

Impact of Type 1 and Type 2 Diabetes on Patterns and Costs of Drug Prescribing

A population-based study

JOSIE M.M. EVANS, PHD
THOMAS M. MACDONALD, MD, FRCP
GRAHAM P. LEESE, MD, FRCP (EDIN)

DANNY A. RUTA, MSC, MFPHM
ANDREW D. MORRIS, MSC, MD, FRCP
(EDIN)

OBJECTIVE — Utilization and costs of prescription drugs were investigated in diabetic and nondiabetic patients.

RESEARCH DESIGN AND METHODS — The study was carried out in Tayside, Scotland, U.K. A validated population-based diabetes register was used to identify patients with type 1 and type 2 diabetes, and a database of all prescriptions dispensed in the community was used to investigate drug utilization in 1995.

RESULTS — In a population of 406,526, there were 974 (0.2%) with type 1 diabetes and 6,869 (1.7%) with type 2 diabetes. The mean dispensed prescribing rates for all drugs (excluding antidiabetic medication) were higher across all age-groups for diabetic patients. After adjusting for age, patients with type 1 diabetes were 2.07 times (95% CI 2.03–2.11) more likely and patients with type 2 diabetes were 1.70 times (1.69–1.71) more likely to be dispensed a drug item than people without diabetes. This likelihood was increased in every drug category, even those not directly related to diabetes, and the proportion and cost of drug items dispensed to diabetic patients was therefore higher than expected given the prevalence of diabetes. Upon projecting these results to the U.K. population, it was discovered that nearly 8% of the U.K. drug budget (£350 million) is accounted for by patients with diabetes (90% of that by patients with type 2 diabetes).

CONCLUSIONS — This study highlights the increased usage and cost of prescription drugs in diabetes, with type 2 diabetes constituting a particular burden. It was discovered that 1.4% of drug usage in the entire population can be accounted for by the increased prescribing rate of diabetic patients compared with that of nondiabetic patients.

Diabetes Care 23:770–774, 2000

The excess burden on the health services of patients with chronic conditions, such as type 1 and type 2 diabetes, is difficult to measure. An important dimension is use of prescription drugs, given that the drug budget constitutes a major proportion of overall health service costs and is increasing. For example, pri-

mary care prescribing costs accounted for 11% of all costs in the U.K. National Health Service (NHS) in 1995, compared with 9.5% 10 years earlier (1).

Compared with the general population, several studies have indicated that diabetic patients have high overall drug usage (especially cardiovascular drugs), independent of

diabetes-specific medication. For example, 2 studies in Sweden and Denmark identified this higher usage in self-report surveys (2,3). However, studies that use routinely collected computerized data are perhaps more reliable, particularly because patient nonresponse to surveys is eliminated and sample sizes are usually bigger (4–6).

Whether the results from these studies carried out in Sweden, Germany (7), and in selected populations in North America can be generalized to the health care situation in the U.K. is not known. Furthermore, few studies have compared the patterns and financial costs of drug usage between type 1 and type 2 diabetes. We have described drug utilization in a population-based sample of diabetic patients drawn from a validated register of type 1 and type 2 diabetic patients in Tayside, Scotland (8). The main objective of the study was to quantify the impact of diabetes on overall drug utilization.

RESEARCH DESIGN AND METHODS

Study population and data sources

The Diabetes Audit and Research in Tayside (DARTS)/Medicines Monitoring Unit (MEMO) Collaboration at the University of Dundee has worked on the record-linkage of health care data to facilitate epidemiological and health services research in the population of Tayside (estimated mid-year resident population of 395,600 in 1995). Tayside is a region in Scotland, U.K., whose residents receive health care through the U.K. NHS. The demographic breakdown of Tayside is broadly similar to that of the rest of Scotland (i.e., with a low proportion of residents from ethnic minority groups), as is the general health status of the population. Record-linkage is enabled by the widespread use of a unique health care identifier known as the Community Health Index Number (CHNo), a 10-digit number incorporating date of birth and sex that is allocated to patients when they register with a general practitioner (GP) in Scotland. Reg-

From the Departments of Medicine (J.M.M.E., G.P.L., A.D.M.), Clinical Pharmacology (T.M.M.), and Epidemiology and Public Health (D.A.R.), Ninewells Hospital, University of Dundee, Dundee, Scotland, U.K.

Address correspondence and reprint requests to Josie M.M. Evans, PhD, Medicines Monitoring Unit, University of Dundee, Ninewells Hospital, Dundee, Scotland, DD1 9SY, U.K. E-mail: josie@memo.dundee.ac.uk.

Received for publication 12 December 1999 and accepted in revised form 28 February 2000.

Abbreviations: BNF, British National Formulary; CHNo, Community Health Index Number; CNS, central nervous system; DARTS, Diabetes Audit and Research in Tayside; GP, general practitioner; MEMO, Medicines Monitoring Unit; NHS, National Health Service; SPA, Scottish Prescribing and Audit.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

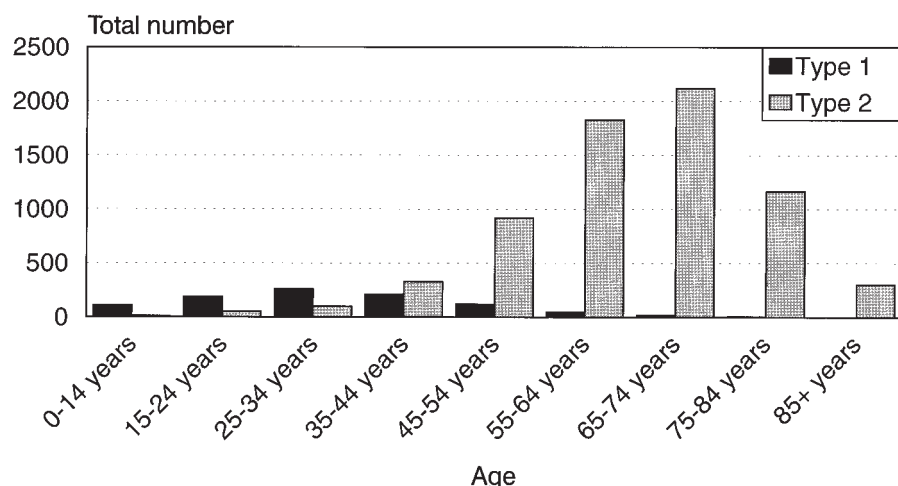


Figure 1—Age distribution of diabetic patients in Tayside.

istration details of these patients are on a central index.

The study was conducted in a defined population of GP-registered patients who were resident in Tayside in January 1995, and were either still resident in December 1995 or had died in Tayside during this period.

DARTS is a validated population-based diabetes information system, compiled by record-linking several independent data sources, including hospital admissions, diabetes clinic visits, and diabetes medication. It has high sensitivity in identifying patients with diabetes and has been described in detail previously (8). In this study, it was used to identify patients in the study population who were diagnosed with diabetes before December 1995. Within the DARTS system, a computer algorithm is used to define diabetes type. Patients diagnosed when younger than 35 years of age and with a requirement for insulin are categorized as patients with type 1 diabetes.

The dispensed prescribing database of MEMO was also used in this study (9). The MEMO database was developed for pharmacoepidemiological research in the population of Tayside and contains records of >15 million prescriptions dispensed in community pharmacies since 1989. Use of the CHNo on both the MEMO and DARTS databases enables record-linkage to investigate drug utilization in diabetic patients (8,9).

Analyses

The MEMO database was used to collate information on all drug items dispensed to patients in the study population dur-

ing a 1-year study period (1995). The overall numbers of drug items dispensed and the proportions of diabetic and nondiabetic patients who received these items were determined.

Mean prescribing rates were calculated. Each rate was the average number of drug items dispensed per patient, stratified by age and sex.

The age-adjusted risk of being dispensed a drug item was estimated by indirect standardization. The ratio of the actual number of items dispensed to diabetic patients to the number that would have been dispensed, had they had the same dispensed prescribing rate as the nondiabetic population, was determined. This was stratified by drug category, as set out in the British National Formulary (BNF) (10). This is a joint publication of the British Medical Association and the Royal Pharmaceutical Society of Great Britain that sets out key reference information on the prescribing, dispensing, and administration of medicines that are used in the U.K. For 4 drug categories of particular interest (gastrointestinal, cardiovascular, central nervous system [CNS], and infections), the drug subcategories were also analyzed.

The population-attributable risk percentage, which is the prescribing that can be attributed to diabetes, was also calculated for type 1 and type 2 diabetes.

To evaluate the impact of diabetes on overall drug utilization and the drug budget, the proportion of drug items dispensed to patients with diabetes was calculated, and also analyzed by BNF subcategory for the 4 categories of interest.

Costs were determined using Scottish Prescribing and Audit (SPA) data, supplied by Tayside Health Board for the population of Tayside in 1995. This information is collected centrally for monitoring purposes and represents data on all prescriptions dispensed in Scotland, but it is not patient specific. Costs were calculated within every BNF subcategory by multiplying the overall number of prescription items dispensed within that subcategory by the estimated unit cost per prescription item derived from SPA.

RESULTS

Study population

There were 406,526 patients in the Tayside study population. Of these, 974 (0.2%) patients had type 1 diabetes and 6,869 (1.7%) had type 2 diabetes. The age distributions are presented in Fig. 1.

Drug utilization

During the study period, a total of 3.41 million prescribed drug items were dispensed to 292,811 of these patients (representing 72% of the total population). The total proportion of patients who dispensed at least 1 item during the study period was 98% in type 1 diabetes, 95% in type 2 diabetes, and 72% in the 398,363 patients without diabetes.

Prescribing rates

The mean dispensed prescribing rates for all drug items (excluding antidiabetic medication), stratified by age, for patients with type 1 and type 2 diabetes, and the nondiabetic population, are shown in Fig. 2. Dispensed prescribing rates are higher for female than male patients, and the rates increase with age. The consistently higher rate in patients with diabetes shows up clearly, with female patients with diabetes having the highest prescribing rates.

After adjusting for age (by indirect standardization), patients with type 2 diabetes were 1.70 times (95% CI 1.69–1.71) more likely to be dispensed a drug item (excluding antidiabetic drug items) than nondiabetic patients. This risk was the same for male and female patients. In type 1 diabetes, the adjusted risk for male patients was 2.37 (2.30–2.44), and for female patients 1.86 (1.81–1.91). Overall, patients with type 1 diabetes were 2.07 times (2.03–2.11) more likely to be dispensed a drug item. These risks, adjusted for age, were also derived by BNF category (Table 1). The risks were increased in every

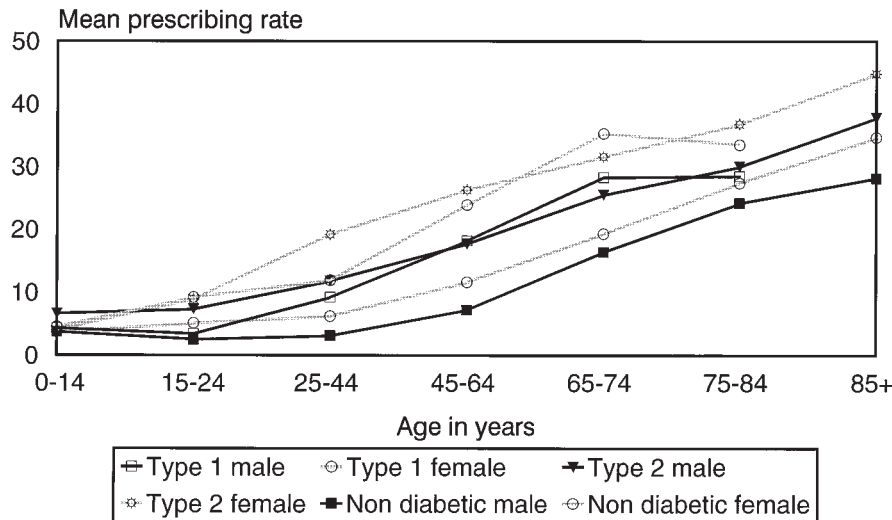


Figure 2—Dispensed prescribing rates by age in male and female patients with and without diabetes in Tayside.

drug category and were particularly high for the cardiovascular system and eye preparations in type 1 diabetes.

There were some interesting observations in the stratified results (Table 2). Within the gastrointestinal category, the marked increase in the use of drugs for intestinal secretions in type 1 and type 2 diabetes was notable. Increased utilization of cardiovascular drugs was mainly for anti-hypertensive drugs, nitrates and vasodilators, and lipid-lowering drugs in type 1 and type 2 diabetes. There was high utilization of drugs for nausea in type 1 diabetes (CNS) and of antifungals for type 1 and type 2 diabetes (infections).

The population-attributable risk percentages were 0.2% in type 1 diabetes and 1.2% in type 2 diabetes: This means that if diabetic patients had the same prescribing rate as the nondiabetic population, prescribing in the entire population would be reduced by 1.4%.

Burden of diabetes

The overall impact of the higher prescribing rates in diabetic patients is also reflected in the proportions of drug items dispensed. Patients with diabetes accounted for 7.3% of the prescriptions dispensed (0.7% to patients with type 1 diabetes and 6.6% to patients with type 2 diabetes). Excluding antidiabetic medication, this proportion was 5.5% (0.3 and 5.2% to patients with type 1 and type 2 diabetes, respectively). For nearly every drug category, diabetic patients accounted

for a higher proportion of drug items dispensed than would be expected given the prevalence of diabetes. The exceptions to this were malignant disease, musculoskeletal disease, and respiratory disease in type 1 diabetes, and obstetrics and gynecology in type 2 diabetes, for which the proportions were the same as the prevalence. Otherwise, in type 1 diabetes, the proportions ranged from 0.3% (cardiovascular disease, gastrointestinal disease, CNS, and endocrine system) to 0.8% (anesthesia). In type 2 diabetes, they

ranged from 3.0% (respiratory disease) to 9.4% (cardiovascular disease).

Cost

The total cost of all prescription items dispensed in the entire Tayside population was £30 million. However, patients with diabetes accounted for £2.37 million, which is 7.9% of the total cost (0.8% to patients with type 1 diabetes and 7.1% to patients with type 2 diabetes). Excluding antidiabetic medication, which cost £144,000 in patients with type 1 diabetes and £557,000 in patients with type 2 diabetes, these proportions were 0.3 and 5.4%, respectively. At the patient level, the average prescribing cost per patient was £75 for a nondiabetic patient, £99 for a patient with type 1 diabetes, and £264 for a patient with type 2 diabetes.

The subanalyses showed that diabetic patients accounted for higher proportions of the costs in nearly every drug category, ranging from 0.2 to 0.8% (anesthesia) in type 1 diabetes, and from 2.6% (endocrine system) to 10.8% (cardiovascular drugs) in type 2 diabetes.

CONCLUSIONS — This study highlights the increased drug-utilization cost of patients with diabetes compared with that of the nondiabetic population. It also describes, for the first time, age-adjusted differential prescribing patterns and drug-utilization costs for people with type 1 and type 2 diabetes in a population-based study. Papoz (11) highlighted some of the

Table 1—Age-adjusted risks (95% CI) of dispensing a drug item for patients with type 1 and type 2 diabetes by BNF drug category

	Diabetes	
	Type 1	Type 2
Gastrointestinal system	1.91 (1.79–2.03)	1.53 (1.51–1.55)
Cardiovascular system	3.48 (3.33–3.63)	1.76 (1.75–1.77)
Respiratory system	1.09 (1.00–1.08)	1.30 (1.27–1.33)
CNS	1.72 (1.64–1.80)	1.70 (1.68–1.72)
Infections	1.76 (1.67–1.85)	1.75 (1.72–1.78)
Endocrine system	2.72 (2.52–2.92)	1.41 (1.38–1.44)
Obstetrics, gynecology, and urinary system	1.12 (1.00–1.24)	1.66 (1.57–1.75)
Malignant disease	1.66 (1.11–2.21)	1.95 (1.83–2.07)
Nutrition and blood	2.90 (2.58–3.22)	1.57 (1.52–1.62)
Musculoskeletal and joint disease	1.41 (1.27–1.55)	1.58 (1.55–1.61)
Eye	3.66 (3.26–4.06)	1.65 (1.60–1.70)
Ear, nose, and oropharynx	1.83 (1.60–2.06)	1.52 (1.46–1.58)
Skin	2.11 (1.98–2.24)	2.08 (2.04–2.12)
Immunology	2.48 (1.95–3.01)	1.61 (1.48–1.74)
Total	2.07 (2.03–2.11)	1.70 (1.69–1.71)

Table 2—Proportions of drugs dispensed to patients with diabetes and age-adjusted dispensing risks (with 95% CI) for 4 drug categories

	Type 1 diabetes		Type 2 diabetes	
	Proportion of drugs (%)	Age-adjusted risk	Proportion of drugs (%)	Age-adjusted risk
Gastrointestinal				
Antacids	0.3	1.99 (1.68–2.30)	4.8	1.43 (1.38–1.48)
Antispasmodics	0.3	1.64 (1.23–2.05)	4.2	1.42 (1.33–1.51)
Ulcer-healing drugs	0.3	1.77 (1.60–1.94)	4.9	1.46 (1.43–1.49)
Antidiarrheal drugs	0.3	1.67 (1.00–2.34)	6.9	2.56 (2.35–2.77)
Chronic diarrhea	0.1	0.65 (0.28–1.02)	3.6	1.28 (1.14–1.42)
Laxatives	0.2	2.36 (2.02–2.70)	5.7	1.60 (1.55–1.65)
Hemorrhoids	0.1	0.78 (0.41–1.15)	4.0	1.39 (1.26–1.52)
Stoma care	—	—	5.3	1.70 (1.15–2.25)
Intestinal secretions	3.1	23.2 (17.0–29.3)	14.7	8.32 (7.31–9.33)
Cardiovascular				
Inotropic drugs	—	0.48 (0.10–0.86)	11.8	2.95 (2.84–3.06)
Diuretics	0.2	2.78 (2.51–3.05)	7.4	1.86 (1.83–1.89)
Anti-arrhythmic drugs	0.1	0.73 (0–1.74)	8.6	2.24 (1.97–2.51)
β -Blockers	0.1	0.87 (0.72–1.02)	5.8	1.65 (1.61–1.69)
Antihypertensives	0.9	9.63 (8.85–10.41)	14.2	4.07 (3.99–4.15)
Nitrates/vasodilators	0.4	4.51 (4.18–4.84)	11.0	2.91 (2.87–2.95)
Anticoagulants	0.2	1.50 (0.92–2.08)	11.2	3.06 (2.92–3.20)
Antiplatelet drugs	0.2	3.31 (2.76–3.86)	10.1	2.52 (2.46–2.58)
Antifibrinolytic drugs	0.5	1.62 (0.03–3.21)	0.8	0.55 (0.14–0.96)
Lipid-lowering drugs	0.8	5.70 (4.76–6.64)	11.3	3.61 (3.45–3.77)
CNS				
Hypnotics/anxiolytics	0.2	1.07 (0.93–1.21)	4.8	1.47 (1.43–1.51)
Drugs for psychoses	0.3	1.43 (1.13–1.73)	4.1	1.45 (1.37–1.53)
Antidepressants	0.4	1.75 (1.58–1.92)	4.3	1.68 (1.63–1.73)
Appetite suppressants	—	—	3.2	1.71 (1.17–2.25)
Drugs for nausea/vertigo	0.4	2.43 (2.01–2.85)	5.0	1.59 (1.52–1.66)
Analgesics	0.3	2.04 (1.91–2.17)	5.6	1.87 (1.84–1.90)
Antiepileptics	0.4	0.32 (0.27–0.37)	3.5	1.11 (1.05–1.17)
Drugs for Parkinsonism	0.2	1.46 (0.90–2.02)	6.1	1.66 (1.56–1.76)
Substance dependence	0.2	0.48 (0.21–0.75)	0.4	0.87 (0.55–1.19)
Infections				
Antibacterial drugs	0.4	1.68 (1.59–1.77)	2.8	1.67 (1.64–1.70)
Antifungal drugs	1.1	4.35 (3.55–5.15)	4.4	2.76 (2.51–3.01)
Antiviral drugs	0.3	1.25 (0.25–2.25)	1.3	0.88 (0.52–1.24)
Antiprotozoal drugs	0.1	1.64 (0.95–2.33)	8.7	2.20 (2.09–2.31)
Anthelmintics	0.4	1.75 (0.35–3.15)	0.3	1.09 (0.14–2.05)

Data are *n* or %.

difficulties involved in carrying out drug-utilization studies in diabetes; hence, these data are invaluable. Although previous studies have evaluated drug prescriptions and costs among diabetic patients in primary health care (7), diabetic patients were ascertained on the basis of antidiabetic drugs, and no valid denominator of all diabetic patients (including people treated with diet therapy alone) or information on diabetes type was available. The DARTS database has been shown to have high sensitivity and specificity in identifying

patients with diabetes, compared with diabetes registers based in primary care (8). Although there may inevitably be some misclassification of diabetes type, as evidenced by the very young patients with type 2 diabetes (Fig. 1), this is unlikely to have a major effect on the study results.

Without exception, within every drug category, diabetic patients were significantly more likely to be dispensed a drug item. This increased likelihood ranged from 1.09 (respiratory system) to 3.66 (eye) in type 1 diabetes, and from 1.30 (respiratory sys-

tem) to 2.08 (skin) in type 2 diabetes. An important reason is the high incidence of long-term complications associated with diabetes. For example, the increased utilization of drugs for the cardiovascular system is the increased risk of heart disease in diabetic patients (cardiovascular drug use accounted for 9.5 and 28.8% of the total prescriptions in type 1 and type 2 diabetes, respectively). Diuretics, calcium antagonists, ACE inhibitors, and nitrates were the most frequently prescribed drugs. This is consistent with the clear relationship between type 2 diabetes and hypertension, hyperlipidemia, and increased cardiovascular risk.

Perhaps more intriguing is the increased drug utilization in drug categories not directly related to diabetes, including drugs for the CNS, drugs for infections, and drugs for musculoskeletal and joint disease. There is some evidence that diabetes is associated with depression and possible suicide/parasuicide (rather like other chronic illnesses) (12), as well as with other cognitive deficits and complaints of memory loss. Antidepressant drugs are also used widely in the treatment of neuropathy. The increased prescribing of antibacterial, antifungal, and antiprotozoal drugs in type 1 and type 2 diabetes is consistent with an increased susceptibility to infection, and perhaps more severe consequences of infections (extensive ulceration, gangrene, and amputations). With respect to musculoskeletal and joint disorders, peripheral neuropathy and peripheral vascular disease may cause soft-tissue damage.

There is also the possibility that increased utilization of drugs can be explained by the presence of conditions that predispose to diabetes. For example, there is the strong association between type 2 diabetes and obesity, which is also a major risk factor for osteoarthritis, perhaps thus explaining the increased use of analgesics in the diabetic population.

Increased drug utilization in other drug categories may represent poorly understood consequences of diabetes. Alternatively, physician and patient factors may account for increased prescribing in diabetic patients. However, similar results were obtained in a previous study using the same data matched by GP practice (thus reducing confounding by prescriber behavior and socioeconomic variation) (13). Another explanation is that diabetic patients may have contact with their general practitioners more regularly, who may, in turn, have different thresholds for pre-

scribing in diabetes. Also, because they receive prescriptions free of charge in the U.K., there is no financial disincentive for diabetic patients to redeem a prescription at a community pharmacy. It should also be noted that although we can be certain that the patients obtained the drugs from the pharmacy, we cannot be sure that they took them as prescribed.

The analyses by subcategory also revealed some interesting patches of under-prescribing. For example, β -blockers were less likely to be prescribed in type 1 diabetes, perhaps reflecting beliefs that they are more harmful or less beneficial in insulin-treated diabetic patients. Deterioration in glycaemic control or blunted counterregulatory responses to hypoglycaemia are seldom clinically important problems, especially with cardioselective β -blockers (14). β -Blocker underuse is a growing concern (15), especially in circumstances in which evidence from large trials suggests that β -blockers are effective in high-risk patients with diabetes after myocardial infarction, particularly in those with left ventricular dysfunction (16).

At the population level, the implications of increased utilization of drugs in diabetic patients are significant. The actual disparity in utilization between diabetic and nondiabetic patients is more pronounced for type 1 diabetes, where background use of drugs in the young healthy group is low. However, type 2 diabetes constitutes the greater burden, because patients with type 2 diabetes are higher absolute users of drugs than patients with type 1 diabetes, as they are a much older population, and there are also 8 times as many of them. Indeed, the population-attributable risk percentages show that 1.4% of drug utilization in the entire population can be accounted for by the increased prescribing rate of diabetic patients compared with nondiabetic patients (1.2% for type 2 diabetes and 0.2% for type 1 diabetes).

The total nationwide expenditure on drugs in the U.K. in 1995 was £4,488 million (1). These results therefore suggest that the overall prescription costs for patients with diabetes in the U.K. could be as high as £355 million, with £319 million spent on patients with type 2 diabetes. Excluding antidiabetic medication, the costs would be £256 million for all diabetic patients, of which £242 million would be spent for type 2 diabetes for causes and

complications of the disease, rather than to achieve glycaemic control. Given predictions that the prevalence of diabetes may reach epidemic proportions by the year 2025 (17), primarily because of the increased incidence of type 2 diabetes, the financial implications are stark.

Data from the U.K. Prospective Diabetes Study (18) suggest that approximately half of patients with type 2 diabetes have complications at diagnosis. It remains to be established, however, whether early detection of diabetes in this group of patients (for example, screening for clinically silent diabetes) would lead to a reduction in the general level of morbidity, and ultimately less health care resource use. The costs incurred by increased expenditure on research into diabetes prevention and detection may ultimately be outweighed by savings in drug expenditure, the burden of which is highlighted in this study.

Acknowledgments — Statistical analysis for this study was partially funded by an unattributed grant from SmithKline Beecham. J.M.M.E. holds a Wellcome Trust Training Fellowship in Health Services Research (Ref. 050212).

MEMO is part of the Medical Research Council Health Services Research Collaboration. Acknowledgments are due to members of the DARTS/MEMO Collaboration who made this work possible, notably D.I.R. Boyle, computer programmer for DARTS. We also thank the following members of the DARTS Steering Group for their support: Kim Boyle, Dr. Alan Connacher, Pauline Clark, Alison Cowie, Dr. Derek Dunbar, Dr. Alisdair Dutton, Dr. Alistair Emslie-Smith, Prof. Roland Jung, Dr. Margaret Kenicer, Dr. Brian Kilgallon, Dr. Graham Leese, Dr. Rebecca Locke, Dr. Sandy McKendrick, Dr. Peter Slane, and Dr. Sandy Young.

References

1. Majeed A, Head S: Controversies in primary care: setting prescribing budgets in general practice: capitation based prescribing budgets will not work. *BMJ* 316:748-750, 1998
2. Gram J, Damsgaard EM: Drug consumption in elderly diabetics. *Diabetes Res Clin Pract* 7:293-298, 1989
3. Wandell PE, Brorsson B, Aberg H: Drug use in patients with diabetes. *Diabetes Care* 19:992-994, 1996
4. Rendell M, Lassek WD, Ross DA, Smith C, Kernek S, Williams J, Brown M, Willinghammyre L, Yamamoto L: A pharmaceutical profile of diabetic patients. *J Chronic Dis* 36:193-202, 1983

5. Isacson D, Stalhammar J: Prescription drug use among diabetics: a population study. *J Chronic Dis* 40:651-660, 1987
6. Glauber HS, Brown JB: Use of health maintenance organization data bases to study pharmacy resource usage in diabetes mellitus. *Diabetes Care* 15:870-876, 1992
7. Rathmann W, Haastert B, Roseman JM, Gries FA, Giani G: Prescription drug use and costs among diabetic patients in primary health care practices in Germany. *Diabetes Care* 21:389-397, 1998
8. Morris AD, Boyle DIR, MacAlpine R, Emslie-Smith A, Jung RT, Newton RW, MacDonald TM, for the DARTS/MEMO Collaboration: The diabetes audit and research in Tayside Scotland (DARTS) study: electronic record-linkage to create a diabetes register. *BMJ* 315:524-528, 1997
9. Evans JMM, McDevitt DG, MacDonald TM: The Tayside Medicines Monitoring Unit (MEMO): a record-linkage system for pharmacovigilance. *Pharmaceut Med* 9:177-184, 1995
10. British National Formulary: Number 36. London, British Medical Association and the Royal Pharmaceutical Society of Great Britain, September 1998
11. Papoz L: Utilization of drug consumption data. In *Diabetes in Europe*. Williams R, Papoz L, Fuller J, Eds. London, John Libbey, 1994, p. 124-130
12. Ingberg CM, Palmer M, Aman J, Larsson S: Social consequences of insulin-dependent diabetes mellitus are limited: a population-based comparison of young adult patients vs healthy controls. *Diabet Med* 13:729-733, 1996
13. Evans JMM, Boyle DIR, Davey PG, Newton RW, MacDonald TM, Jung RT, Morris AD: What is the drugs' bill for diabetes? A population-based study (Abstract). *Pharmacoepidemiol Drug Safety* 7 (Suppl. 1):S102, 1998
14. Viskin S, Barron HV: Beta blockers prevent cardiac death following a myocardial infarction: so why are so many infarct survivors discharged without beta blockers? *Am J Cardiol* 78:821-822, 1996
15. MacDonald TM, Butler R, Newton RW, Morris AD: Which drugs benefit diabetic patients after acute myocardial infarction? *Diabet Med* 15:282-289, 1998
16. Lager I, Blohme G, Smith U: Effect of cardioselective and non-selective beta blockade on the hypoglycaemic response in insulin-dependent diabetics. *Lancet* i:458-462, 1979
17. King H, Aubert RE, Herman WH: Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care* 21:1414-1431, 1998
18. U.K. Prospective Diabetes Study (UKPDS) VIII: Study design, progress and performance. *Diabetologia* 34:877-890, 1991