibility to care, patient satisfaction, or coordination among the different health professionals involved in the care of a diabetic patient can have a major impact on the acceptability of medical recommendations (9–11). Equally important in determining good compliance and adequate self-care are factors such as

age, comorbidity, socioeconomic status, and social support (12,13).

Starting from these premises, representatives of the government health departments and patient organizations met with diabetes experts under the aegis of the regional offices of the World Health Organization (WHO) and the International Diabetes Federation (IDF) in St. Vincent, Italy, in October 1989. As a result of the meeting, 5-year targets were defined, directed primarily at the reduction of major diabetic complications (14). The underlying assumption of the suggested targets was that a large fraction of diabetic complications are avoidable by improving the quality of care.

Further to this end, we designed a study to identify and to quantify risk factors for the development of long-term diabetic complications (i.e., critical limb ischemia, amputation, chronic renal failure [creatinine >3 mg/dl], dialysis treatment, proliferative retinopathy, blindness). In particular, we evaluated the overall impact of pathophysiological and quality of care–related factors on diabetic complications, with particular emphasis on those factors that can be considered "avoidable" because they are related to patients' and doctors' practices and attitudes.

RESEARCH DESIGN AND METHODS

Inclusion criteria

The study was carried out between December 1993 and June 1994. We designed a case-control study (15) in which cases were identified in outpatient diabetes clinics, in general practitioners' offices, and in hospital departments (surgery, nephrology, and ophthalmology) where patients were admitted because of a major diabetic complication. All patients with NIDDM or IDDM with a duration of at least 5 years were included in the study as cases if they met one or more of the following criteria: admission to a hospital for amputation or amputation within the previous 12-month period; critical limb ischemia (foot ulcer, gangrene, ischemic rest pain for ≥15 days, or bypass surgery or angioplasty for peripheral vasculopathy); dialysis initiated within the previous 12-month period for diabetic nephropathy; serum creatinine levels of ≥3 mg/dl; blindness developed within the previous 12-month period; and proliferative retinopathy or diabetic maculopathy.

Patients were considered eligible as control subjects if they had NIDDM or IDDM with a duration of at least 5 years and if they were not affected by any of the complications under study. If patients suffered from claudication, early renal impairment (serum creatinine <3 mg/dl or micro- and macroalbuminuria), or nonproliferative retinopathy, they were still considered eligible as control subjects.

Patient identification and accrual

Patients were recruited from 35 diabetic clinics in 17 out of the 20 Italian regions. For each diabetic clinic at least two general practitioners (GPs) from the same health district were identified. Out of the 90 GPs contacted, 49 accepted the invitation to participate in our study.

Identification of cases. In outpatient diabetes clinics, patients eligible as cases were identified among all subjects seen during the study period. In GPs' offices, cases were identified among all diabetic patients in the practice, using computerized clinical records, where possible, to trace them. In hospital departments, all eligible patients who were seen during the study period and were referred to a diabetic clinic or a GP participating in the study were enrolled.

Identification of control subjects. Control subjects were identified in outpatient diabetes clinics and in GPs' offices. In diabetes clinics, a random sample of eligible patients was recruited. In GPs' offices, all eligible patients in their charge were enrolled as control subjects.

Measurements

All patients enrolled in the study as cases or control subjects received a 45-min interview by trained physicians, focusing on exposures of interest, including demographic and socioeconomic characteristics, health care information (accessibility, self-care, social support, type, modality, and frequency of received educational interventions), smoking history, and alcohol consumption. In order to verify the clarity and acceptability of the questionnaire, a pretesting of the interview was performed on 30 patients. All data concerning general medical history and specific diabetes history were collected by interview with the patient's physician and by review of his or her medical records.

For the purposes of our study, patients were considered as affected by hypertension only if the diagnosis preceded the development of diabetic end-stage renal failure. Hypertension was considered uncontrolled by treatment (difficulty in obtaining blood pressure values <160/90 mmHg with chronic treatment) on the basis of clinical judgment and was confirmed by the presence in the medical records of values >160/90 mmHg. Similarly, information on the compliance with scheduled visits and dietary recommendations was based on the physician's evaluation. For the classification of employment status, the husband's employment was considered for housewives, while the status of last employment was considered for retired patients.

All data referred to existing situations; we also collected information on the accessibility of health care facilities and on health habits relative to the previous 5 years, a period of time presumably prior to the development of complications.

Sample size estimation

The number of subjects to be included in a case-control study depends on the specification of four values: *1*) the relative frequency of exposure among control subjects in the target population; *2*) a hypothesized relative risk associated with exposure that would have sufficient biological or public health importance to warrant its detection; *3*) the desired level of significance, α; and *4*) the desired study power, $1-\beta$. In our case, assuming that a hypothetical factor has a prevalence in the control population of 10% and is associated with a relative risk of developing the disease of two or more, the number of cases required is 322 (with $\alpha = 0.05$ and $1-\beta = 0.95$), assuming a case-control rate of 1:2 (16). Thus, the actual sample of more than 800 cases also allows for the reliable detection of risk factors with a lower prevalence in the control group or those presenting a weaker association with the outcome of interest.

Statistical analysis

Analysis was initially carried out based on a series of univariate comparisons. In order to control simultaneously for the possible confounding effect of the variables, a multiple logistic regression analysis with

stepwise variable selection was utilized for the final analysis (17). Thus, in both univariate and multivariate analyses, the association between exposures and outcomes is expressed as an odds ratio (OR) with its 95% CI. ORs >1 suggest an increased risk, while those <1 indicate a protective effect. When the 95% CIs include the null value of 1, no statistically significant difference (at the 5% level) is present. In the final analysis, ORs are controlled for all the variables retained in the model.

For age, employment categories, duration of self-monitoring, frequency of educational interventions, and smoking habits, nonsignificant terms for specific levels of these characteristics were forced into the final logistic model to obtain OR estimates across the entire spectrum of characteristics. This did not affect the estimation of the coefficients of the significant independent variables of the reduced model.

All categorical covariates were coded as 0,1. Covariates considered for the analysis were: age: <50 (reference category [RC]), 50–69, ≥70; sex: women (RC) vs. men; occupation: professional/managerial (RC), technical/clerical, skilled workers/artisans, unskilled workers, other (including housewives, unemployed, retired); marital status: married (RC), single, divorced/separated/widowed; level of education, 0–5 years (RC) vs. >5 years; type of diabetes: NIDDM (RC), IDDM, insulin-treated NIDDM; diabetes duration: <10 years (RC), 10–20 years, > 20 years; hypertension: no (RC), yes (controlled by treatment), yes (uncontrolled by treatment); history of myocardial infarction or stroke: yes versus no; comorbidity: 1 controlled comorbid condition (RC), 2 controlled comorbid conditions, >2 controlled or any uncontrolled comorbid conditions; time spent to reach the health facility in minutes 5 years previous: continuous variable; distance from the health facility in kilometers for previous 5-year period: continuous variable; need of assistance to reach the health facility for previous 5-year period: yes vs. no; regular attendance to visits: yes vs. no; compliance with dietary recommendations: yes vs. no; self-adjustment of insulin doses: yes vs. no; self-monitoring: no (RC), yes (<5 years), yes (≥5 years); frequency of educational intervention: on a regular basis (RC), occasionally, never; kind of educational intervention: individual vs. group; presence of a family member during the educational intervention: yes vs. no; duration of the intervention in min: continuous variable; smoking: nonsmoker (RC), current smoker, quit smoking (<5 years), quit smoking (≥5 years); alcohol consumption in the past 5 years: no alcohol consumption (RC), moderate alcohol consumption, heavy consumption.

Since we had no a priori hypothesis regarding possible interactions among the variables mentioned above and in order to avoid overfitting of the logistic model, no interaction term was included in the analysis.

To estimate the fraction of the total number of patients affected by complications that would not have occurred if the effects associated with the avoidable risk factors were absent, we also obtained the adjusted individual and summary attributable risks from the logistic regression (18).

Table 1—*Patients' characteristics*

	Case subjects	Control subjects	Univariate
n	886	1,888	
Sex			
Female	427 (48)	1,022 (54)	1
Male	459 (52)	866 (46)	1.27 (1.08–1.49)
Age			
<50	97 (11)	209 (11)	1
50–70	440 (50)	926 (49)	1.01 (0.78–1.33)
>70	349 (39)	753 (40)	0.99 (0.75–1.30)
Occupation			
Professional/manager	35 (4)	95 (5)	1
Technical/clerical	133 (15)	326 (18)	1.11 (0.71–1.71)
Skilled workers	194 (22)	341 (18)	1.54 (1.01–2.36)
Unskilled workers	357 (41)	780 (41)	1.24 (0.83–1.87)
Other	159 (18)	330 (18)	1.31 (0.85–2.02)
Not assessable	8	16	—
Years of education			
0–5 years	589 (67)	1,229 (65)	1
>5 years	297 (33)	659 (35)	0.94 (0.93–1.03)
Marital status			
Married	580 (67)	1,258 (68)	1
Single	102 (12)	165 (9)	1.34 (1.03–1.75)
Divorced/separated/widowed	184 (21)	434 (23)	0.92 (0.75–1.12)
Not assessable	20	31	—
Type of diabetes			
NIDDM	212 (24)	1,178 (62)	1
IDDM	185 (21)	194 (10)	5.30 (4.13–6.80)
Insulin-treated NIDDM	489 (55)	516 (28)	5.26 (4.35–6.38)
Diabetes duration			
<10 years	150 (17)	664 (35)	1
10–20 years	334 (39)	815 (44)	1.81 (1.45–2.25)
>20 years	394 (44)	388 (21)	4.49 (3.58–5.63)
Not assessable	8	21	—
Hypertension			
No	409 (47)	1,083 (57)	1
Yes, controlled	339 (38)	661 (35)	1.15 (0.97–1.35)
Yes, uncontrolled	126 (14)	130 (7)	2.24 (1.73–2.90)
Yes, unknown	12 (1)	14 (1)	—
Cardiac-cerebrovascular disease			
No	723 (82)	1,679 (89)	1
Yes	163 (18)	209 (11)	1.81 (1.45–2.26)

Data are *n* (%) or OR (95% CI).

Table 2—*Patients' characteristics*

	Case subjects	Control subjects	Univariate
n	886	1,888	
Comorbidity			
No	403 (46)	953 (50)	1
1 comorbid condition	337 (38)	666 (36)	1.19 (1.00–1.42)
2 comorbid conditions	119 (13)	224 (12)	1.25 (0.97–1.61)
>2 or any uncontrolled	27 (3)	45 (2)	1.42 (0.87–2.32)
Need of help to reach the health facility within last 5 years			
No	356 (42)	1,304 (72)	1
Yes	490 (58)	512 (28)	3.50 (2.95–4.15)
Not assessable	40	72	—
Compliance with visit scheduling			
Yes	635 (73)	1,540 (83)	1
No	233 (27)	320 (17)	1.76 (1.45–2.14)
Not assessable	18	28	—
Self-management of insulin therapy			
No	394 (60)	335 (49)	1
Yes	258 (40)	355 (51)	0.61 (0.49–0.76)
Not applicable	234	1,198	—
Blood glucose self-monitoring			
No	475 (54)	1,233 (65)	1
Yes, ≤5 years	123 (14)	187 (10)	1.71 (1.33–2.19)
Yes, >5 years	132 (15)	185 (10)	1.85 (1.45–2.37)
Yes, unknown	156 (17)	283 (15)	—
Frequency of educational interventions			
Regularly	241 (30)	578 (32)	1
Occasionally	557 (68)	1,190 (67)	1.12 (0.93–1.31)
Never	16 (2)	13 (1)	2.95 (1.39–6.23)
Not assessable	72	107	—
Smoking			
No	531 (60)	1,169 (62)	1
Yes	121 (14)	318 (17)	0.84 (0.66–1.06)
Ex, <5 years	74 (8)	86 (5)	1.89 (1.36–2.62)
Ex, ≥5 years	160 (18)	315 (16)	1.12 (0.90–1.39)
Alcohol consumption			
No	556 (63)	1,090 (58)	1
1–3 cups/day	282 (32)	683 (36)	0.81 (0.68–0.96)
≥4 cups/day	48 (5)	115 (6)	0.82 (0.58–1.16)

Data are *n* (%) or OR (95% CI).

RESULTS

General characteristics of the study population

A total of 886 cases (682 from diabetic clinics, 59 from GPs' offices, 145 from hospital departments) and 1,888 control subjects (1,345 from diabetes outpatient clinics, 543 from GPs' offices) were recruited. Among cases, 349 had proliferative retinopathy, 72 maculopathy, 68 blindness, 215 end-stage renal disease, 195 ulcers/critical limb ischemia, and 125 lower limb amputation. The clinical, sociodemographic, and care-related characteristics of the study population, together with the results of univariate analyses, are reported in Tables 1 and 2.

Mean ± SD systolic and diastolic blood pressure values were 138 ± 17 over 81 ± 8 mmHg, 151 ± 17 over 84 ± 9 mmHg and 172 ± 18 over 95 ± 11 mmHg for patients with no hypertension and controlled and uncontrolled hypertension, respectively.

Results of the logistic regression analysis

Results of the multivariate logistic regression are summarized in Table 3.

Sociodemographic characteristics. Male sex was associated with an 80% increase in the risk of complications, compared with female sex, while patients over 50 years of age showed a higher probability of being a case, particularly in the age-group between 50 and 69 years.

No association emerged with marital status, occupation, or level of education.

Clinical variables. After adjusting for the potential confounding effect of other variables, diabetes duration was a strong predictor for the development of major diabetic complications. Patients with diabetes for 10–20 years showed a 45% increased risk of developing a complication, while the risk was almost three times greater for patients with diabetes lasting >20 years than for patients with a diabetes of shorter duration (i.e., <10 years).

The type of diabetes was also associated with the outcome of interest. Patients with IDDM and those with insulin-treated NIDDM had an increased probability of being a case, compared with NIDDM patients. The presence of hypertension was also significantly associated with an increased risk of complications, particularly when the disease was poorly controlled. A previous history of cardiac or cerebrovascular disease, as well as the presence and severity of other comorbid conditions, were not independently associated with the outcome.

Accessibility to health facilities. Patients who 5 years earlier needed assistance to reach the health facility showed a 53% increased risk of developing a major complication, while the distance and the time spent to reach the facility were not related to the outcome. Patients who did not attend visits on a regular basis also had an increased risk of experiencing a complication.

Patient practices, education, and habits. Self-management of insulin therapy was associated with a 40% risk reduction. The association between self-monitoring of metabolic control and the development of complications was more difficult to interpret. While patients who practiced self-monitoring for >5 years did not differ significantly from those who did not test their blood glucose, subjects who practiced self-monitoring for <5 years showed a 48% increased probability of having a complication.

With regard to diabetic health education, patients who had not received

Table 3—*Results of the multivariate logistic regression analysis*

Variable	OR	95% CI
Age (RC = <50 years)		
50–69 years	1.69	1.18–2.43
≥70 years	1.41	0.95–2.09
Sex (RC = women)	1.82	1.45–2.29
Type of diabetes (RC = NIDDM)		
IDDM	5.93	3.11–11.27
Insulin-treated NIDDM	3.04	1.74–5.30
Diabetes duration (RC = <10 years)		
10–20 years	1.45	1.15–1.84
>20 years	2.74	2.12–3.54
Hypertension (RC = no hypertension)		
Controlled	1.49	1.22–1.83
Uncontrolled	3.11	2.27–4.26
Access to health facilities 5 years previous (RC = autonomous)		
Need of help	1.53	1.23–1.90
Noncompliance with visit scheduling	1.71	1.35–2.16
Adjustment of insulin doses (RC = no)	0.61	0.46–0.80
Self-monitoring of blood glucose (RC = no)		
Yes, ≤5 years	1.48	1.12–1.97
Yes, >5 years	1.05	0.77–1.43
Frequency of educational interventions (RC = regularly)		
Occasionally	1.07	0.86–1.32
Never	4.06	1.69–9.75
Smoking habits (RC = nonsmokers)		
Current smoker	0.67	0.50–0.89
Ex-smoker ≤5 years	1.82	1.22–2.71
Ex-smoker >5 years	0.99	0.74–1.31

Data are OR or 95% CI. RC, reference category.

any kind of outpatient education showed a more than fourfold increased risk of developing a major complication, opposed to patients who received some form of education. The type, modality (individual versus group), frequency, and duration of educational interventions were not related to the outcome.

Analysis of health habits showed that patients who had quit smoking within 5 years had an almost twofold risk of developing a major complication, opposed to nonsmokers, while current smokers had a lower probability of disease. Current and past alcohol consumption were not related to the probability of being a case.

Attributable risks. The attributable risks associated with risk factors considered potentially avoidable (i.e., no educational interventions, uncontrolled hypertension, no compliance with visit scheduling, no self-management of insulin treatment), after adjusting for all other clinical and patient-related characteristics, are reported in Table 4. The summary attributable risk—that is, the proportion of cases associated with the four risk factors mentioned above—was equal to 39%.

CONCLUSIONS— To our knowledge, this is the largest case-control study conducted to date that is aimed at identifying risk factors for the development of major diabetic complications. It was designed to investigate the relative importance of both disease- and setting-related factors in the development of any one of the major diabetic complications. The focus on the problem of avoidability and thus on quality of care–related issues required the involvement of a large number of patients, reflecting different settings and practice styles. Furthermore, patients were enrolled from most of the Italian regions, making the results more generalizable.

Our data showed that several factors related to patient characteristics, clinical variables, and the delivery of care play an important role in the development of complications. Among patient factors, sex and age were related to the outcome. As a matter of fact, men and patients ≥50 years of age had an increased risk of having a major complication. The magnitude of the risk was greater for patients between 50 and 69 years of age. The moderate risk for older patients (i.e., ≥70 years of age) may be at least partially caused by the "healthy worker effect": because of the major burden of diabetic complications and other comorbid conditions, older patients may be less likely to attend the health care facilities and thus not be sampled for the study. Furthermore, the presence of complications may be responsible for a higher mortality rate before 70 years of age, thus leading to an apparent lower risk in this age category. Education and occupation were not associated with the outcome. The importance of patient autonomy is supported by the findings relative to the increased risk of complications for those who needed assistance to reach the health facility.

Among the clinical variables, diabetes type and duration were the strongest predictors of the outcome. The presence of hypertension inadequately controlled by treatment was associated with an almost threefold increase in the probability of being a case, while the excess risk was moderate (i.e., 50%) when hypertension was well controlled. It is worthwhile to mention that overall almost half of the patients in our study were hypertensive and about 17% of these were judged by their doctors to be poorly controlled by the treatment. Clinical judgment was confirmed by blood pressure values, which clearly exceeded normal limits in this subgroup. The presence of macrovascular involvement, defined by a past history of cardiac or cerebrovascu-

Table 4—*Attributable risks for the factors considered avoidable*

Risk factor	Attributable risk
No educational interventions	0.03
Uncontrolled hypertension	0.07
No compliance with visit scheduling	0.10
No self-management of insulin treatment	0.25
All four risk factors	0.39

Attributable risks have been adjusted for all other clinical and patient-related characteristics.

lar disease, was not related to the development of major complications.

Poor compliance with visit scheduling was also associated with an increased risk of being a case, while no association emerged for inadequate compliance with diet recommendations.

Self-care also proved to be an important prognostic factor: those patients able to adjust insulin doses were less likely to develop a major complication. Self-monitoring of blood glucose concentration was, on the contrary, related to a 50% increased risk of being a case. Such a counterintuitive result can be explained by the fact that many patients are given advice on self-monitoring only after the development of complications. Nevertheless, even patients who started self-monitoring >5 years previously, a period of time probably before the onset of the complication, did not show a decreased complication risk as opposed to patients not practicing self-monitoring.

The relevance of diabetes education is further confirmed in our study. Those patients who never received information on specific aspects of diabetes care (e.g., self-management, foot care, physical activity) showed a striking fourfold increased risk of a major complication as opposed to patients receiving some kind of educational intervention. While a large body of literature has already shown that patient education is related to metabolic control (19), our data also document a more direct relationship with clinically relevant outcomes, such as the development of major complications. The probability of being a case was not related to any particular feature of the educational intervention (type, frequency, duration, presence of a family member). Far from considering the characteristics of the educational intervention unimportant, it is more likely that such a result reflects the difficulty in reliably measuring these aspects solely by interviewing patients. Independent verification and more detailed, specifically developed instruments will probably be needed to address this issue better.

As far as lifestyle is concerned, patients who had quit smoking in the last 5 years showed an increased risk of having a major complication, compared with nonsmokers, while current smokers and those patients who stopped smoking more than 5 years previously did not show an increased complication risk. These results could be explained by the fact that patients had stopped smoking as a consequence of the development of a complication. The low complication risk for current smokers suggests that smoking can be considered as a sort of "health status indicator." The lack of association between smoking and major complications has already been reported in a case-control study on diabetic amputations (20).

The results relative to attributable risk deserve particular attention. Attributable risk takes into account not only the strength of the association between a risk factor and the outcome of interest but also the number of patients exposed to the risk factor. It is therefore a very important indicator of the relative impact of different risk factors on public health, and it can help policy makers in choosing among different preventive strategies (21). From our data it emerges that more than one third of the cases could be avoided by better controlling hypertension and by improving patient education, awareness, and compliance. The crucial role of patient education is certainly underestimated in this study. As a matter of fact, many patients may have received information on specific aspects of diabetes care only after the development of a complication. For example, in our study 68% of the patients with foot complications received adequate information on foot care, opposed to 59% of those without such a complication. The data on self-monitoring further support this hypothesis.

As a final point, some possible limitations of our study need to be discussed. As in any case-control study, the design of the study is by definition retrospective. It is thus impossible to draw any conclusion about the causal relationship between the variables investigated and the outcome of interest. Even in interpreting the attributable fraction, it should be borne in mind that we assume that a cause-effect relationship exists and that effective interventions are available. Nevertheless, these limitations are balanced by the possibility of rapidly monitoring the clinical practice, identifying avoidable risk factors on large populations, and setting priorities for preventive strategies.

As a second point, the presence of a major complication could be responsible for recall bias in regard to the kind of education received. In other words, patients suffering from a complication may be more prone to deny having had adequate diabetic care information. Nevertheless, the results are consistent with those coming from randomized clinical trials, showing the efficacy of educational interventions. Furthermore, the previously reported figures on foot care information seem to exclude this problem.

Another possible limitation of case-control studies depends on the correct choice of the control group. Some of the findings, such as the moderate excess risk for patients >70 years of age, could in fact be related, as previously discussed, to differential survivorship between cases and control subjects. Such bias, if present, is much less likely to be relevant for those variables describing the process of care, which represent the major interest of our study. In that sense, covariates such as age and gender are to be considered as adjusting variables rather than as explanatory ones. From this point of view, patients in our study were randomly selected from a very large population, reflecting the different settings of care and practice styles; it is thus very likely that they represent a realistic picture of the true prevalence of the risk factors investigated in the general population.

This project was undertaken in the framework of the initiatives for the implementation of the recommendations of the St. Vincent Declaration in Italy, which aimed at achieving a substantial reduction in the rate of major diabetic complications.

The study helped to identify factors that are likely to be related to an adverse outcome and to distinguish avoidable from nonavoidable factors. Among the former, the control of hypertension and adequate educational interventions seem to be the most effective tools for reducing the incidence of complications. This calls for more intensive efforts that are devoted to informing patients and promoting self-management of the disease. The study also emphasizes the need for setting priorities and tailoring specific interventions for those patients who, on the basis of their characteristics, are more likely to develop a diabetic complications.

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APPENDIX

THE SID-AMD ITALIAN STUDY GROUP FOR THE IMPLEMENTATION OF THE ST. VINCENT DECLARATION

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