Screening to prevent renal failure in insulin dependent diabetic patients: an economic evaluation

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Abstract

***Objective*—To examine the conditions necessary to make screening for microalbuminuria in patients with insulin dependent diabetes mellitus cost effective.**

***Design*—This economic evaluation compared two strategies designed to prevent the development of end stage renal disease in patients with insulin dependent diabetes with disease for five years. Strategy A, screening for microalbuminuria as currently recommended, was compared with strategy B, a protocol in which patients were screened for hypertension and macroproteinuria.**

***Intervention*—Patients identified in both strategies were treated with an angiotensin converting enzyme inhibitor.**

***Setting*—Computer simulation.**

***Main outcome measures*—Strategy costs and quality adjusted life years (QALYs).**

***Results*—The model predicted that strategy A would produce an additional 0·00967 QALYs at a present value cost of $261.53 (1990 US$) per patient (or an incremental cost/QALY of $27 041.69) over strategy B. The incremental cost/QALY for strategy A over B was sensitive to several variables. If the positive predictive value of screening for microalbuminuria (impact of false label and unnecessary treatment) is <0·72, the effect of treatment to delay progression from microalbuminuria to macroproteinuria is <1·6 years, the cumulative incidence of diabetic nephropathy falls to <20%, or >64% of patients demonstrate hypertension at the onset of microalbuminuria, then the incremental costs/QALY will exceed $75 000.**

***Conclusions*—Whether microalbuminuria surveillance in this population is cost effective requires more information. Being aware of the costs, recommendation pitfalls, and gaps in our knowledge should help focus our efforts to provide cost effective care to this population.**

Introduction

Diabetic nephropathy is the leading cause of end stage renal failure in many countries.[1,2] Several studies have demonstrated the importance of control of blood pressure in delaying progression to end stage renal failure.[3,4] More recently captopril, an angiotensin converting enzyme inhibitor, was shown to have the additional benefit of a delay in progression in patients with overt diabetic nephropathy.[5] There are many reports showing that most patients pass through a stage of "incipient" nephropathy (microalbuminuria) before developing overt diabetic nephropathy.[6-8] More recently treatment with an angiotensin converting enzyme inhibitor at the stage of microalbuminuria has been shown to prevent the progression to clinical proteinuria.[9] Ideally if patients destined for diabetic nephropathy could be identified and treated early to delay progression, valuable health care savings and improvements in patient outcomes could be realised. Whether microalbuminuria is a good predictor is controversial.[10]

Two cost effective analysis studies support screening for microalbuminuria.[11,12] These models, however, assumed a high incidence of diabetic nephropathy in the population, incorporated high efficacy rates of treatment to prevent end stage renal disease, and did not specifically examine the effect of false positive results of microalbuminuria on cost effectiveness. This study examines these variables and also examines whether screening for microalbuminuria (>20 μg/minute) and treatment with an angiotensin converting enzyme inhibitor is cost effective compared with a strategy not requiring microalbuminuria testing.

Methods

This economic evaluation compared two strategies for the follow up and treatment of patients with insulin dependent diabetes mellitus. Strategy A consisted of screening for microalbuminuria in patients with more than five years of diabetes and treatment with an angiotensin converting enzyme inhibitor (equivalent to captopril 25 mg thrice daily) if two out of three tests were positive (>20 μg/minute).[5,13] Strategy B consisted of treating patients with hypertension or macroproteinuria, or both (dipstick >0·3 g/l or positive Albustix confirmed with >300 mg/day or >200 μg/minute proteinuria). A Markov model incorporating relevant outcomes for a cohort of patients with insulin dependent diabetes was created based on previous models.[11,12] Strategy A (fig 1) is similar to these previously published models. A portion of the patients destined for diabetic nephropathy will be hypertensive at the onset of microalbuminuria.[14,15] Therefore a portion of patients in strategy B will be treated with angiotensin converting enzyme inhibition at the same time as in strategy A without the costs of screening for microalbuminuria. The remaining patients destined for diabetic nephropathy in strategy B will either develop hypertension sometime thereafter and be started on the drug or develop macroproteinuria and be treated. Patients in strategy B destined to diabetic nephropathy without concomitant hypertension are assumed to progress from microproteinuria to macroproteinuria at a faster rate (compared with strategy A) because of a delay in treatment (fig 1).

To determine which of these two strategies were superior, probabilities, costs, and utilities were assigned to each treatment and health state (tables 1 and 2). Direct costs from the perspective of the patient and provider (third party and government) were included. Utilities were used to calculate QALYs (cost effective and cost utility are used interchangeably in

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BMJ 1995;311:1595-9

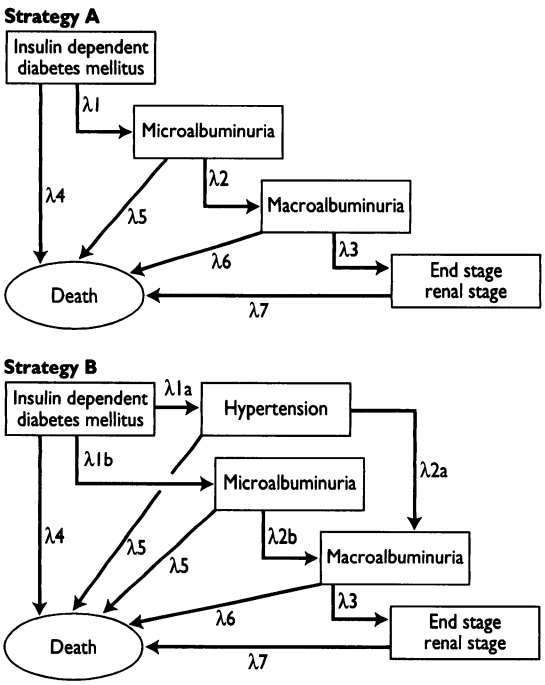

Fig 1—*Flow charts for strategy A and strategy B. Shaded boxes represent treatment with angiotensin converting enzyme inhibitor. Transition probabilities (λ) are shown in table 1. Patients with hypertension at onset of microalbuminuria (strategy B) will be treated at same time as strategy A. Others will have treatment delayed until onset of macroproteinuria*

this report).[16] Traditionally utilities vary between 1·0 (perfect health) and 0 (death). As there are no published utilities for our purpose, we determined utilities from 17 health care workers (four nephrologists, six house staff, six nurses, and one social worker) not associated with the study. Six states were presented to each subject in random order (present health; hypertension requiring medication; and insulin dependent diabetes alone, requiring blood pressure pills, with a functioning renal transplant, or on dialysis). Subjects first ranked and then assigned values to the states by using the time trade off method.[17] Costs and outcomes were then calculated over a 60 year period. A sensitivity analysis was performed to calculate the threshold values for choosing strategy A over B. This report used guidelines recommending that a technology costing <$15 000 US dollars (<$20 000 Canadian) per additional QALY be readily implemented and that one costing >$75 000 (>$100 000 Canadian) be considered poor evidence for adoption.[18]

Results

The baseline model predicted the life expectancy for a diabetic subject from the time of diagnosis for strategy B would be 39·56 years. For this strategy a patient was also predicted to accrue 12·51 QALYs from the time of screening. Strategy A produced an additional 0·1287 years but only 0·0097 more QALYs (3·5 days). Only 0·039 of the additional undiscounted life years produced accrued in the first 30 years. A physician following the recommendations of strategy A must screen and treat 103 (1/0·0097) patients over a 60 year period to produce an additional QALY. From a different perspective he or she must screen and treat 423 patients for 10 years to prevent one year of dialysis. The incremental cost/QALY of A over B was $27 041·69. As costs differ widely from centre to centre a wide range of values were examined (table 3). Costs for screening and treatments with drugs and for renal failure as well as the effect of drug treatment on quality of life had important effects; most changes, however, maintained the incremental cost/QALY in an acceptable range.

Screening tests for microalbuminuria have a high coefficient of variation and can yield positive results in normal subjects.[14 19 20] The potential to diagnose patients falsely with incipient nephropathy will lower the positive predictive value of the test. The sensitivity and specificity of the test are reported to be high (>0·90); the precision (wide confidence intervals) of these estimates, however, is low.[14] With an annual incidence of microalbuminuria of 1·7% the positive predictive value for a single test (0·97 sensitivity and 0·96 specificity) is 0·3.[21] To what extent repeat testing increases the positive predictive value is unclear (not likely to exceed 0·8). If the predictive value is low many patients will be treated needlessly. The positive predictive value must be >0·72 if strategy A is to be preferred (fig 2). Lower screening costs with poor predictive value or more frequent testing (at higher costs) with modestly better predictive value will both result in higher costs/QALY. Even if annual drug costs drop to $250, strategy A will not be cost effective if the predictive value falls below 0·65.

The Collaborative Study Group showed that

Table 1—*Baseline probability inputs (see fig 1)*

Baseline probabilities	Range
λ1=0·017/year	0·008-0·051
λ1a=λ1×fraction with concomitant microalbinuria and hypertension=0·085/year	
λ1b=λ1-λa=0·085/year	
λ2=λ2a=0·10/year*	0·05-0·15
λ2b=0·125/year*	0·06-0·25
λ3=0·067/year*	0·05-0·10
λ4=0·001+(0·0009* duration of diabetes)†	
λ5=1·045×λ4†	
λ6=1·09×λ4†	
λ7=0·15/year†	0·10-0·20
Positive predictive value of screening for microalbuminuria=0·80	0·4-1·00
Fraction of patients with concomitant microalbuminuria and hypertension=0·50	0·2-1·00

*Model assumed transition from microproteinuria to macroproteinuria without treatment is eight years,[14] with treatment is 10 years, and a transition from macroproteinuria to end stage renal failure without angiotensin converting enzyme inhibition is 10 years and with treatment is 15 years.[12] Association of λ2b and λ2 is described as λ2=1/((1/λb2)+delay in years from microproteinuria to macroproteinuria with drug treatment).[33]
†Annual patient mortality was estimated from known mortality statistics.[34 35] The 1·09 multiplier (λ6) accounts for excess cardiovascular mortality documented in proteinuric diabetic patients.[36] An intermediate value was assumed for microalbuminuric patients (λ5).

Table 2—*Baseline cost and utility assignment*

Measure	US$ (range)
Costs:	
Annual screening for microalbuminuria	24 (15-72)
Annual screening for macroproteinuria	4 (2-8)
Angiotensin converting enzyme inhibition	500 (250-750)
Treatment of end stage renal failure	44 800 (35 000-60 000)
Utilities:	
Insulin dependent diabetes mellitus	0·838
Angiotensin converting enzyme inhibition	0·826 (0·814-0·838)
End stage renal failure†	0·567
Discount rate	0·05 (0·04-0·06)

*Costs for drug and renal failure treatment costs were taken from published reports.[11 12 37 38] Drug wholesale costs were increased by 0-40% to account for dispensing fees, pharmacy overhead costs, and drug monitoring. Drug costs also vary widely with drug, dose, and frequency of prescription. Renal failure treatment costs represent pooled average for all patients, and all treatments including transplantation. Costs ($20 per test) for microalbuminuria will vary according to method, frequency, and from centre to centre. Model assumed 10% duplicate retest rate for positive screens. As current recommendations for strategy A call for ongoing microalbuminuria testing after drug treatment, additional monitoring costs were included during microalbuminuria stage.
†End stage renal disease value (0·35×0·762+0·65×0·462) is combined value for transplant recipients (0·762) and dialysis patients (0·462).

Table 3—*Sensitivity analysis*

	Costs		Corresponding incremental cost/QALY	
	Minimum	Maximum	Minimum	Maximum
Screening for microalbuminuria	15	72	15 122	90 612
Angiotensin converting enzyme inhibition costs	250	750	-5467*	59 551
End stage renal failure costs†	35 000	60 000	42 831	2551
Utility:				
Angiotensin converting enzyme inhibition	0·814	0·838	-48 251‡	10 560
Discount rate	0·04	0·06	18 271	41 292

*Lower drug treatment costs produce more QALYs at less cost for strategy A over B.
†Higher renal failure costs favour strategy A as reflected in lower incremental cost/QALY for A over B.
‡Disutility of drug treatment at 0·814 results in fewer QALYs and more cost for strategy A.

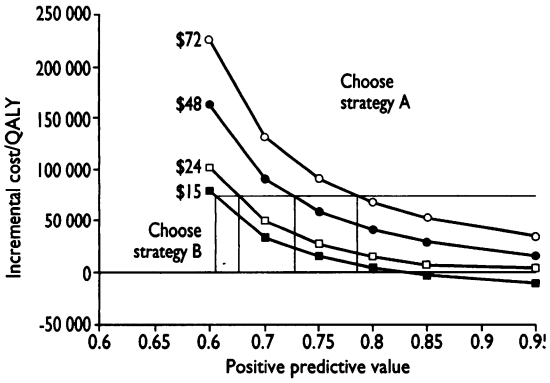

Fig 2—*Effect of positive predictive value of screening test on strategy choice. The lower the positive predictive value, the more falsely labelled and treated patients and the higher the incremental cost/QALY of strategy A over B. Four different annual screening cost ($72, $48, $24, and $15) curves are shown. Higher screening costs were included to reflect more frequent testing in some centres*

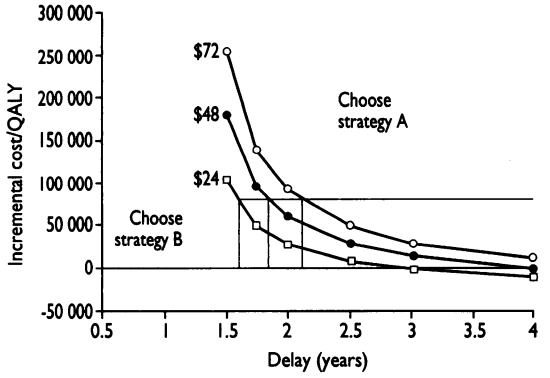

Fig 3—*Effect of early drug treatment to delay transition from microalbuminuria to macroproteinuria on strategy choice. Curves shown for three different annual microalbuminuria screening costs ($72, $48, and $24)*

captopril slows progression of diabetic nephropathy in patients with renal impairment.[5] There was no evidence that earlier treatment had an additional effect. The baseline model states that treatment will delay the transition from microalbuminuria to macroproteinuria by two additional years. For strategy A to be preferred, delayed treatment under B must result in premature macroproteinuria by >1·6 years (fig 3). If early treatment delays the transition by four additional years more QALYs are produced for less cost in strategy A.

A recent study reports that the cumulative incidence of diabetic nephropathy 25 years from initial diagnosis has fallen, from 30% to <9%.[22] It is not clear whether this same change is being seen elsewhere. This model predicts a lifetime (25 year) cumulative incidence of 36·2% (15·7%) and 37·8% (16·8%) for strategy A and B, respectively. If the cumulative lifetime incidence falls below 20% (25 year to 8·1%) and all other assumptions hold, however, strategy A would not be cost effective (fig 4).

A number of patients will develop hypertension before or at the time of onset of microalbuminuria.[14,15] Therefore screening for hypertension will already detect many patients destined for diabetic nephropathy and eliminate the need to screen for microalbuminuria in some patients. If the percentage of such patients with concomitant hypertension exceeds 64% then strategy A is not cost effective (fig 5).

Recently a report showed that patients with poor glucose control (haemoglobin A_{1c} >8·1%) developed microalbuminuria early and frequently.[23] These patients may well have proteinuria on the basis of poor control. If the rate of development of sustained "true" microalbuminuria (0·051) was three times our baseline value (0·017), however, even a lower positive predictive value of 0·65 would result in a cost/QALY of only $24 310. The present recommendations also include follow up microalbuminuria testing twice a year. If this practice were eliminated without compromising efficacy the cost/QALY falls from $27 041 to $18 821.

Conclusions

The high incidence of renal failure in patients with insulin dependent diabetes and the high costs and consequences of end stage renal failure make screening an attractive technology. If screening and treatment costs are low then quick calculations show that even a short delay will be "cost effective." Undeniably better blood pressure control and the additional benefits of captopril will forestall the progression in patients with overt nephropathy. Although not the purpose of this report, our model does show that initiation of treatment at the start of hypertension or macroproteinuria not only increases QALYs but also reduces costs compared with conventional treatment (data not shown). Screening for microalbuminuria, however, introduces variables which impact on cost effectiveness. These include balancing more distant future savings with upfront costs (discounting), balancing present health over future health, and estimating efficacy without the benefit of a randomised control trial. Two previous studies concluded that screening would be cost

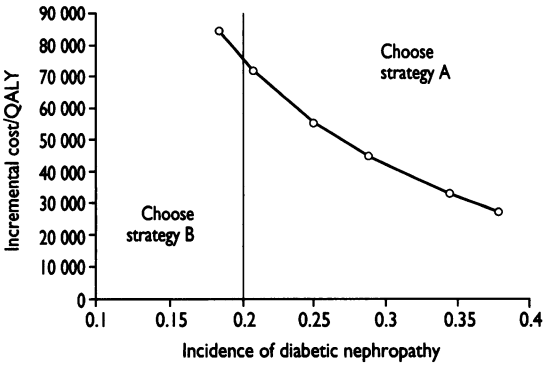

Fig 4—*Effect of cumulative lifetime incidence of diabetic nephropathy on incremental cost/QALY for strategy A over B*

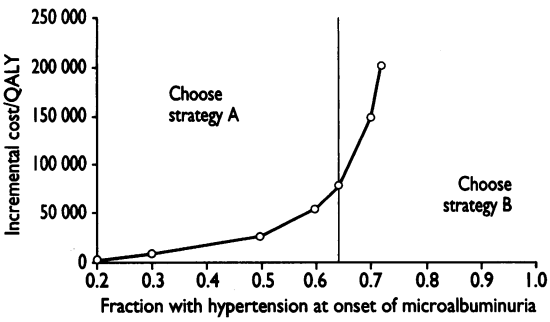

Fig 5—*Effect of concomitant hypertension and microalbuminuria on strategy choice. The fewer the number of patients identified early with hypertension the more that will benefit from screening*

effective.[11 12] The European study did not discount outcomes whereas the Joslin Clinic study did not assign utilities, and neither study considered the effect of false labelling, the fact that hypertension would reduce the need for screening in some patients, nor the impact of a change in the incidence of diabetic nephropathy.

This analysis shows screening to be cost effective if our baseline values and assumptions are correct. Screening for microalbuminuria will not be cost effective if these values and assumptions deviate significantly (and quite realistically) from baseline. From the above, research should be directed at the following.

Firstly, the effect of early treatment with angiotensin converting enzyme inhibitor (onset of microalbuminuria) to delay the onset of diabetic nephropathy and subsequent renal failure must be quantified. Simply stating there is a delay is insufficient.

Secondly, the positive predictive value and costs of the best microalbuminuria test should be determined. The positive predictive value will be much lower when testing is done annually (low incidence) than done in an unselected cross section of diabetic patients. At present several methods are being used. Some advocates suggest using two different screening methods with each patient visit.[24] The trade off between higher screening costs (more testing) and better precision in diagnosis must be carefully considered (fig 2).

Thirdly, updated information on the cumulative incidence of diabetic nephropathy in North America and Europe should be collected.

Fourthly, the incidence of associated hypertension before, at the onset of, or just after the development of microalbuminuria should be determined.

Fifthly, the effects of treatment with angiotensin converting enzyme inhibitors on quality of life may be contentious. None the less, economic appraisals include this disutility in their analysis and further research in this area is warranted.[25 26].

Finally, the additional impact of non-compliance, inappropriate testing, and loss to follow up must be considered on the overall costs of screening. Large numbers of patients will be tested and either refuse treatment or be lost to follow up. Nearly half of all patients identified with microalbuminuria in a recent large study were lost to follow up.[15] This increases screening costs without improving outcomes.

For those centres already screening there are several important recommendations. Firstly, to be cost effective screening must maintain a high positive predictive value. To reduce false positive results screening should be done in patients who are otherwise well.[24 27] Poor glucose control, acute illness, high protein intake, urinary tract infection, and heavy exercise are causes of increased albumin excretion in diabetic patients who would not necessarily have incipient nephropathy. Despite best intentions and well known warnings, many tests are being inappropriately ordered.

Secondly, there is no evidence to support microalbuminuria testing in patients already on angiotensin converting enzyme inhibitors, those in whom the drug and other antihypertensive agents would be contraindicated or not considered, or those with macroproteinuria. Further research is needed to determine whether quantifying the effect of treatment on microalbuminuria is important. It is not known whether it is better to start treatment at a low dose and monitor or start at a higher dose and not retest. Given the high coefficient of variation many samples (at additional cost) would be needed to ensure confidence in monitoring.[14 19 28]

Thirdly, each centre should strive to minimise drug and screening costs and ensure compliance. Longer prescription orders, cheaper drugs, and careful testing are important. Finally, early angiotensin converting enzyme inhibition does not assure that a delay in progression will occur. There is some evidence that the response may also depend on blood sugar control, and good glucose control remains an important goal.[29 30]

Like many other promising screening strategies the evidence is not always available to support widespread implementation.[31 32] None the less, there is some evidence to support screening for microalbuminuria in insulin dependent diabetic patients. What remains to be determined is at what level and how. With ongoing research more precision in the above analysis should be possible. Until then this analysis shows screening for low levels of microalbuminuria to be unproved and potentially costly. We hope this report provides a balanced perspective on screening for microalbuminuria and focuses the issues for practising physicians.

Key messages

- At least 423 fully participating patients must be screened for microalbuminuria for 10 years to prevent one year of dialysis
- Treatment with angiotensin converting enzyme inhibitors at the start of microalbuminuria must delay progression to macroproteinuria by on average 1·6 years to be cost effective
- The positive predictive value of the test is important; physicians must also avoid inappropriate testing
- Twice yearly testing for microalbuminuria after the start of treatment with angiotensin converting enzyme inhibitors is probably not cost effective

Funding: None.
Conflict of interest: None.

1 US Renal Data System. USRDS 1994 annual data report. The National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, July 1994. *Am J Kidney Dis* 1994;**24**: 48-S56.
2 Canadian Organ Replacement Register. *1992 Annual report*. Ontario: Canadian Institute for Health Information, 1994.
3 Mogensen CE. Long term antihypertensive treatment inhibiting progression of diabetic nephropathy. *BMJ* 1982;**285**:685-8.
4 Parving H-H, Andersen AR, Smidt UM, Svendsen Paa. Early aggressive antihypertensive treatment reduces the rate of decline in kidney function in diabetic nephropathy. *Lancet* 1983;i:1175-9.
5 Lewis EJ, Hunsicker LG, Bain RP, Rohde RD, for the Collaborative Study Group. The effect of angiotensin-enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993;**329**:1456-62.
6 Mogensen CE, Christensen CK. Predicting diabetic nephropathy in insulin dependent patients. *N Engl J Med* 1984;**311**:89-3.
7 Viberti GC, Jarret RJ, Mahmud U, Hill RD, Argyropoulos A, Keen H. Microalbuminuria as a predictor of clinical nephropathy in insulin dependent diabetes mellitus. *Lancet* 1982;i:1430-2.
8 Parving H-H, Oxenboll B, Svendsen Paa, Christensen JS, Andersen AR. Early detection of of patients at risk of developing diabetic nephropathy: a longitudinal study of urinary albumin excretion. *Acta Endocrinol* 1982;**100**: 550-5.
9 Viberti GC, Mogensen CE, Groop LC, Pauls JF, for the European Microalbuminuria Captopril Study Group. Effect of captopril on progression to clinical proteinuria in patients with insulin-dependent diabetes mellitus and microalbuminuria. *JAMA* 1994;**271**:275-9.
10 Forsblom CM, Groop P-H, Ekstrand A, Groop LC. Predictive value of microalbuminuria in patients with insulin dependent diabetes of long duration. *BMJ* 1992;**305**:1051-3.
11 Borch-Johnsen K, Wenzell H, Viberti GC, Mogensen CE. Is screening and intervention for microalbuminuria worthwhile in patients with insulin dependent diabetics? *BMJ* 1993;**306**:1722-3.
12 Siegel JE, Krolewski AS, Warram JH, Weinstein MC. Cost-effectiveness of screening and early treatment of nephropathy in patients with insulin dependent diabetes mellitus. *J Am Soc Nephrol* 1992;**3**:S111-9.
13 Bennett PH, Haffner S, Kasiske BL, Keane WF, Mogensen CK, Parving H-H, *et al.* Screening and management of microalbuminuria in patients with diabetes mellitus: recommendations to the scientific advisory board of the National Kidney Foundation from an ad hoc committee of the Council on Diabetes Mellitus of the National Kidney Foundation. *Am J Kidney Dis* 1995;**25**:107-12.

14 Mogensen CE, Hansen KW, Sommer S, Klebe J, Christensen CK, Marshall S, *et al.* Microalbuminuria: studies in diabetes, essential hypertension, renal diseases as compared with background population. *Adv Nephrol Necker Hosp* 1991;20:191-8.
15 Mangili R, Defarrari G, Di Mario U, Giampietro O, Navalesi R, Rigamonti G, *et al* for the Italian Microalbuminuria Study Group. Arterial hypertension and microalbuminuria in IDDM: the Italian microalbuminuria study. *Diabetologia* 1994;37:1015-4.
16 Drummond MF, Stoddart GL, Torrance GW. *Methods for the economic evaluation of health care programs.* New York: Oxford University Press, 1987.
17 Froberg DG, Kane RL. Methodology for measuring health-state preferences. II. Scaling methods. *J Clin Epidemiol* 1989;42:459-71.
18 Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for clinical and economic evaluations. *Can Med Assoc J* 1992;146: 473-81.
19 Howey JEA, Brawning MCK, Fraser CG. Selecting the optimum specimen for assessing slight albuminuria, and a strategy for clinical investigation. In: Mogensen CE, ed. *The kidney and hypertension in diabetes mellitus.* Boston: Martinus Nijhoff Publishing, 1988:41-50.
20 Cohen DL, Close CF, Viberti GC. The variability of overnight urinary albumin excretion in insulin dependent diabetic and normal subjects. *Diabetic Med* 1987;4:437-40.
21 Fletcher RH, Fletcher SW, Wagner EH. *Clinical epidemiology: the essentials.* 2nd ed. Baltimore: Williams and Wilkins, 1988:42-75.
22 Bojestig M, Arnqvist HJ, Hermansson G, Karlberg BE, Ludvigsson J. Declining incidence of nephropathy in insulin-dependent diabetes mellitus. *N Engl J Med* 1994;330:15-8.
23 Krolewski AS, Laffel LMB, Krolewski M, Quinn M, Warram JH. Glycosylated hemoglobin and risk of microalbuminuria in patients with insulin-dependent diabetes mellitus. *N Engl J Med* 1995;332:1251-5.
24 Mogensen CE, Vestbo E, Poulsen PL, Christansen C, Damsgaard EM, Eiskjaer H, *et al.* Microalbuminuria and potential confounders. *Diabetes Care* 1995;18:572-81.
25 Nease Jr RF, Owens DK. Cost-effectiveness of preference incorporation. *Med Decis Making* 1994;14:382-92.
26 Krahn M, Naylor CD, Baskinski AS, Detsky AS. Comparison of an aggressive (US) and a less aggressive (Canadian) policy for cholesterol screening and treatment. *Ann Intern Med* 1991;115:248-5.
27 WHO Study Group on Diabetes of Prevention. Prevention of diabetes. *World Health Organ Tech Rep Ser* 1994;844:55-9.
28 Johnston J, Paterson KR, O'Reilley DStJ. Estimating urinary albumin excretion rate of diabetic patients in clinical practice. *BMJ* 1993;306:493-4.
29 Reichard P, Nilsson B-Y, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. *N Engl J Med* 1993;329:304-9.
30 Mathisen ER, Ronn B, Jensen T, Storm B, Deckert T. Relationship between blood pressure and urinary albumin excretion in development of microalbuminuria. *Diabetes* 1990;39:245-9.
31 Krahn MD, Mahoney JE, Eckman MH, Trachtenberg J, Paulker SG, Detsky AS. Screening for prostate cancer: a decision analytic view. *JAMA* 1994;272:773-80.
32 Kattlove H, Liberati A, Keeler E, Brook RH. Benefits and costs of screening and treatment for early breast cancer. *JAMA* 1995;273:142-8.
33 Beck JB, Pauker SG, Gottlieb JE, Klein K, Kassirer JP. A convenient approximation of life expectancy (the 'DEALE'). II. Use in medical decision-making. *Am J Med* 1982;73:889-97.
34 Gleeson RE. Endocrine and metabolic systems. In: Lew EA, Gajewski J, eds. *Medical risks: trends in mortality by age and time elapsed.* Vol 2. New York: Praeger, 1990:11-60.
35 US Renal Data System, National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases. USRDS 1992 annual report. *Am J Kidney Dis* 1992;20(suppl 2):55-60.
36 Borch-Johnsen K, Kreiner S. Proteinuria: value as predictor of cardiovascular mortality in insulin dependent diabetes mellitus. *BMJ* 1987;294:1651-4.
37 US Renal Data System, National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases. USRDS 1993 annual report. *Am J Kidney Dis* 1993;22(suppl 2):21-9.
38 The Medical Letter on Drugs and Therapeutics. *Three new ACE inhibitors for hypertension.* New York: New Rochelle, 1991;33:83-4.

(Accepted 31 October 1995)

Commentary: Economics of diabetes care must move forwards

P D Home

A problem of clinical science, albeit ultimately a happy one, is that it does not stop moving forwards. Even this autumn, the observations by the Gentofte group that percentage survival after onset of diabetic nephropathy over 16 years has quintupled and that median survival time has trebled, in association with lower blood pressure, will lead many to intensify their efforts to control even minor degrees of hypertension (>140/90 mm Hg) in these patients.[1] So much is consistent with the current paper, but meanwhile the Gentofte group has also defined a 75% reduction (40% to 10%) over eight years in progression to proteinuria (albumin excretion >300 mg/day) in those patients with type 1 diabetes treated with angiotensin converting enzyme inhibitors who have microalbuminuria but not hypertension (mean blood pressure 127/78 mm Hg).[2] Can this be reconciled with the concerns evidently felt by Kiberd and Jindal that microalbuminuria screening may fail the test when it comes to increased quality of life for the sums invested?

The management of diabetes mellitus is for the most part preventive medicine in that a high proportion of the efforts expended by people with the disease and professionals give no immediate return in health. In the primary prevention of microvascular complications the lead times are particularly great (several decades), and this results in particularly difficult judgments between the present and the future in both health (hypoglycaemia now or blindness later) and economic (intensive insulin therapy now, renal replacement therapy later) terms. Evidently the only appropriate way to answer these questions is to perform modelling along the lines that Kiberd and Jindal describe, but in doing so these authors also illustrate that there are fundamental unmet needs in defining some of the parameters that underlie their model.

Such is evident from the sensitivity analysis (shown in their table 3) with sixfold variations shown in cost per QALY for microalbuminuria screening methods, and infinite variation for costs for angiotensin converting enzyme inhibitors (lower drug costs actually giving more QALYs for less total health care costs). More troublesome, however, are the assumptions about degree of benefit of this method of treatment, the length of the period of microalbuminuria before hypertension and of hypertension or proteinuria to renal failure, and the survival time and costs of management of renal replacement therapy. Indeed this poses another problem, for we are talking about medicine 20 years hence; will medical inflation continue to exceed underlying inflation (implying that discount rates should be adjusted downwards), or will novel cheaper forms (pig kidneys) of management of end stage renal disease be the rule?

But even in its present form we can derive some useful messages from the present paper. Firstly, to be cost effective the prevention of complications several decades in the future must use methods (drugs, investigations, consultations) that are similar in cost (fully applied) to those in the cheaper industrialised nations today. Secondly, we need further economic studies, but perhaps preferably those which start from an acceptable cost/QALY, and work back to appropriate costs of management. Thirdly, there are still too few data on which to base reliable estimates of the effectiveness of treatment, as needed for this type of study; the bias against funding such studies of the natural and medical history of disease needs to be reduced.

Perhaps the newly announced initiative of the International Diabetes Federation will help us to a better understanding of the economics of diabetes care and its needs.[3]

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1 Rossing K, Jacobsen P, Smidt U, Rossing P, Parving H-H. Past and present prognosis in nephropathy. *Diabetologia* 1995;38(suppl 1):A46 (abstract).
2 Mathiesen ER, Hommel E, Smith U, Parving H-H. Efficacy of captopril in normotensive diabetic patients with microalbuminuria—8 years follow up. *Diabetologia* 1995;38(suppl 1):A46 (abstract).
3 Williams R. Quantifying the benefits and investing in prevention. *Diabetic Med* 1995:12:849.