

## UK NATIONAL SCREENING COMMITTEE

### POPULATION SCREENING FOR BLADDER CANCER AND GLOMERULONEPHRITIS

13 September 2002

A Review of the Evidence with Policy Recommendations

#### 1 Purpose

This paper, together with the accompanying appendices, provides a synopsis of the evidence of the risks and benefits of population screening for bladder cancer and glomerulonephritis (kidney inflammation which can lead to kidney failure).

Information is provided to enable the National Screening Committee (NSC) to make a policy decision as to whether an adult programme of population (low risk, asymptomatic individuals) screening should be instituted for these diseases.

Screening for bladder cancer in high-risk individuals, such as rubber workers, is currently being reviewed by the Health and Safety Executive in conjunction with the NSC and is not considered in this paper.

Investigation of symptomatic individuals is beyond the scope of this paper and is unaffected by any of its conclusions.

#### 2 Background

A “dipstick” urine test is commonly performed when a patient registers with a general practitioner and a “new patient health check” is carried out. During this assessment the medical, social and lifestyle history is taken together with a general examination, which usually includes measurement of body mass index and blood pressure, together with a urine dipstick test. The urine test is able to detect small quantities of blood, protein and glucose, which should be considered as population screening tests for urological neoplasms, renal disease and diabetes.

A urine dipstick testing is also often undertaken a part of a pre-operative assessment in hospital.

Because blood and protein is a common finding on urine dipstick testing (in about 5% or more of those tested) a large number of referrals are made to urology and nephrology departments because of such findings, in the absence of symptoms or other risk factor in the individual.

In 2000 an audit was undertaken of referrals to Urology outpatients in one PCG. A small sample of 32 referrals, were randomly selected from all referrals in a one-year period. Four referrals (12%) were for microscopic haematuria.

### **3 Results**

#### **3.1 Bladder Cancer**

Appendix A details the findings of a literature review of the evidence for screening for bladder cancer against National Screening Committee criteria.

The main findings are as follows:

- 3.1.1 About seven times as many people die per year in the UK from lung cancer and three times as many from bowel cancer when compared with bladder cancer deaths.
- 3.1.2 Smoking probably accounts for about *half* the cases of bladder cancer, and as many as 10% may currently be attributable to past occupational exposure.
- 3.1.3 Most bladder cancer (70-80%) presents clinically as early-stage, superficial disease.
- 3.1.4 As bleeding from bladder cancer can be intermittent repeated urine tests over consecutive days, rather than a single sample, would be necessary as a sensitive screening test.
- 3.1.5 The prevalence of asymptomatic microscopic haematuria in the population varies between less than 1% and 20% depending on the age and gender profile of the population.
- 3.1.6 In a large population study of testing for asymptomatic microscopic haematuria in men aged over 35 and women aged over 55 the positive predictive value for bladder cancer of a positive urine dip test for haematuria was less than 0.2%.  
  
Similar rates of urological cancer were found in those who tested positive and those who tested negative to microscopic haematuria.
- 3.1.7 Diagnostic tests in the investigation of microscopic haematuria such as cystoscopy are unpleasant and not without risk.
- 3.1.8 There is no evidence that screening for bladder cancer can reduce the morbidity or mortality associated with the disease.

## **3.2 Glomerulonephritis**

Appendix B details the findings of a literature review of the evidence for screening for glomerulonephritis against National Screening Committee criteria.

The main findings are as follows:

- 3.2.1 An estimated 540 adults, who have a primary renal diagnosis of glomerulonephritis, start renal replacement therapy (dialysis) each year.
- 3.2.2 There are a number of glomerulonephritides, each of which has an individual natural history and prognosis.
- 3.2.3 The most common form of glomerulonephritis, IgA nephropathy, has a highly variable and unpredictable clinical course and there is no proven specific treatment.
- 3.2.4 About 1%-6% of the adult population will have a positive urine dip test for protein. In a large population study of over 100,000 Japanese adults, 5% tested positive for protein.
- 3.2.5 Proteinuria is a strong clinical risk factor for end stage renal failure (ESRF) with a relative risk of about 15.
- 3.2.6 A urine dipstick test has a sensitivity of 90% and a specificity of 67% when compared with a 24-hour urine sample for protein excretion.
- 3.2.7 The positive predictive value of a urine dipstick test for protein as a test for significant renal disease is 0%- 1.4%.
- 3.2.8 There is no reliable evidence that screening the population for proteinuria will reduce the morbidity or mortality from renal disease.
- 3.2.9 A feasibility study has predicted that 15,384 people would need to be screened and 77 of those treated with ACE inhibitors for 2-3 years to prevent one case of ESRF.

## **4 Conclusions**

Microscopic haematuria and proteinuria are common findings in an asymptomatic adult population, with a likely prevalence of around 5%.

The positive predictive value of a positive test for either blood or protein is low and in the order of 0%-1.4%.

It has not been established that early diagnosis of bladder cancer or glomerulonephritis by screening will confer a significant prognostic advantage. If any prognostic advantage is conferred by early diagnosis this is likely to be in a small minority of cases.

Screening for bladder cancer and glomerulonephritis has not been proved to be effective in a randomised controlled trial.

Because of this and the poor performance of the tests, population screening for bladder cancer and glomerulonephritis cannot be recommended.

A previous NSC review has highlighted the poor performance of the urine test for glucose as a screening test for diabetes.

**Dipstick urine testing in asymptomatic individuals is therefore not recommended.**

## **5 Recommendations**

**5.1 The NSC adopt a policy that population screening for bladder cancer and glomerulonephritis is NOT recommended.**

**5.2 The NSC supports the limitation of urine dipstick test screening of asymptomatic individuals in primary and secondary care.**

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## Appendix A

### Evaluation of Urinary Tract Malignancy (Bladder Cancer) Screening against NSC Criteria

Criteria	Evidence
<b>6 The condition</b>	
<p><b>6.1 The condition should be an important health problem</b></p>	<p><b>Urinary tract malignancy (UTM) is an important health problem, yet the number of people developing and dying from bladder cancer and kidney cancer is small compared with the more common cancers.</b></p> <p><b>In the UK, in 1996, 13,600 people developed bladder cancer and in 1998, 5,000 died from bladder cancer. The corresponding figures for kidney cancer were 5,600 developed kidney cancer and 3,100 died from kidney cancer<sup>1</sup>.</b></p> <p>Comparative mortality data (1998) for the major cancers are <b>34,900 deaths from lung cancer, 17,100 deaths from colorectal cancer and 13,200 female deaths from breast cancer<sup>1</sup>.</b></p>
<p><b>6.2 The epidemiology of the condition should be known</b></p>	<p><b>Bladder cancer is almost 4 times as common in men than women and kidney cancer is just over twice as common in men than women. Bladder cancer predominantly occurs in adults aged over 50 years<sup>2</sup>.</b></p> <p><b>The known risk factors for bladder and kidney cancer are smoking and occupational exposure to aromatic amines and amides (some chemical industries such as rubber and dye manufacture). Also cytostatic drugs such as Cyclophosphamide and radiotherapy to the pelvis are known to increase the risk of bladder cancer<sup>3</sup>.</b></p> <p>Individuals who smoke have a 4-7x increased risk of developing bladder cancer compared with individuals who never smoked<sup>4-6</sup>.</p> <p><b>Smoking probably accounts for about half of the cases of bladder cancer in the UK<sup>7</sup>.</b></p> <p>As many as 10% of bladder cancer cases have been</p>

	<p>attributable to occupational causes in Britain and North America but the proportion should now be less<sup>2</sup>.</p>
<p><b>6.3 The natural history of the condition should be understood.</b></p>	<p>The most common type of bladder cancer in the UK is transitional cell cancer of which there are two distinct types. One is a low-grade papillary tumour that frequently recurs and the second is a high grade malignancy which can present as dysplasia or carcinoma in situ, but which frequently presents as invasive disease<sup>3</sup>.</p> <p>Bladder cancer appears to be associated with premalignant changes elsewhere in the urinary tract. Tumours at multiple sites and recurrence is common.</p> <p>90% of bladder cancer is transitional cell cancer (TCC) which is a heterogeneous neoplasm with a variable natural history and behaviour pattern. 70 - 80% of bladder cancers present as early stage, superficial papillary lesions; 20% are initially diagnosed as invasive disease. Superficial tumours have a great propensity to recur, and 10-20% progress to invasion of the bladder wall. Patients with invasive tumours are at high risk for disease progression, and despite definitive therapy (frequently cystectomy), the overall 5-year mortality rate is almost 50%<sup>8</sup>.</p> <p>Haematuria is a presenting feature in 90% of cases. Hesitancy, urgency, frequency, dysuria and post voiding discomfort are other symptoms<sup>9</sup>.</p> <p>Macroscopic and microscopic haematuria are intermittent in bladder cancer.</p>
<p><b>6.4 There should be a recognised latent period or early symptomatic stage</b></p>	<p>The majority (76%) of bladder cancer presenting clinically (without screening) is superficial disease<sup>10</sup>. For these cases it is unlikely that earlier detection would offer any advantage.</p> <p>In one study a greater proportion (95%) of bladder cancer detected through screening for microscopic haematuria is superficial. It is argued that bladder cancer which would have presented clinically as invasive disease is picked up during an earlier latent stage through screening whilst it is still superficial disease<sup>10</sup>. However there were other differences between the screened and the non-screened group, including the prevalence of current smoking, which is known to cause a less favourable stage distribution of bladder cancer<sup>10,11</sup>. The authors acknowledge that a</p>

	<p>randomised trial would be necessary to confirm the efficacy of bladder cancer screening.</p> <p>Bladder cancer does not have a long pre-clinical stage<sup>10</sup>. Urine testing would therefore need to be carried out frequently in order to be able to detect potentially invasive tumours.</p>
<p><b>6.5 All the cost effective primary prevention interventions should have been implemented as far as practicable</b></p>	<p><b>Smoking accounts for roughly 50% of bladder cancer cases<sup>7</sup>. About 12 million adults in England smoke cigarettes (29% of adult population)<sup>12</sup>. About 200,000 adults (1.7% of the smoking population) received NHS smoking cessation services in 2001 and about half of these were (0.85% of the smoking population) were abstinent four weeks after their quit date<sup>13</sup>. It is predicted that only half of those smokers who are abstinent four weeks after their quit date will still be abstinent at one year<sup>14</sup></b></p> <p>Less than 0.5% of the smoking population are likely to have stopped smoking for one year as a result of NHS smoking cessation services in 2001. It can be argued that primary prevention interventions could be enhanced, for example through more brief intervention by GPs and more workplace interventions.</p>
<p><b>7 The Test</b></p>	
<p><b>7.1 There should be a simple, safe, precise and validated screening test.</b></p>	<p><b>Urine dip testing for small quantities of blood in asymptomatic individuals, [asymptomatic microscopic haematuria (AMH)] is used in some settings (such as new patient examinations in general practice, private medical screening and insurance medical examinations) as a screening test for various renal and urological conditions including bladder cancer.</b></p> <p>A single urine test in a health care setting is simple and safe, but screening for microscopic haematuria requires repeated testing due to the intermittent nature of blood loss from urological cancers. In one study patients self-tested their urine daily for 14 days and repeated the 14 days of testing nine months later<sup>10</sup>.</p> <p>Subsequent testing of patients found to be positive for AMH (which may be up to one fifth of patients, the majority of which will be free of cancer<sup>10,15-17</sup>) is not simple or safe. Cystoscopy is the only means of excluding bladder cancer but it requires sedation and carries the risks</p>

of infection and bleeding.

The positive predictive value (PPV), of microscopic haematuria for urological cancer is very low and especially low in patients aged less than 50.

Studies of outpatients aged over 50 (mean age 65) and aged over 60 have demonstrated a PPV of microscopic haematuria for bladder cancer of 8% and 5% respectively<sup>10,15</sup>.

In another study of over 20,000 members of a health plan in California, 4.3% were found to be positive for microscopic haematuria on urine dipstick testing. The PPV for bladder cancer in this study was less than 0.2%, possibly due to the younger age profile and that a significant proportion of those found dip test positive were excluded because of evidence of previous urological disease.. **However similar rates of urological cancer was found on follow-up in those who tested negative to blood as those who tested positive.** With multivariate analysis of these results, adjusting for age, gender and race, the risk of urological cancer was slightly elevated among those dipstick positive to blood (relative risk of 2.1) but this was not significant (confidence interval 0.7-6.6)<sup>16</sup>.

In another study of almost 2,700 outpatients the PPV for bladder or renal cell carcinoma was 0.5%<sup>17</sup>.

In another cross-sectional population study, patients who tested positive and negative for microscopic haematuria (MH) were followed up to determine risk of urological disease. Urological cancer was found in 1.2% of MH positive patients and 0.2% of MH negatives (P=0.04). **On sub-analysis of the urological cancers, only prostate cancer was found in significantly higher percentage of those with positive tests (P=0.047)**<sup>18</sup>.

In three separate studies 46-55% of men with AMH had no identifiable source of bleeding after further investigations<sup>15,19,20</sup>

In summary the positive predictive value of microscopic haematuria is low and may not confer a significantly higher risk for bladder cancer than a negative result for MH. For this reason MH is not considered a valid test for bladder cancer in the context of population screening.

<p><b>7.2 The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed</b></p>	<p><b>In population surveys the prevalence of asymptomatic microscopic haematuria varies between 0.19% and 21% depending on the age and gender of the population screened and the number of screening tests performed<sup>21</sup>.</b></p> <p>The dipstick test is generally regarded as having a binary result, positive or negative, irrespective of the degree of haematuria demonstrated by the test strip. However it is suggested that all positive results are followed up by urine microscopy. Microscopic haematuria is defined as three or more red blood cells per high-powered microscopic field in urinary sediment from two of three properly collected urinalysis sediments<sup>21</sup>.</p> <p>The cut off level is regarded as any amount of MH (trace upwards). Due to the large number of patients testing positive (up to 21%) and the low PPV of the test for urological cancer (0.2-8%, see above) a large number of patients would need to undergo invasive tests such as cystoscopy to detect bladder cancer in a small number of cases.</p>
<p><b>7.3 The test should be acceptable to the population</b></p>	<p><b>Dipstick testing of urine is acceptable to the vast majority of population in a health care setting. Self-testing of urine at home may be found less acceptable.</b></p> <p><b>However because of the intermittent nature of MH caused by urological tumours, studies of screening programmes have used repeated self-testing, which many of the participants found unacceptable. In one study the participants were asked to test their urine daily for five days then once a week for one year. A later group in the same study were asked to test daily for 14 days then daily for 14 days nine months later. Only 45% agreed to participate<sup>10</sup>.</b></p> <p><b>The invasive tests which are recommended after a positive test for AMH such as cystoscopy and intravenous urography are less acceptable, with one third of men in two studies refusing further investigations or having incomplete workup<sup>15,19</sup>.</b></p>
<p><b>7.4 There should be an agreed policy on the further diagnostic investigation of individuals with a</b></p>	<p><b>Most authorities recommend cystoscopy and intravenous urography for patients found to have microscopic haematuria confirmed on urine microscopy. However as discussed above the yield of</b></p>

<p><b>positive test result and on the choices available to those individuals</b></p>	<p><b>these investigations is small.</b></p>
<p><b>7.5 There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.</b></p>	<p><b>There are agreed evidence based policies for the treatment of the different grades and stages of bladder cancer<sup>9,22</sup>.</b></p>
<p><b>8 The treatment</b></p>	

<p><b>8.1 There should be an effective treatment or intervention for patients identified through early detection</b></p>	<p>Survival in patients with bladder cancer is strongly associated with stage at diagnosis. Although most cancers are superficial at diagnosis, with a 90% five-year survival, 10-20% have invaded the bladder muscle when first diagnosed with a five-year survival of less than 50%<sup>23</sup>.</p> <p>However as aggressive cancers may invade early, periodic screening will have a limited potential to detect invasive cancer at an early, more treatable stage<sup>24</sup>.</p> <p>Some studies have shown that screening can pick up more disease at a superficial stage than routine care and that survival in those cases of bladder cancer picked up by screening is superior<sup>10,15,19,25</sup>.</p> <p>However these studies suffer from a number of biases including lead-time bias, length time bias and selection bias and no firm conclusions can be drawn without randomised trials of screening, or at least without a comparable unscreened control group. However, even with the latter length time bias would remain.</p> <p>Even in the screened group in one study 10 of 16 cancers detected by screening recurred within three years<sup>25</sup>.</p> <p>Many intravesical chemotherapeutic agents have been shown to reduce tumour recurrence when used in conjunction with transurethral tumour resection. Unfortunately, however, none of these agents have proved to be of benefit in preventing disease progression<sup>26</sup>.</p>
<p><b>8.2 There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.</b></p>	<p><b>Evidence based treatment regimes exist for the various grades and stages of bladder cancer<sup>9,22</sup>.</b></p>

<p><b>8.3 Clinical management of the condition and patient outcomes should be optimised by all health care providers prior to participation in a screening programme</b></p>	<p><b>In 2001, in more than 32% of bladder cancer cases the diagnosis was made more than 4 weeks after GP referral with suspicion of cancer<sup>27</sup>.</b></p> <p>For bladder cancer the median time to definitive treatment from GP referral with suspicion of cancer was 47 days (range 1-353)<sup>27</sup>.</p>
<p><b>9 The screening programme</b></p>	
<p><b>9.1 There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity.</b></p>	<p><b>This evidence does not exist and despite calls from leading researches in the US the National Cancer Institute would not support such a study.</b></p>
<p><b>9.2 The opportunity cost of the screening programme (including testing, diagnosis and treatment) should be economically balanced in relation to expenditure on medical care as a whole.</b></p>	<p><b>There is insufficient evidence to suggest that a screening programme for bladder cancer would benefit the population. There is no need to consider opportunity costs and cost-effectiveness until there is reliable evidence that screening for bladder cancer is effective.</b></p>

## Conclusions

There is currently no evidence that screening for bladder cancer will reduce morbidity or mortality from the disease. Testing asymptomatic individuals for microscopic haematuria will cause unnecessary anxiety and subject many disease-free individuals to invasive tests.

The majority of bladder cancer detected through screening is low grade superficial disease, which would still be superficial disease if it presented clinically later with macroscopic haematuria (visible blood in the urine) or other urinary symptoms.

In order to detect high-grade, potentially invasive disease before invasion of the bladder muscle wall, screening would need to take place at such frequent intervals to make it

unacceptable. In addition as bleeding from bladder tumours is intermittent each screen would itself need to involve repeated daily testing.

### **Implications for policy**

Urine testing for microscopic haematuria should not be undertaken for asymptomatic individuals.

Such testing currently takes place in new patient health checks in primary care, routine urine testing of emergency admissions to hospital, pre-operative screening and medical insurance, occupational and private health screening examinations.

The department of health's policy on screening for bladder cancer and routine urine testing for microscopic haematuria should be made in light of this evidence.

### **Implications for research**

Although a randomised trial of bladder cancer screening in the population would be able to provide a definitive answer to the effectiveness, there may be insufficient evidence from other studies to justify the cost of such research.

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**Appendix B**  
**Evaluation of Glomerulonephritis against the NSC Handbook**

Criteria	Evidence
<p><b>10 The condition</b></p> <p><b>10.1 The condition should be an important health problem</b></p>	<p>About 5,300 adult patients in England &amp; Wales started renal replacement therapy (RRT) in 2000 giving an estimated incidence rate of 89 per million population<sup>1</sup>.</p> <p>In 14% (170) of those aged &lt;65 and 6% (70) of those aged ≥65 who were reported to the Renal Registry as starting RRT in 2000, the primary renal diagnosis reported was glomerulonephritis. The diagnosis was uncertain in 16% and 24% and no diagnosis was sent in 15% and 20% in the &lt;65 and the ≥65 year age groups respectively. It is likely that glomerulonephritis will have been the cause of the end stage renal failure in a proportion of these patients<sup>1</sup>.</p> <p><b>It is estimated that at least 540 adults with a primary renal diagnosis of glomerulonephritis start RRT each year.</b></p> <p>Renal Replacement Therapy consumes 2% of the NHS budget and is predicted to reach 3% within five years. In the UK more than 500 patients per million population are receiving RRT<sup>2</sup>.</p>
<p><b>10.2 The epidemiology of the condition should be known</b></p>	<p><b>Some of the epidemiology of End Stage Renal Disease (ESRD) and glomerulonephritis is understood but in 16-24% of cases the cause of ESRD is unknown<sup>1</sup>.</b></p> <p><b>A large cohort study of over 300,000 men followed up for an average of 16 years found that the major risk factors for ESRD were: old age; low income; cigarette smoking; diabetes; black race and hypertension<sup>3</sup>.</b></p> <p>A further cohort study of over 100,000 Japanese people attending a mass screening programme who were followed up for ten years found that proteinuria was the strongest risk factor for ESRD with a relative risk of 14.9<sup>4</sup>.</p> <p>Glomerulonephritis (GN) covers a group of conditions in which inflammation of the glomerulus (the kidney's filter system) is present. GN depends on the histological analysis of a renal biopsy. The estimated incidence of 17-60 per million population will therefore depend on renal biopsy policies. Asymptomatic proteinuria is a recognised means of</p>

	<p>presentation of glomerulonephritis. Other clinical presentations include nephrotic syndrome (severe proteinuria, hypoproteinaemia and oedema) microscopic haematuria, hypertension and renal failure<sup>5</sup>.</p>
<p><b>10.3 The natural history of the condition should be understood.</b></p>	<p><b>Glomerulonephritis is divided into histological subtypes, which have specific clinical features and natural history:</b></p> <p><b>Minimal-change Nephropathy</b></p> <p>Minimal-change nephropathy is most common in children. It presents with nephrotic syndrome and responds to high dose steroids<sup>5</sup>.</p> <p><b>Focal Segmental Glomerulosclerosis (FSGS)</b></p> <p>FSGS presents with nephrotic syndrome and may be associated with hypertension, microscopic haematuria and impaired renal function. The disease often progresses to ESRD despite treatment<sup>5</sup>.</p> <p><b>Membranous nephropathy (MN)</b></p> <p>MN typically presents with proteinuria, which may be severe enough to cause nephrotic syndrome. This disease may be secondary to drugs, tumours or infections. The prognosis is dependent on the underlying disease. Where there is no underlying cause at least 25% undergo spontaneous remission. Treatment is generally reserved for those with nephrotic syndrome and renal failure<sup>5</sup>.</p> <p><b>Mesangiocapillary GN (MCGN)</b></p> <p>MCGN is uncommon and presents with proteinuria, haematuria, hypertension and impaired renal function. It tends to have a progressive course with 50% of patients having chronic renal failure within 10 years<sup>5</sup>.</p> <p><b>Focal necrotising GN (FNGN)</b></p> <p>FNGN usually presents with acute renal failure, haematuria and proteinuria and is a medical emergency<sup>5</sup>.</p> <p><b>IgA Nephropathy</b></p> <p>IgA nephropathy is the most common form of glomerulonephritis worldwide and is predominantly a disease</p>

	<p>of young males<sup>6</sup>. The typical clinical presentation is haematuria, which may be macroscopic. Without proteinuria the prognosis is good, if proteinuria is more than 1g/ 24 hours the risk of ESRD is about 25%<sup>5</sup>.</p> <p>There is no proven treatment for IgA nephropathy<sup>5</sup>.</p> <p>IgA nephropathy is characterised by extreme variability in the clinical course and sometimes by the unpredictability of the ultimate outcome<sup>7</sup>.</p>
<p><b>10.4 There should be a recognised latent period or early symptomatic stage</b></p>	<p><b>There is a long latent phase (from onset of proteinuria to ESRD) in some of the glomerulonephritides such as IgA nephropathy but not in others such as FNGN.</b></p> <p>However it is unpredictable if ESRD will follow the onset of proteinuria.</p>
<p><b>10.5 All the cost effective primary prevention interventions should have been implemented as far as practicable</b></p>	<p><b>The main preventable causes/ risk factors of ESRD are low income; cigarette smoking; diabetes; and hypertension<sup>3</sup>.</b></p> <p>Primary prevention of these risk factors would include antipoverty policies, smoking cessation and smoking uptake prevention, diet and exercise modification.</p> <p>It is unlikely that all these interventions have been implemented as far as is practicable.</p>
<p><b>11 The Test</b></p>	
<p><b>11.1 There should be a simple, safe, precise and validated screening test.</b></p>	<p><b>A urine dipstick test is simple and safe.</b></p> <p><b>Dipstick urinalysis detects albumin at a sensitivity of 100-200 mg/litre.</b></p> <p>Dipsticks provide semi quantification but 24-hour urine collection is required for formal quantification.</p> <p>When the gold standard of a 24-hour urinary excretion of protein of 300 mg or more is used the dipstick has a sensitivity of 90% at a specificity of 67%<sup>8</sup>.</p> <p>About 30% of those who are dipstick positive will have a positive 24-hour urine protein test. Of these 13% will be assessed as having a “moderate” to “high risk” of ESRD in the future . This gives an overall positive predictive value (PPV) of about 4% for a positive urine dip test for protein as an assessment of moderate to high risk of ESRD in the</p>

	<p>future<sup>8</sup>.</p> <p>Rates of definitely significant disease in asymptomatic individuals with proteinuria have been in the range of 0.0% and 1.4%<sup>9</sup>.</p>
<p><b>11.2 The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed</b></p>	<p><b>In two population studies the prevalence of proteinuria was between 1% and 6%. In one Japanese study of over 100,000 adults the prevalence of dipstick proteinuria was 5%<sup>4</sup>. From a 16 years study of over 5,000 men and women in the Framingham cohort the prevalence of proteinuria was between 1% and 6% depending on age and gender<sup>10</sup>.</b></p>
<p><b>11.3 The test should be acceptable to the population</b></p>	<p><b>A simple urine dip test is likely to be acceptable to the population. A 24-hour urine test, which would be required in about one in twenty adults, would be less acceptable.</b></p> <p>The follow up tests, which would be advocated in about a third of those undergoing 24-hour urine testing, may not be acceptable. These would include blood tests, further urine tests, possible renal biopsy (e.g. for proteinuria &gt; 1g/24 hours) and indefinite follow up.</p>
<p><b>11.4 There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals</b></p>	<p><b>There are agreed policies on the investigation of proteinuria<sup>11</sup>.</b></p>

<b>11.5 There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.</b>	<b>There are agreed policies on the treatment of glomerulonephritis<sup>12</sup>.</b>
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<b>12 The treatment</b>	
<b>12.1</b> There should be an effective treatment or intervention for patients identified through early detection	<p>Patients with glomerulonephritis benefit from vigorous treatment of hypertension, preferably with an ACE inhibitor. Prednisolone and other immunosuppressive drugs are beneficial in some forms of glomerulonephritis<sup>12</sup>.</p> <p>Fish oil supplementation and anticoagulation is also recommended in some instances <sup>12</sup>.</p>
<b>12.2</b> There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.	There are agreed evidence based policies <sup>12</sup> .
<b>12.3</b> Clinical management of the condition and patient outcomes should be optimised by all health care providers prior to participation in a screening programme	A screening programme has not been advocated
<b>13 The screening programme</b>	
<b>13.1</b> There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity.	<p>No randomised control trial of screening for proteinuria was found.</p> <p>A feasibility study has predicted 1.3 cases of ESRD prevented over 2-3 years for every 20,000 people screened for proteinuria<sup>8</sup>.</p> <p>Number needed to screen (NNS) = <u>15,384</u>.</p> <p>Number needed to treat (NNT) (ACE inhibitors for 2-3 years) = <u>77</u></p>

<p><b>13.2 The opportunity cost of the screening programme (including testing, diagnosis and treatment) should be economically balanced in relation to expenditure on medical care as a whole.</b></p>	<p><b>The opportunity costs of a population screening programme for proteinuria would be large with about 5% of the population testing positive and requiring further investigation.</b></p> <p>There is no evidence that there would be any improvement in the health of the screened population.</p>
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## Conclusions

There is currently no good evidence that population screening for proteinuria will reduce morbidity or mortality glomerulonephritis. Testing asymptomatic individuals for proteinuria will cause unnecessary anxiety and subject many disease-free individuals to invasive tests, life-long follow-up and pharmacological treatment.

## Implications for policy

Urine testing for proteinuria should not be undertaken for asymptomatic individuals.

Such testing currently takes place in new patient health checks in primary care, routine urine testing of emergency admissions to hospital, pre-operative screening and medical insurance, occupational and private health screening examinations.

The department of health's policy on screening for renal disease and routine urine testing for proteinuria should be made in light of this evidence.

## Implications for research

Research should be carried out on the most effective means to change the current practice of routine population screening for proteinuria in primary care.

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