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IS SCREENING FOR MICROALBUMINURIA IN TYPE 2 DIABETIC PATIENTS FEASIBLE IN THE PUBLIC SECTOR PRIMARY CARE CONTEXT: A COST AND CONSEQUENCE STUDY IN ELSIES RIVER COMMUNITY HEALTH CENTRE.

In partial fulfillment of the MMed degree in Family Medicine.

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Declaration:

I, hereby declare that the work contained in this research assignment is my original work and that I have not previously submitted it at any university for any degree.

Signature:
Date: 26 August 2011

Abstract

Background: The epidemic of type 2 diabetes poses an enormous and growing burden on health care globally. While the prevalence of diabetes is increasing worldwide, the developing countries will bear the greatest burden of this disease. Diabetes is one of the most common causes of kidney failure and nephropathy is a strong predictor of cardiovascular complications and death in these patients. Microalbuminuria represents a latent and early pre-symptomatic phase of nephropathy which can be stopped from progressing to an advanced stage if detected and treated early. The cost effectiveness of this screening and intervention has been researched and proven in the developed world, however similar studies in developing countries are non-existent. Microalbuminuria is not currently tested for in the public primary care sector.

Aim and objectives: The aim was to assess the feasibility of introducing a screening test for microalbuminuria and the associated costs and consequences at Elsies River Community Health Centre (CHC) in the Metropolitan District of Cape Town. The objectives of the study are to assess the feasibility of implementing the test in our context, to assess any additional cost to the health services, to assess any measurable benefits in the quality of care for the patients, to extrapolate the likely long term consequences in terms of health outcomes, use of resources and costs and to make a policy recommendation to the Department of Health.

Method: A cost and consequence study that describes the introduction of microalbuminuria testing in a cohort of type 2 diabetic patients at Elsies River Community Health Centre, Metro District Health Services, Cape Town, South Africa. Point of care status analyser microalbuminuria screening was introduced to the CHC after training of the chronic care team, and their fidelity to the protocol measured. All patients who met the inclusion criteria were screened. Patients whose first results were abnormal had a repeat test after 3-6 months, if both results were abnormal patient was diagnosed microalbuminuria positive, however a patient with a second normal result required a third test. Interventions included addition of an Angiotesin Converting Enzyme inhibitor to their treatment, more intensive glycaemic, blood pressure or lipid control via medication or lifestyle changes and treatment adherence health education. Field notes were taken by the researcher during visits and a recorded focus group interview conducted with the health workers to explore their views on the feasibility of the screening and intervention. Cost was assessed by the estimation of the

additional resources required and the likely long term health outcomes extrapolated from available data and literature.

Results: 15.2% of the sample population was noted to be microalbuminuria positive and they all received interventions. Additional cost required to screen a cohort of 100 patients was R1,109.40 per annum, out of which 15 patients at risk of developing nephropathy were identified and the cost of treating these patients was R1,393.20 for the first year. Qualitative data revealed that the test and interventions are feasible with an additional cost of staff time, medication and other materials which have been included in the cost above.

Conclusion: This study represents the first attempt to successfully introduce screening for microalbuminuria in our public primary health care context. The chronic care team showed reasonable fidelity to the protocol and demonstrated the feasibility of screening and treating patients. The balance of costs and long term benefits suggests that this represents excellent value for money in a South African primary care setting.

Introduction and background

The epidemic of type 2 diabetes poses an enormous and increasing burden on health care globally.(1) It is estimated that the number of people with type 2 diabetes worldwide will rise from 151 million in the year 2000 to 300 million by the year 2025.(2) Of particular concern is that most of the increase will occur in the developing world where the resources are scant and limited to deal with the problem.(1)

Complications associated with diabetes are devastating to patients and lead to increased morbidity and mortality as well as premature death. Adults with diabetes have an annual mortality that is double that of their non-diabetic counterparts.(3) Diabetes is recognised as a major risk factor for cardiovascular and neurological complications that manifest as visual loss, leg ulcers, amputation, atherosclerosis, myocardial infarction, thromboembolism and stroke.(4)

Diabetes is essentially a metabolic disease associated with the development of chronic kidney disease and cardiovascular complications. According to the World Health Organisation (WHO), about 50% of patients with diabetes mellitus will die from cardiovascular disease.(5) Well recognised is the significance of proteinuria as a risk marker for progressive deterioration in

kidney function.(6) The link between proteinuria or early kidney disease as an independent risk factor for cardiovascular morbidity and mortality has been established by meta-analysis of 22 separate general population, cohort studies in older (>65) and younger people of different nationalities and races.(7) Early intervention can reduce chronic kidney disease progression and cardiovascular risk by 50% and consequently improve quality of life.(6)

Microalbuminuria, defined as an increase in urinary albumin levels to between 20 and 200mg/L, represents elevated levels of urinary albumin that cannot be detected with standard urine dipstix analysis and is a reliable tool to identify and recognize early kidney damage.(8) Early screening and detection or diagnosis of microalbuminuria can lead to effective interventions to prevent progression and complications, particularly nephropathy and cardiovascular end points.(9) Detection of macroalbuminuria defined as urinary albumin levels above 200mg/L however is often too late to make as effective an intervention as nephropathy is already established.(9) It is of significant note that microalbuminuria (albumin excretion of 30-300mg/day), unlike macroalbuminuria (albumin excretion of >300mg/day), is not considered to be synonymous with the presence of kidney disease as has been noted in recent analysis, because microalbuminuria is reversible if diagnosed and correct interventions commenced.(10,11) Microalbuminuria was found to be associated with carotid atherosclerosis in middle aged individuals, and has been shown to predict cardiovascular outcome in older individuals.(12) The Heart Outcomes Prevention Evaluation study, demonstrated that even a small increase in albuminuria increased the risk of cardiovascular events.(13)

Currently public sector health centres in Africa only test patients for macroalbuminuria even though all the national, regional and international guidelines recommend testing annually for microalbuminuria.(14,15,16) The District Health Services have struggled to provide an adequate standard of care for diabetic patients and there have been doubts as to whether microalbuminuria testing is both feasible and affordable in our context.(17,18) This study therefore aims to explore the feasibility and costs of introducing the test at Elsies River Community Health Centre and to provide practical information for a policy decision on this issue.

The World Health Organisation (WHO) principles of screening for disease which were published over four decades ago are excellent guiding principles for the introduction of a screening test and they are discussed in relation to diabetes and microalbuminuria

as follows:

Diabetes is a common and important disease in our setting.

There are no current or very recent national prevalence statistics for diabetes available in South Africa neither are there current information on the numbers or outcomes of patients with diabetic nephropathy. However based on the available epidemiological data, approximately 1-1.5 million South Africans are considered to have diabetes.(4) The South African National Burden of Disease Study reported that diabetes was the tenth leading cause of death among persons of all ages in 2000, accounting for an estimated 13,500 deaths (2.6% of the total).(4) In Cape Town up to 11% of the adult population is thought to be diabetic.(19)

Nephropathy can be detected and prevented in a sub-clinical stage

Nephropathy develops gradually in diabetic patients over a period of years. There is an early sub-clinical latent phase with the development of microalbuminuria being the first sign. After this the patient develops macroalbuminuria, which is a sign of more established disease and consequently patients may have a raised creatinine and low glomerular filtration rate. The patient is then likely to progress to a more advanced stage of kidney damage which may become chronic and eventually develop into end-stage renal failure.(20) Microalbuminuria is a sign of more widespread endothelial dysfunction and is also a predictor of complications elsewhere.(21)

Microalbuminuria has been shown to be a strong predictor of progression to advanced stages of nephropathy, but can also regress with intensive blood glucose control, reduced serum lipids and lowered systolic blood pressure. In addition to the prevention of development of microalbuminuria, renal outcomes are improved after development of microalbuminuria with excellent control of glycaemia and blood pressure, even without the use of a Renin Angiotensin Aldosterone System (RAAS) inhibitor.(22) Angiotensin Converting Enzyme (ACE) inhibitors are particularly effective at reducing blood pressure and improving endothelial function with a reduction in albumin excretion.(16,23) The HOPE and the micro-HOPE studies showed that the reduction in microalbuminuria with ACE inhibitor Ramipril improved cardiovascular outcomes.(24,25) Effective inhibition of RAAS is demonstrated to provide renal protection in patients with type 1 and type 2 diabetes.(26) Systematic reviews showed that treatment with ACE inhibitors provide

significant reduction in albumin excretion rate in type 1 and type 2 diabetes. It was also shown that albumin excretion was reduced in normotensive diabetic patients and an increase in blood pressure was also prevented in the patients.(16)

The potential benefits in terms of prevention outweigh the potential harms of ACE inhibitors in terms of adverse side effects, such as angio-oedema or anaphylaxis.(27)

Microalbuminuria can be reliably detected in primary care

Urinary albumin levels follow a circadian rhythm and are affected by many factors. A single positive test may be due to vigorous exercise in the last 24 hours, a fever, heart failure, urinary tract infections, prostatitis (in men) or even menstrual contamination (in women) and therefore a diagnosis of microalbuminuria is based on 2 positive tests on 2-3 separate occasions 3-6 months apart.(28) Results of a meta-analysis, comparing albumin-creatinine ratio in a random specimen to albumin excretion rate from a 24 hour sample; showed that the benefit of a 24 hour collection is small and not worth the cost and inconvenience.(28,29) Albumin measurement in a first morning urine are more reliable and more correlated with 24 hour protein excretion than measurement in a random spot urine sample for the diagnosis and monitoring of microalbuminuria.(28,32) Alternative methods of screening include timed (4 hour or overnight) urine collection, however the National Kidney Foundation guideline stated that it is usually not necessary to obtain a timed urine collection for evaluation of microalbuminuria, albumin should be measured in a spot urine sample using either an albumin specific dipstix or urinary albumin to creatinine ratio.(28-30)

Several investigators and guidelines have advocated use of separate albumin creatinine ratio (ACR) cut off points for the detection of microalbuminuria in men and women of different racial groups.(33,34) This is because urine creatinine concentrations differ between men and women and between racial groups. Future research studies that use the ACR to define microalbuminuria should use sex specific ACR cut offs to help avoid the potential problems of underestimating microalbuminuria in subjects with higher urine creatinine excretion (e.g men) and overestimating microalbuminuria in subjects with lower urine creatinine excretion (e.g. women).(35) Microalbuminuria is hereby defined to be 17-250mg/g or 2.5-25mg/mmol and 25-355mg/g or 3.5-35mg/mmol in spot urine albumin-creatinine ratio in male and female patients respectively.(36) Screening for microalbuminuria has a sensitivity of 76% and a specificity of 96%.(37) However sensitivities and specificities range between

69-96% and 41-97% respectively.(28)

Microalbuminuria test is acceptable to the population

The national kidney foundation(38) recommends the use of spot urine specimens obtained under standardised conditions (first voided morning midstream urine) to detect microalbuminuria and this may require the patient to collect the specimen bottle from the hospital and carefully collect the specimen at home and bring to the hospital on the day of visit. This is cumbersome, can be potentially unacceptable to patients and lead to poor compliance. Taking into consideration convenience, accuracy and cost, the measurement of urine albumin concentration in a random urine sample is the best choice for microalbuminuria screening in diabetic patients.(39) This makes the screening simple and readily acceptable to the patients as the specimen collected for the routine macroalbuminuria dipstix can be used for the microalbuminuria test.

Microalbuminuria testing is cost-effective elsewhere

Intensive treatment of microalbuminuria may stop chronic progression to end stage renal impairment and consequently reduce associated renal and cardiovascular morbidity and mortality with a potential decrease in overall costs of management.(41) Cost-effectiveness of screening for microalbuminuria has been researched in USA and Europe. Optimized treatment is associated with increased life expectancy, quality-adjusted life years and lifetime costs compared to conventional treatment. It has been shown that though it is more expensive to provide more intensive treatment, in the long run, it saves money on treating renal and cardiovascular complications, prolongs life and improves quality of life. Looking at the direct medical costs for intervention and control groups, it was projected that the cost was higher for intervention group. However, breakdown of costs revealed that incremental costs for the intervention group were less than those for the control group for all complications and interventions, despite patients living longer in the intervention group. The study showed that optimized treatment was cost-effective compared to conventional treatment.(9,42-44) The other alternative to screening for microalbuminuria and treatment of positive patients is the routine prescription of ACE inhibitor but it has been shown to be more costly than screening for microalbuminuria, albeit it is also cost effective as it increased Quality Adjusted Life Year (QALY) and life expectancy.(43)

Testing for nephropathy with microalbuminuria therefore meets all of the WHO criteria for secondary prevention which include the following:

- Diabetes with diabetic nephropathy and cardiovascular complications is an important and common health problem.
- There is a recognizable latent or early pre-symptomatic phase.
- The natural history of the condition, including the development from latent to advanced disease is adequately understood.
- There is a suitable test to detect the condition during this latent or pre-symptomatic phase.
- No further diagnosis is required other than ensuring 2 out of 2-3 tests are positive.
- The test is acceptable to the population.
- There are effective interventions to treat the condition and prevent the development of nephropathy.
- Early detection and treatment improves the final outcome.
- The intervention has been shown to be cost-effective in other settings.

The only remaining issues, which this study addressed, are whether it is feasible or practical in our public sector primary care setting and whether it is affordable.

Aim

The aim of this study was to assess the practicality of introducing a screening test for microalbuminuria and the associated costs and consequences at Elsies River Community Health Centre (CHC) in the Metropolitan District of Cape Town.

Objectives

- To assess feasibility of implementing the test in our context (i.e. can it be done within existing staffing levels and organization of care?)
- To assess any additional cost to the health services (i.e. staff time, resources, equipment, changes in medication)
- To assess any measurable benefits in the quality of care for the patients
- To extrapolate the likely long term consequences in terms of health outcomes, use of resources and costs
- To make a policy recommendation to the Department of Health

Study design

A cost-and-consequence or cost and outcome study that describes the implementation of microalbuminuria testing on a cohort of type 2 diabetic patients in public sector CHC and evaluates the consequences for quality of care and the immediate costs involved. This can also be regarded as translational research – evaluating the implementation of evidence in clinical practice.

Setting

The study is part of a bi-centre study which is being conducted in the Metropolitan District of the City of Cape Town, South Africa. Elsies River CHC serves large numbers of diabetic patients from the uninsured population of Cape Town. Patients are mostly from low socio-economic backgrounds and historically disadvantaged black Xhosa speaking and coloured Afrikaans or English speaking communities. The other centre was Kraaifontein CHC which involved another MMed student who will report in a separate research assignment.

Elsies River CHC runs diabetic "clubs", on two days each week, Mondays and Thursdays, when diabetic patients are seen for review. Patients are seen 3 to 6-months depending on their glycaemic control. The diabetic clubs are run by teams of primary care providers (typically several nurses, 2 clinical nurse practitioners, a pharmacist and a health promoter), under the supervision of the family physician. The diabetic clubs are meant to perform the following tests and activities routinely on every patient:

- Weight (every visit)
- Body mass index (annually)
- Blood pressure (every visit)
- Urinalysis (every visit)
- Random capillary glucose (every visit)
- HbA1c (annually)
- Cholesterol (annually)
- Visual acuity and fundoscopy (annually)
- Foot screening (annually and if at-risk every visit)
- Education (every visit)

Sampling procedure

A disease register of all the diabetic patients attending the facility over a 6-month period was created and 581 patients were registered. Although the test was offered to all eligible type 2 diabetic patients, a representative sample of 171 patients was

randomly selected from the disease register of 581 numbered patients using random numbers generated in an excel spreadsheet, to evaluate the screening process and this resulted in a 95% confidence interval that has a width/accuracy of 7.5% points. The records of all patients who screened positive for microalbuminuria from the total diabetic population of 581 were used to assess the implementation of interventions.

The screening test, training and interventions

Equipment for screening of microalbuminuria consisted of a point-of-care portable diagnostic machine (Status Analyser) and urine testing strips. Equipment and strips were donated by Siemens Medical Diagnostic Solutions. According to the manufacturer, the status analyser machine has a specificity of 98.2%, sensitivity of 96.9% and the equipment calibrates itself automatically at intervals with a lifespan of about 5 years on average.

The chronic care team was trained in the use of the equipment and how to interpret and act on the results. The researcher did help the team to plan a realistic organizational framework for testing, interpreting, recording and acting on the results at the clinic level. A standard operating procedure (SOP) was constructed for performing, interpreting and reacting to the test, full details are given in appendix 1.

The routine urine dipstix for protein (macroalbuminuria) was done for each patient at the clinic. If negative, urine testing for the albumin:creatinine ratio (microalbuminuria) was then performed using the Status Analyser.
If the ratio was normal, the test was repeated after one year.
If the ratio was abnormal, a repeat urine test was performed at the second visit (when the patient next returns for a routine visit after 3-6 months as the case may be) and if the second test was negative a third test was performed at the third visit.
Single testing is not reliable, but with multiple testing, reliability is improved to 98%. False positives may be seen in those with recent (last 24 hours) vigorous exercise, fever, heart failure, urinary tract infection, prostatitis (in male) and menstruation (in female, patients in these categories were excluded from the screening. The possibility of false positives is accounted for by repeated testing.
It may take 3-6 months to perform the two tests and 6-12 months to perform all three tests, if this was necessary, as patients only attend every 3-6 months.
If there was an abnormal result in two out of the three tests then the result for microalbuminuria was said to be positive and

this implies early renal disease. The clinic staff then attempted to improve overall diabetic control (glycaemia, lipids, weight, blood pressure). In particular the blood pressure should be reduced to the target of <130/80mmHg. If the patient was not on an ACE inhibitor this was started by the doctor or CNP. If the patient was already on an ACE inhibitor the need to increase the dose was considered. These interventions are in line with the published national and international guidelines for evidence-based practice and are not regarded as experimental.(6,9).
Those who tested positive should have a repeat test after receiving the interventions for at least 12-months.

The results of the microalbuminuria tests were recorded in a test register which was kept with the Status Analyser machine (Name, folder number, date and result of 1st, 2nd and 3rd tests), and the original result slip taken by the patient to the club room where it was attached to the chronic diseases summary sheet in the patient's folder by the staff nurse. Testing was performed in the preparation room by a nurse and patients who tested positive for microalbuminuria were further managed by the clinical nurse practitioner (CNP).

At the beginning, on-going support and supervisory visits by the researcher were done weekly (for one month) and then two-weekly (for two months). Once testing was established the researcher only visited monthly and as required. At these visits the researcher received feedback on the feasibility of performing, interpreting and responding to the test from the clinic staff and ensured that the protocol was being correctly followed.

Assessment

The disease register and the test register were used to select patients for different aspects of the assessment.

Structural, process and outcome criteria were developed to monitor changes in the quality of care following the introduction of the test. This was to enable an assessment of how well the screening was implemented as well as the likely consequences in terms of additional resources used or required. Patients included in the study were followed up over the study period. A representative random sample selected from the disease register was used to evaluate the process and outcome criteria. Structural criteria were evaluated by the researcher at each clinic visit. Data was also recorded to give a profile of the diabetic patients.

Structural Criteria

- SOP is in place for microalbuminuria testing
- Microalbuminuria machine is in working order
- Microalbuminuria testing strips available
- Printing paper roll available
- ACE inhibitor in stock

Process criteria:

- % of patients tested for macroalbuminuria
- % of patients tested for creatinine
- % of patients tested for HbA1c
- % of patients tested for cholesterol
- % of patients tested for microalbuminuria
- % of patients with a positive first test
- % of patients with a positive first test receiving a second test
- % of patients with two tests (one negative / one positive) receiving a final test
- % of patients with final results clearly recorded in the folder

Outcome criteria:

- % of patients with macroalbuminuria
- % of patients with microalbuminuria

Profile criteria:

- Age and sex
- % of patients with increased creatinine (>107mmol/l in Female & >115mmol/l in male)
- % of patients with raised cholesterol (>5mmol/l)
- % of patients with raised HbA1c (>7%)
- Mean creatinine amongst those with no albuminuria, macroalbuminuria and microalbuminuria
- Mean HbA1c amongst those with no albuminuria, macroalbuminuria and microalbuminuria
- Mean systolic BP amongst those with no albuminuria, macroalbuminuria and microalbuminuria
- Mean diastolic BP amongst those with no albuminuria, macroalbuminuria and microalbuminuria

All those who tested positive for microalbuminuria were identified from the testing register and their folders examined to record information on the interventions that they received for the prevention of nephropathy and associated cardiovascular

complications.

- % of patients with a final positive test result not on Angiotensin Converting Enzyme Inhibitor (ACEI)
- % of patients with a final positive test receiving ACEI for the first time
- % of patients with a final positive test already on ACEI
- % of patients with a final positive test already on ACEI who have the dose increased
- % of patients with a final positive test result receiving other additional treatment (dose increase or new medication)
- % of patients with a final positive test result receiving additional health education or lifestyle advice

The regular meetings with the chronic care team was recorded and used as qualitative data on the feasibility of introducing the screening test.
The researcher also directly observed the screening process and noted any key positive or negative aspects of performing the test (i.e. time taken, mistakes made…). A focus group interview was held with the chronic care team at the end of the study period to explore their experience of using the new test. The interview was recorded, transcribed verbatim and then analysed as part of the qualitative data. Participants in the focus group interview were 8 in total, excluding the researcher; doctor (n=1) Clinical Nurse Practitioners (n=2), staff nurses (n=2), nursing assistants (2) and volunteer (n=1). The family physician directly supervises the CNPs on management and intervention, one of the staff nurses work in the club room sorting out the club patients, the other nurses work at different times in the preparation room while the volunteer (student of public health at the University of the Western Cape) helped with data collection most especially folder review. The length of the interview was 50 minutes and it was conducted in the quiet club room after the day's work.

The assessment of cost included the following data, which was reported on, in terms of additional costs required to test and treat 100 patients for a year:
Status analyzer
Testing strips and paper required to test all patients 1-3 times
Additional medication used per month
Additional staff time in minutes.

The cost of identifying one person with microalbuminuria can also be calculated by dividing the cost of all the tests done by the number of diagnosed patients.

Data analysis
MS Excel was used to capture the quantitative data and STATISTICA version 8 (StatSoft Inc. (2008) STATISTICA (data analysis software system), _ HYPERLINK "http://www.statsoft.com" _www.statsoft.com_.) used to analyse the data with the help of the Centre for Statistical Consultation.

Summary statistics were used to describe the variables. Distributions of variables was presented with histograms and frequency tables. Means were used as the measures of central location for ordinal and continuous responses and standard deviations and quartiles as indicators of spread.

The relationships between continuous variables and nominal variables were analysed using analysis of variance (ANOVA). A p-value of $p < 0.05$ represented statistical significance in hypothesis testing and 95% confidence intervals were used to describe the estimation of unknown parameters.

Recording of the team meetings were analyzed qualitatively using the framework approach and key themes relating to the feasibility and organization of care reported.(45)

Extrapolation
The likely impact of testing on secondary and tertiary level of care were extrapolated from the analysis. The likely long term costs and benefits in terms of testing, medication, preventing renal failure, avoiding dialysis, transplantation and hospital admissions were extrapolated using the literature and also based on a hypothetical cohort of 100 patients.

Ethical consideration

Relevant ethical issues for the study were:

Permission: Ethical approval was obtained for the bi-centre study from the Health Research Ethics Committee of the Faculty of Health Sciences, University of Stellenbosch. The Western Cape Provincial Health Department granted permission for the study to be conducted in the two CHCs and the facility manager of Elsies River CHC permitted this study in her facility.

Informed consent: Screening for microalbuminuria is already recommended by our national guidelines and therefore providing the test was aligned with normal and accepted standards of care and was in essence an expected improvement in the quality of care, it was not an evaluation of a new diagnostic test or a new

treatment. Therefore informed written consent for an experimental intervention from the patients was not necessary. No additional data was collected from patients beyond the usual clinical requirements and no patient identifiers were used in the analysis by the researchers. Clinic staff were required to explain the test to patients and obtain the usual level of verbal consent that is customary for a diagnostic test and the usual medical record. As with any diagnostic test patients could refuse.

Written informed consent was obtained from the chronic care staff, who participated in the process and the interviews, details in appendix 2.

Confidentiality: The disease register and testing register were kept and maintained by staff in the CHC and only used to sample patients. Data collection and subsequent analysis did not include any patient identifiers. Qualitative data from the chronic care staff were reported anonymously and names were excluded from the transcripts.

Staff training: The adequate training of staff in performing the test, interpretation of the test, deciding on appropriate interventions and explanation of the test result to patients were of ethical necessity. The researcher provided training to everybody in the chronic care team. A SOP was provided for all these steps.

Benefits and harms: Patients in the study benefited from a higher quality of care and possible prevention of chronic renal failure and cardiovascular complications. Patients might have been more motivated to engage with self-care activities as a result of the testing. Possible harms include false positive results leading to unnecessary interventions and worry regarding the possibility of renal disease. However the interventions to improve control of diabetes would be indicated even without a positive result. Patients who had adverse reactions to ACE inhibitors that were started or increased, as a result of the test may experience harm. As ACE inhibitors were already widely used amongst diabetic patients these risks were not more than those faced by other diabetic patients.

Conflict of interest: The status analyser equipment and packet of test strips donated by Siemens were used in the research project without fear or favour and the donation did not constitute any conflict of interest whatsoever.

Results

Assessment of screening process

This was based on a randomly selected sample of 171 patients from the 581 patients in the disease register. Out of these patients 42 (24.6%) were male and 129 (75.4%) were female. Their mean age was 59.9 years and the distribution of age is shown in Figure 1.

Figure 1: Age distribution of study sample (n=171)

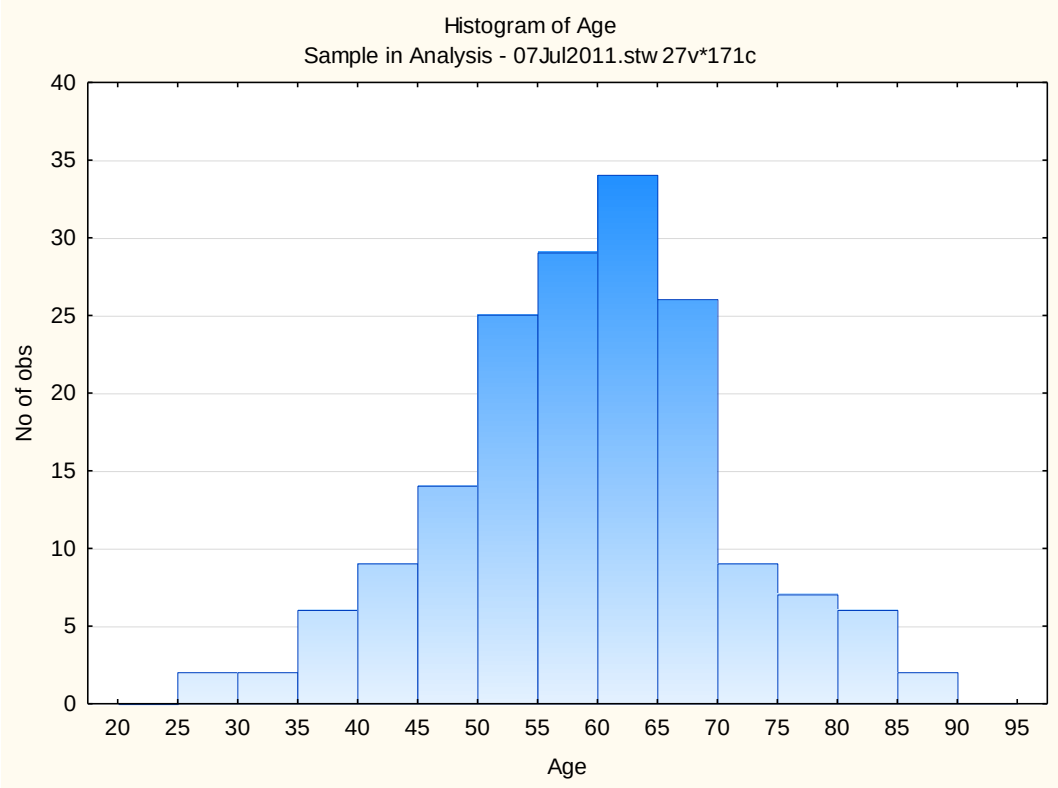

Table 1 below presents a profile of key diabetes indicators in this diabetic population.

Table 1: Profile of key diabetes indicators (N=171)

Indicators	**N**	**%**
Patients tested for HbA1c	99	57.9
Patients with raised HbA1c (>7%)	81	47.4
Patients tested for creatinine	113	66.1
Patients with raised creatinine	21	18.6
Patients tested for cholesterol	110	64.3
Patients with raised cholesterol	63	36.8
Mean Systolic Blood Pressure (mmHg)	146.0	
Mean Diastolic Blood Pressure (mmHg)	86.0	

Overall 20 patients (11.7%) were noted to have macroalbuminuria and an additional 26 patients (15.2%) were diagnosed with microalbuminuria. Key indicators that describe the screening process are shown in Table 2.

Table 2: Indicators of the screening process (N=171)

Indicators	**N**	**%**
Patients tested for macroalbuminuria	171	100.0
Patients tested for microalbuminuria	151	88.3
Patients with positive first test	57	33.3
Patients with positive first test receiving a second test	35	20.5
Patients with 2 tests(one negative/one positive) receiving a final test	3	1.8
Patients with final results clearly recorded in the folder	171	100.0

All patients were tested for macroalbuminuria and the number of patients tested for microalbuminuria was the total number of those eligible for the test 151/151 (100%), as the 20 patients with macroalbuminuria did not need to be tested. Of those who had a positive first test 35/57 (61.4%) received the necessary second test. This implies that 22/57 (38.6%) of patients were not screened completely at this stage. Ten patients were found to have an abnormal first test and a normal second test of whom 3/10 (30.0%) received the necessary third test. Overall therefore 25/57 (43.8%) of patients with an initial abnormal result did not complete the screening process.

Table 3 below shows the comparison of key diabetic indicators among patients with normal results, macroalbuminuria and microalbuminuria. There were no significant differences in diabetic indicators among the three groups, although the study was not designed to make this comparison.

Table 3: Comparison of key diabetic indicators among those with normal results, macroalbuminuria and microalbuminuria

Profile	**Normal**	**Macro.**	**Micro.**	**P-values**
Mean creatinine	78.8	100.9	91.8	**0.8720**
Mean HbA1c	9.3	8.5	8.4	**0.3868**

Mean systolic BP	145.5	144.5	150.1	**0.8964**
Mean diastoloic BP	86.0	84.3	82.5	**0.7327**
Mean cholesterol	5.2	5.4	4.8	**0.7534**

Abbreviations: Macro = macroalbuminuria; Micro = microalbuminuria.

The key results for the structural criteria are shown in Table 4 below. Altogether structural criteria were evaluated at 25 visits made to the facility during the study period. The result of the structural assessment were close to perfection, except for the status analyser machine that was reportedly faulty for a short period, only for the technician to discover that it was the newly inserted wrong size paper that was responsible.

Table 4: Results for the structural criteria (N=25)

Structure	**Frequency (n)**	**%**
SOP in place for microalbuminuria screening and intervention	25	100.0
Microalbuminuria machine in working order/calibrated	24	96.0
Microalbuminuria testing strips available	25	100.0
Microalbuminuria results printing paper available	25	100.0
Angitensin Converting Enzyme Inhibitor (Enalapril) in stock	25	100.0

Abbreviation: SOP=standard operating procedure

The researcher observed during these visits that each test took an average of two minutes to do, while it took another 2-3 minutes to record each result for the purpose of the study in the test register. The original results were then taken by respective patients to the club room. It took only a few seconds for the staff nurse in the club room to staple the original result to the chronic care summary sheet in the patient's folder.

Assessment of intervention in patients with microalbuminuria

A total number of 74 patients were diagnosed with microalbuminuria as recorded in the test register. The interventions received by this group as a direct result of the diagnosis are described in Table 5. Data for two patients were

unavailable as one patient died and the other patient's folder was missing.

Table 5: Frequency of interventions on those who tested microalbuminuria positive (N=72)

Intervention	Frequency(n)	Percentage(%)
Patients with final positive test result not on ACEI	7	9.7
Patients with final positive test receiving ACEI for the first time	36	50.0
Patients with final positive test already on ACEI	29	40.3
Patients with a final positive test already on ACEI who had the dose increased	28	38.9
Patients with final positive test result receiving other additional treatment(dose increase or new medication)	23	31.9
Patients with final positive test result Receiving additional health education or lifestyle advice	40	55.6

The table shows that the opportunity to initiate ACEI was missed in 9.7% of patients, while the benefits of ACEI were increased in 88.9% of patients.

Cost analysis

From the screening sample of 171 the total number of tests performed was 189. The total time spent in performing 189 tests and in identifying 26 positive patients was estimated as 378 minutes. The cost of the intervention was based on the cost of additional medication and the staff's extra time spent on education. It was estimated that 200 minutes in total (5 minutes per patient) was spent in educating the 40 patients. The cost of the analyser and strips to the public sector were quoted from the manufacturer as of May 2011, while the cost of the paper was

the retail cost as of August 2011. The cost of the staff time was based on the salary scale of full time clinical nurse practitioner (for education) and staff nurse (for testing) grade one, notch one (new OSD salary notches/total 'CTE' packages on 1 July 2010) while the cost of additional medication was based on the cost as purchased by Metro District Health Service (MDHS) in August 2011. The amount and cost of the additional medication for the 72 patients diagnosed from the total disease population is shown in Table 6.

Table 6: Additional prescriptions and costs per month

Medication	Dose started or added	Cost per month (rands)	Number of prescriptions	Total cost (rands)
Enalapril	5mg BD	4.96	35	173.60
	10mg BD	5.36	27	144.72
	15mg BD	10.32	2	20.64
Amlodipine	5mg	2.99	2	5.98
	10mg	4.99	2	9.98
Hydrochlorothiazide	12.5mg	2.26	2	4.52
Gliclizide	40mg BD	5.66	3	16.98
Metformin	850mg	3.96	3	11.88
Protophane	10 Unit	24.55	2	49.10
	2 Unit	1.60	2	3.20
Simvastatin	10mg	3.94	9	35.46
			Total	476.06

Table 7 summarises the additional costs of the screening process based on the 171 patients sampled and the actual performance achieved in this health centre. It was assumed that the analyser would last for a period of five years before replacement and during this study a total of 581 patients were screened over a 12 months period. The proportion of the cost for 171 patients could therefore be calculated.

Table 7: Cost of screening process

Item	Cost
Portion of capital cost of analyser	901.00
189 test strips	949.54
Rolls of printing paper for analyser	4.50
378 minutes of staff nurse time for screening	68.04
Total cost to screen 171 patients	1923.08
Total cost to screen 100 patients	1124.61
Total cost to identify one patient with microalbuminuria	73.96

Table 8 summarises the additional costs of the intervention for the first month. This was based on the 72 patients diagnosed in this study and according to the level of performance obtained in this health centre. It was assumed that additional health education took on average 5 minutes and was given by a clinical nurse practitioner.

Table 8: Cost of the interventions

Item	Cost (Rands)
Cost of additional medication	476.06
200 minutes of CNP time for education	81.26
Cost of intervention for 72 patients	557.32
Cost of intervention for 100 patients	774.06
Cost of intervention for 1 patient	7.74
Cost of intervention for 1 year per patient	80.50

Qualitative Data Analysis

The staff needed to be motivated before the screening process could take off and the first few weeks of the study was eventful as a lot of mistakes were made in performing the test, but this was largely due to repeated replacement of the staff nurses in the preparation room with new nurses that warranted repeated training of the nurses. It ended as an advantage as many nurses in the facility became more aware of the programme and some of them became expert in the process and later helped in training others. However some patients were missed because patients threw away their urine specimen while the nurse was busy with their dipstix macroalbuminuria test as clear instructions were not given by the nurse. Individual meetings of the researcher with every member of the chronic care team, collaboration with the family physician at the facility and the power point presentation at the start of the research served as strong motivation to the staff of the CHC. By the end of the first month the team adapted the screening to their daily routine to the extent that it was difficult to convince them to stop the process at the end of the research period. The CNPs involved with the interventions were the most motivated, they used their cell phones to call me sometimes when they needed to seek clarification on certain aspects of the management especially

when the only patient with intolerable cough due to Enalapril presented to the facility.

The following themes were derived from the focus group interview and regular meetings with the chronic care team.

1a: Ease and feasibility of doing the test

Respondents reported that the test was easy to do and could be introduced into the primary care practice. They appreciated the benefits the patients will derive from the introduction of this test:
"I think it is feasible, to prevent renal failure in the long term. To pick it up if there is any protein in the urine or not, so the doctor can start immediately with treatment on the patient."
"I think to the people that are involved in this whole exercise it is feasible, there is no doubt about it because even the ones who have come so far you can see the result for yourself and overall it's the patient that will benefit."

1b: Ease and feasibility of interpreting and acting on the result

The respondents involved with interpretation and intervention also recognised the importance of introducing the test and so they also believed that it was easy and feasible:
"It's actually very easy because the patients know themselves that if they are diabetic their heart and their kidneys are at stake, so it's much easier to explain it to them that this treatment is something that will prevent them to get into renal failure in the future. Most of them do understand it and it's only a few patients, a little number that are negative towards it."

2a: Time required for carrying out the test

Participants in the preparation room did spend significantly more time on patients who are eligible for the test and this is quantified as five minutes which was inclusive of time spent in documenting the result in test register for the purpose of the study:
"It takes about 5 minutes, may be less but let's keep it at 5 minutes."

2b: Time required for interpreting and acting on the result

CNPs believed the time spent acting on the positive result was small and did not significantly increase their work or constitute a burden:
"I am coping and it's only a few extra minutes with each patient and you only react on the abnormals and only on seeing the abnormality do you intervene with the medication. It's also not every patient that is like that. May be there are a few hypertensives and may be then another diabetic, so it's not a huge burden."

3a: Additional staff requirement for introducing the test

All the respondents from the preparation room believed that additional staff would be required if the test was introduced as it added to their already busy schedule because the only nurse in the preparation room was already overworked:
"It is possible if there are more staff because we are sitting with plus or minus 600 diabetic patients in total and for one nurse in the prep room to do it for all those patients is not possible."

3b: Additional staff requirement for interpreting and acting on the results

Participants in this category believed they do not need additional staff because of the microalbuminuria test:
"With us we are fine because it doesn't take much time to talk to the patient and put the patient on the new treatment but it could be more time consuming in the preparation room but not for us, its okay with us we don't need any additional staff."

4: Other issues relevant to the testing and intervention

One of the participants acting on the result also raised the question of certain patients with allergy to Enalapril to which the doctor responded:
"We are actually in the process of submitting a motivation for Lorsatan to be prescribed in place of Enalapril in instances where we have adverse reactions or side effects that prevent the patient from taking the Enalapril."

Discussion

This study represents the first attempt to assess the feasibility of introducing microalbuminuria screening in diabetic patients to public sector primary health care in South

Africa. Microalbuminuria screening was successfully introduced into the care of diabetic patients at Elsies River CHC. Under normal working conditions the study found that if 100 patients were screened then 12 patients would be diagnosed with macroalbuminuria, another 15 diagnosed with microalbuminuria and it will cost the health system an additional R1225.50 to screen for and treat these patients in the first month. The cost of identifying a patient with microalbuminuria was R73.96 and the cost of treating a patient with the ACEI Enalapril per month was R7.74. The total cost therefore of identifying and treating one patient for one year with microalbuminuria in this health centre was R154.40. It should be noted that screening was completed in only 56.2% of all patients with a positive first test in this CHC, but almost all patients who were diagnosed received intervention.

Staff found the testing and intervention easy and feasible to integrate into their daily routine. Although it only took an extra two minutes to perform the test, staff in the preparation room felt that additional staff capacity would be needed if this test became part of the normal protocol. Alternatively other unnecessary tasks could be stopped to increase the capacity of existing staff.

It was generally observed that the screening can be introduced into the primary health care context with sufficient reliability. Approximately 56.2% of the eligible patients completed the screening process, when this is compared with data from the other routine annual investigations like serum creatinine (66.1%), HbA1c(57.9) and cholesterol(64.0%) which are only one time screening, it is a comparable result.

Screening and prompt treatment with an ACEI leads to a gain in Quality Adjusted Life Years (QALY) and 88.9% of diagnosed patients received the benefit of increased ACEI therapy.(43) Stricter glycaemic and blood pressure control, lipid lowering therapy, dietary and weight control education were other interventions that were instituted as a direct response to a positive result. These interventions should be instituted in the normal day to day care of patients with type 2 diabetes irrespective of microalbuminuria however positivity for microalbuminuria is a red flag that these need to be carried out more intensively. Screening for microalbuminuria followed by

optimized interventions is found to lead to a 44% reduction in cumulative incidence of end stage renal disease (ESRD), the benefits of which are noted from two years after commencement of screening and intervention.(9) Although the effect of the health education is likely to be small, especially if it is a once off intervention, the benefits of intensified treatment should be long term. Based on the literature it is anticipated that there should be better clinical outcomes such as reduced incidence of ESRD and its associated reduction in cardiovascular complication as well as improved life expectancy and quality adjusted life expectancy, if these patients are followed up long term.(9)

Diabetes is one of the commonest causes of kidney failure accounting for 44% new cases (47) and 40% of patients with diabetes are likely to develop nephropathy.(23) By extrapolation this is 40% of 1-1.5 million patients living with diabetes in South Africa.(4) In the current budget it is not possible to dialyse or transplant all of these patients and many are left untreated to die of ESRD. Investment in early screening and treatment may therefore be the only viable strategy to prevent premature deaths. The projected ESRD related costs for this population are shocking. In Tygerberg Hospital (TBH) the average annual cost of dialysis per patient is R120,000.00 and about R78,000.00 is spent yearly on every transplanted patient (personal communication with Prof Moosa and Prof Razeen Davids, Nephrology Unit, Department of Medicine TBH). It is difficult to quantify the cost of recurrent cardiovascular complications and repeated hospitalisations prior to dialysis and transplantation. One must also keep in mind the cost to the government of disability grants that are also paid to patients with ESRD. Nevertheless it is evident that the cost of treating one patient with dialysis for one year is at least the equivalent cost of screening 3000 diabetic patients and treating 450 patients at risk of renal disease, who would be identified, for at least 24 months. In this context, early identification and immediate treatment has a potential to have a huge economic savings with substantial clinical gains and improved quality of life. Money is not always the most significant component of cost as future life years have a value that is difficult to quantify.

The evidence base for cost savings and clinical benefits of screening for microalbuminuria as well as the intervention is very sound. A multinational review of evidence concluded that

screening for microalbuminuria and many other interventions intended to control for diabetes and its complications are cost saving and very cost effective and they are supported by strong evidence, policy makers should consider giving these interventions a higher priority.(48)

Strengths and limitations

The results are clearly influenced by the motivation and performance levels of the staff and degree of organisation within the CHC chosen. Here the motivation and performance appeared quite high as indicated by 100% of patients receiving the initial tests. The results represent the likely effect of screening under these normal working conditions and performance might be worse in CHCs with a more chaotic organizational framework or de-motivated staff. It is difficult therefore to generalize performance to the district or province as a whole. The possibility of a false positive result due to initial staff mistakes could not be ruled out despite taking all the necessary precautions to prevent it and this could lead to unnecessary intervention and attendant cost as well as worry for the patient.

The qualitative data was collected by the researcher who might have been perceived by the health workers as having a vested interest in a more positive viewpoint and who was also responsible for analysing and interpreting the data.

Recommendations

The demonstrated feasibility of testing in the current system, small relative cost, likely long terms benefits to patients and future cost savings, make the introduction of testing for microalbuminuria in public sector primary care a recommendation of this study. Attention should be given to adequate capacity in the preparation room. Future research should focus on long term follow up of patients on interventions in order to be able to chart the impacts of the interventions on an individual patient and calculate the exact QALYs gained in our setting.

Conclusion

This study demonstrated that it is feasible to introduce microalbuminuria testing into routine chronic care of diabetic patients in a public sector primary care facility. The immediate additional costs of screening and treating are overshadowed by the anticipated short term reduction in cardiovascular events and the avoidance of long term end stage renal disease. The benefit to the patients in terms of quality of life, and to the government in terms of future savings make this a cost-effective intervention.

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HEALTH WORKER INFORMATION LEAFLET AND CONSENT FORM

Is screening for microalbuminuria in Type 2 Diabetic patients feasible in the public sector primary care context? A cost and consequence study in two Community Health Centres.

REFERENCE NUMBER:

PRINICIPAL INVESTIGATOR: Prof RJ Mash

CO-INVESTIGATORS: Dr H.O Ibrahim and Dr D Stapar

.

ADDRESS: Family Medicine and Primary Care, Stellenbosch University, Box 19063, Tygerberg, 7505

CONTACT NUMBER: 021 938 9061 / 9449 / 9170

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Committee for Human Research at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

The study aims to assess how practical and affordable it is for a typical community health centre to implement testing for microalbuminuria in diabetic patients.

Why have you been invited to participate?

You have been invited to participate because, as a member of the chronic care team at your community health centre, you may have experience of testing patients for microalbuminuria, interpreting the results, deciding on what to do next and explaining the results to patients.

What will your responsibilities be?

You will be responsible to meet with the researcher when they visit the site to discuss any practical difficulties or clinical uncertainties related to the test. Your feedback on your experience will be recorded as part of the research study. The researcher will visit weekly in the first month, fortnightly in the next 2 months and then monthly thereafter for the 12 month duration of the study. You should also contact the researcher by telephone at any time if you have any questions when using the test.

You will be responsible for ensuring that if/when you are personally involved in microalbuminuria testing that you follow the standard operating procedures for the test, the interpretation and any subsequent interventions as provided by the research study during training.

Will you benefit from taking part in this research?

The study will help policy makers and managers in the District Health Services decide whether it is practical and affordable to introduce this test at all community health centres.

Are there in risks involved in your taking part in this research?

There are no risks to you personally.

If you do not agree to take part, what alternatives do you have?

Your health centre will have made a collective decision to take part in the study and your role in the testing will be clarified by the facility manager and family physician. You do not have to agree to be interviewed and

can also withdraw your consent for this at any time.

Will you be paid to take part in this study and are there any costs involved?

There are no costs for you and you will not be paid to take part.

Is there any thing else that you should know or do?

- You can contact Prof RJ Mash at 0723419542 or 021 938 9061 or your local researcher if you have any further queries or encounter any problems.
- You can contact the Committee for Human Research at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.
- You will receive a copy of this information and consent form for your own records.

By signing below, I…… agree to take part in a research study entitled:- Is screening for microalbuminuria in Type 2 Diabetic patients feasible in the public sector primary care context? A cost and consequence study in two Community Health Centres.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalisd or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*)……..on (*date*) …….. 2004

…….. ……

Signature of Participant Signature of Witness.

Declaration By Investigator

I (name) ……declare that:-

- I explained the information in this document to ……..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use a translator. (*If a translator is used then the translator must sign the declaration below.*

Signed at (*place*)……..on (*date*) …….. 2004

……. ……

Signature of Investigator Signature of Witness.