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#### **Key Messages**

- Type 2 diabetic patients with chronic kidney disease receiving structured care (SC) by a diabetologist-nurse team or usual care (UC) had a similar incidence of end-stage renal disease (24 of 104 vs 24 of 101) after intervention for 2 years.
- 101) after intervention for 2 years.
  Patients receiving SC were three times more likely to attain three or more predefined treatment targets than those receiving UC (63 of 104 vs 28 of 101).
- Of 91 patients who attained three or more treatment targets, 14 died or developed end-stage renal disease, compared to 34 of the remaining 114 patients. This amounted to a 60% risk reduction in favour of SC.
- 4. The total number of hospital days was 933 in the SC group and 1169 in the UC group, with a cost difference of HK\$631 300 over a 2-year period.
- Using trained nurses to review these patients under medical supervision which incurred an extra cost of HK\$476 736 in the SC model was cost-saving in a public health care setting.
- Assuming all eight extra out-patient visits were medical consultations during the 2-year period, an extra cost of HK\$322 172 would have been incurred for the whole group.
- Using a traditional medical model, additional yearly cost of HK\$2557 to 40 272 would be required for a patient to attain multiple treatment targets or save one major clinical event if all review visits were by doctors.

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# Cost implication of team-based structured versus usual care for type 2 diabetic patients with chronic renal disease

# Introduction

Multifaceted care delivered by a multidisciplinary team and attainment of multiple treatment targets are associated with reduced rates of premature mortality and new onset of cardiovascular disease in type 2 diabetes.<sup>1,2</sup> In a quality improvement programme involving type 2 diabetic patients with chronic kidney disease, those managed by a pharmacist-diabetologist team using a structured care (SC) protocol were more likely to attain multiple treatment goals and had 50% lower risk of death or end-stage renal disease than those treated with usual care (UC).<sup>3</sup>

# **Patients and methods**

In a 2-year multicentre study conducted between 2004 and 2007,<sup>4</sup> 205 type 2 diabetic patients aged 35 to 75 years from nine public hospitals were randomised to receive either SC delivered by a diabetes specialist team using a protocol with predefined treatment targets or UC. Their serum creatinine levels were 150 to 350 µmol/L. None had biopsy proven glomerulonephritis or surgically remediable renal disease. The primary renal endpoint was defined as death and/or end-stage renal disease (need for dialysis or plasma creatinine level of  $\geq$ 500 µmol/L). The composite cardiovascular endpoint consisted of acute myocardial infarction, lower extremity amputation, revascularisation procedures, heart failure, unstable angina, and arrhythmia precipitating hospital admission. The study protocol was approved by the ethics review committee of the participating hospitals.

The treatment targets were defined as blood pressure of <130/80 mm Hg, HbA<sub>1c</sub> of <7%, LDL-C of <2.6 mmol/L, triglyceride of <2 mmol/L, and treatment with angiotensin-converting enzyme inhibitors and/or angiotensin II receptor blocker provided that the patients did not develop persistent hyperkalaemia ( $\geq$ 5.5 mmol/L) or acute deterioration in plasma creatinine (eg 30% increase) upon introduction or dose titration of these drugs.

Patients randomised into the SC group were seen by a dietician to reinforce adherence to a low protein and low potassium diet. Patients were first started on either an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker, and their renal function was monitored at week 2, and then 4-weekly for 12 weeks, and every 8 to 12 weeks thereafter. All patients were seen at the diabetes centre by a diabetologist (or endocrine trainee) and a diabetes nurse at least four times each year, and more often if indicated. Between each medical review, patients were followed up by the diabetes nurse for blood taking, measurement of body weight and blood pressure, and reinforcement of self-care and treatment compliance. All laboratory results were available for medical review at the next visit for decision making.

Patients randomised into the UC group were managed according to the usual practice of the participating hospitals. Thus, patients might attend a diabetes clinic or a general medical clinic, usually at 3 to 4 monthly intervals. All clinical decisions or referrals for investigations or education were at the doctor's discretion.

# Results

The results of this study have been reported.<sup>4</sup> In brief, 24 of the 104 patients receiving SC and 24 of the 101 patients receiving UC reached the primary renal endpoint. After adjusting for age, gender, and study sites, the SC group had lower diastolic blood pressure ( $68\pm12$  vs  $71\pm12$  mm Hg, P=0.02) and HbA<sub>1c</sub> levels ( $7.3\pm1.3\%$  vs  $8.0\pm1.6\%$ , P<0.01) and was more likely to attain three or more treatment goals (61% [63/104] vs 28% [28/101]). Patients who attained three or more treatment goals (n=91) had 60% risk reduction in reaching the primary renal endpoint than those who did not (n=114) [14 vs 34; RR=0.43; 95% confidence interval, 0.21-0.86].

The clinical events and hospitalisation days in patients randomised to SC or UC group are summarised (Fig 1). Using Kaplan-Meier plots, the time to first clinical event (including death, renal and cardiovascular endpoints) is shown (Fig 2). The cost estimates for the SC and UC groups are shown (Table). The total number of hospital days during the 2-year study period was 933 in the SC group and 1169 in the UC group, with a difference in hospitalisation costs of HK\$631 300 (US\$80 935). In the SC group, 35 more patients attained multiple treatment targets, and there were four fewer composite renal endpoints and six fewer combined clinical endpoints than in the UC group. In a traditional medical model, each patient in the SC group would need eight extra medical consultations during the 2-year period incurring an extra cost of HK\$322 172 (US\$41 410) after deducting savings from hospitalisation costs. Based on these estimates, an additional yearly cost of HK\$2557 to 40 272 (US\$329 to 5176) would be required for a patient to attain multiple treatment targets or save one major clinical event. In this team-based model, we used trained nurses to review these patients which was cost-saving in a public health care setting, even if we factored medical input (eg 20% of a medical clinic visit) into the calculation.

#### Discussion

In this multicentre, randomised translational study, although we failed to show that SC was more effective than UC in reducing the renal endpoint, three times more patients in the SC group attained multiple treatment targets compared to the UC group. Patients who attained multiple treatment targets had 60% risk reduction in death and end-stage renal disease.<sup>4</sup> When the study was first conceived in 2000, the sample size was estimated using data available at that time.<sup>3,5</sup> In earlier studies conducted between 1997 and 2002 which recruited patients with similar characteristics, the incidence of the primary renal endpoint was 30 to 50% over a 2-year period. In the present study, a rate of 24% was noted for the primary renal endpoint in both the SC and UC groups. This suggests that increasing awareness of the beneficial effects of intensive risk factor control and inhibition of the reninangiotensin system had led to improvement in care standard



Fig 1. Recruitment, randomisation, and clinical outcomes of type 2 diabetic patients with chronic kidney disease

and reduced rates of clinical endpoints. The involvement of specialist care in the UC group in some of the hospitals might have reduced the effect size of SC. Furthermore, the lack of an audit to reinforce adherence to protocols and attainment of multiple treatment targets in the SC group might also explain the apparent failure to benefit in the SC group.<sup>4</sup>

The three-fold higher rate for attaining multiple treatment targets in the SC group translated to a lower mortality rate, fewer clinical events and hospitalisation days, which are all in agreement with other studies.<sup>1,2</sup> In an observational study of 6386 type 2 diabetic patients, attainment of two or more treatment targets was associated with 30 to 50% risk reduction in new onset of cardiovascular disease.<sup>2</sup> In the Steno-2 study, patients receiving multifaceted care were more likely to attain multiple treatment targets than those receiving usual care. This translated to 20 to 60% risk reduction in death, microvascular, and macrovascular complications.<sup>1</sup>

From a public hospital perspective, the additional costs incurred in the SC group were mainly due to extra clinic visits, laboratory tests, and drug costs. Taking into consideration of lower hospitalisation costs in the SC group, we estimated an additional yearly cost of HK\$2557 to HK\$40 272 (US\$328 to 5176) would have been needed to treat one patient to attain multiple treatment targets or save one clinical event if only doctors were used to manage these high-risk patients. In this team-based model, our patients were reviewed by trained nurses (supervised by a specialist) in the SC model which became cost-saving. In the United Kingdom Prospective Diabetes Study, the cost per quality-adjusted life year (QALY) for intensive blood glucose control with insulin or sulfonylureas was £6028 higher than for conventional treatment, whereas that with metformin in overweight patients was £1856 less than conventional treatment. The cost per QALY gained for tight blood pressure control was £369.6 According to the Centers for Disease Control in the USA, the incremental cost:effectiveness ratio for intensive glycemic control was US\$41 384 per QALY. On the other hand, intensified blood pressure control and reduction of serum cholesterol were cost-saving with US\$1959 and US\$51889 gained per OALY, respectively. These interventions were most costeffective when instituted early during the course of disease.7 In the Steno-2 Study, the incremental cost:effectiveness ratio for multifaceted care versus conventional treatment was €3927 and €2538 per life year and per QALY gained, respectively. These incremental costs were mainly attributed to increased pharmacy and consultation costs.8

There are multiple barriers in delivering SC at the levels of patients, care providers, and health care systems. In most clinical audits, <10% of type 2 diabetic patients attained three or more treatment targets (namely blood pressure, LDL-C, and HbA<sub>1c</sub>).<sup>9</sup> Apart from patient noncompliance, clinical inertia of physicians with delayed commencement



Fig 2. Kaplan-Meier plots showing the cumulative incidences of the (a) primary renal endpoint, (b) composite renal endpoint, and (c) combined endpoint during a 2-year period

Primary renal endpoint is defined as death or need for dialysis or serum creatinine level of  $\geq$ 500 µmol/L; composite renal endpoint is defined as primary renal endpoint or doubling of the serum creatinine level; and combined endpoint is defined as composite renal or cardiovascular endpoints

Table. Comparison of treatment costs between the structured ca	are (SC) and usual care	(UC) groups during a 2-year period
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Cost (HK\$)	SC (n=104)	UC (n=101)
Treatment costs		
No. of clinic review by doctors per year per patient	4	4
Extra No. of clinic review by nurses per year per patient	4	0
Cost of each clinic review by doctors (Hospital Authority statistical report, 2004-5)	1146	1146
Cost of each clinic review by nurses (estimated 50% of above)	573	-
Additional costs		
Extra cost of nurse review per patient (573×4 visits×2 years)	4584	0
Total extra cost of nurse visits in 2 years (4584×104 patients)	476 736	0
Assuming all additional visits are medical consultations (1146×8 visits×104 patients)	953 472	-
Hospitalisation costs		
Mean/median (IQR) days of hospitalisation per patient	8.97/2 (0-10)	11.57/2 (0-15)
Total days of hospitalisation of the whole arm	933	1169
Cost per hospitalisation day (Hospital Authority statistical report 2004-5)	2675	2675
Total cost spent on hospitalisation	2 495 775	3 127 075
Cost saving in SC group (if extra visits by nurses)	-154 564	-
Extra cost in SC group (if extra visits by doctors)*	322 172	-
Clinical outcome		
No. of patients attaining ≥3 treatment targets	63	28
No. of patients reaching composite renal endpoint (death+need for dialysis+doubling of serum	24	28
creatinine level)		
No. of patients reaching combined endpoint (death+cardiovascular-renal endpoint)	31	37

During a 2-year period, extra cost needed to (1) treat one patient to attain multiple treatment targets (35 more patients in SC group): HK\$322 172÷35=5114,
 (2) prevent one composite renal endpoint (four fewer endpoints in SC group): HK\$322 172÷4=80 543, and (3) prevent one combined endpoint (six fewer endpoints in SC group): HK\$322 172÷6=53 695

or escalation of therapy might also reduce the likelihood of achieving multiple treatment targets.<sup>10</sup> To this end, our results strongly support the cost-effective nature of using a doctor-nurse team to implement structured care. Increasing the sample size, lengthening the follow-up period and introducing an audit system to improve protocol compliance and attainment of multiple treatment targets will be necessary to confirm these encouraging findings.

## Conclusions

In this 2-year study, although type 2 diabetic patients treated with SC had a similar incidence of death or end-stage renal disease as those treated with UC, they were more likely to attain multiple treatment targets and had reduced hospitalisation rates. Given the silent nature of diabetes and the complex nature of care protocols, an integrated and team-based approach (including early diagnosis, risk stratification, use of protocol with predefined targets and management plans, and decision support) further augmented by regular feedback and patient empowerment is needed to achieve favourable outcomes.

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