Urinalysis self-testing in pregnancy

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Clinical Question:

In pregnant women, what is the accuracy, feasibility and utility for self-testing of proteinuria?

Background, Current Practice and Advantages over Existing Technology

Protein leaking into the urine combined with high blood pressure defines pre-eclampsia, a condition affecting 2-8% of pregnancies in the UK *(1, 2)*. Pre-eclampsia can lead to eclampsia; a serious condition with seizures and a high mortality rate (0.83). There are around 300-400 confirmed cases of pre-eclampsia in the UK every year (*3*). A recent audit of maternal deaths in the UK reported 19 deaths from pre-eclampsia and eclampsia during 2006-2008 indicating that the number of deaths from pre-eclampsia has not fallen since the 1991-1993 report (*4*).

Diagnosing pre-eclampsia requires monitoring of blood pressure and proteinuria, typically by midwives at intermittent times during pregnancy, generally coinciding with antenatal visits (*5*). Standard reagent strips are used with further testing in the case of a positive result (24 hour sample testing and spot testing urine protein:creatinine ratio (uPCR) as per NICE and PRECOG guidelines) (*6, 7*). Meta-analysis has shown that the uPCR optimum threshold is between 0.3-0.35mg/mmol and this provides a sensitivity and specificity of above 0.75 (*8*). Values in excess of 150 mg/L or 300 mg/24 hr during pregnancy are usually associated with either pre-eclampsia or underlying renal disease. Routine care appears to be similar in the U.S.A: the recent American congress of obstetricians and gynaecologists (ACOG) guidelines suggest that a dipstick reading of 1+ suggests proteinuria, but should only be used when quantitative methods are not available (ACOG 2013). The report recommended weekly proteinuria testing and weekly, or home BP monitoring in hypertensive pregnancy, suggestive of a move towards home monitoring. The development of proteinuria in a hypertensive pregnancy is universally agreed to be significant (*9*).

A significant number of women in the UK develop pre-eclampsia within the interval between antenatal visits (*3*). Furthermore a significant proportion of deaths from pre-eclampsia also had

serious disease present between normal antenatal visits (*10*). Regular self-monitoring of blood pressure and self-testing for proteinuria could improve detection of pre-eclampsia in the higher risk pregnant population, as well as reducing the time, cost, stress and inconvenience of frequent appointments without compromising the ability to detect and monitor a potentially serious disease.

Self-testing of urine for glucose or albumin is becoming increasingly common in diabetic care (*11, 12*). The pregnant population are also well accustomed to urine testing with the use of home pregnancy tests as the standard means of diagnosing pregnancy for women in the UK (*13, 14*). However, there are surprisingly little data on self-testing of proteinuria in the pregnant population. Several studies describe providing pregnant patients with urine dipsticks to periodically check for protein alongside self-monitoring blood pressure (*15-18*) but have not formally evaluated test performance, effect on frequency of visits to clinics and pregnancy outcome. Large screening studies have been carried out within the general population (excluding pregnancy) with the aim of improving early detection of renal disease. These studies found that self-testing improved the chances for an early diagnosis and therapy, though the study concluded that participants had a tendency to over diagnose proteinuria (*19, 20*).

Details of Technology:

Urinalysis reagent strips are visually read tests used to detect protein in urine samples. A large number of urinalysis reagent strips are commercially available, all of which follow a similar testing methodology (Table 1).

The reagent strip is dipped briefly into a fresh, mixed first-pass (non-centrifuged) urine sample, ensuring all test pads are fully immersed. Upon removal, some products state to touch side of strip against container or to blot the strips lengthwise onto absorbent paper to remove excess. At times ranging from 30 seconds to 2 minutes, the reagent areas can be compared to the corresponding colour blocks on the colour chart, giving a semi-quantitative result. An automated reader can also be used to reduce operator/reader variability *(21)*.

The stated sensitivities of these tests range from 50-300mg/L. Normal levels of protein are around 50mg/L in the first and second trimesters and <100mg/L in the third. Values in excess of 150mg/L are associated with either pre-eclampsia, underlying renal disease or a urinary tract injection and correspond to 1+ or greater on the dipstick (*9*).

There has been limited evaluation of the diagnostic accuracy of dipstick analysis for proteinuria, when performed by health care professionals. A 2004 meta-analysis of studies comparing point of care testing to laboratory testing concluded that the accuracy with a 1+ threshold for predicting proteinuria is poor, with a positive likelihood ratio of 3.5. Accuracy at higher protein thresholds was

not analysed, due to sparse data. This study concluded that significant proteinuria could not be accurately detected or excluded at the 1+ threshold and should not be used to diagnose pre-eclampsia (*22*).

A prospective study carried out in Australia analysed 503 urine samples from 170 hypertensive pregnant women using an automated dipstick reader found that using a dipstick proteinuria 1+ to diagnose pre-eclampsia provided an overall accuracy of 70% and a false positive rate of 71%. However, a dipstick proteinuria of 2+ provided a significant improvement with an overall accuracy of 82% and false positive rates reduced to 7% at the 3+ level. Interestingly, they reported that incorrect urinalysis by dipstick was significantly more likely (p=0.032) if the blood pressure was below 90mmHg (*23*).

Patient Group and Use:

- Pregnant women

Importance:

The incidence of pre-eclampsia is around 5%, and severe pre-eclampsia and eclampsia in the UK are estimated to occur in 5/1,000 pregnancies *(24)* and 4.9/10,000 pregnancies (*3*), respectively. Around 6 mothers die each year in the UK from the complications of pre-eclampsia (*1, 25*). The 8th Confidential Inquiry into Maternal and Child Health *(2)* found that pre-eclampsia and eclampsia combined were the second leading cause of direct maternal death in the UK, with 19 women dying due to pre-eclampsia between 2006-2008 and the mortality rate is not declining. Furthermore around 1,000 babies die each year in the UK because of the condition, mostly because of complications of early delivery (*1*).

A significant number of women in the UK have been reported to develop pre-eclampsia during the interval between antenatal visits with 22% of women (64/291 women with complete antenatal records) experiencing their first convulsion while under community care in 1992 (*3*), furthermore a significant proportion of deaths from pre-eclampsia also had serious disease present between normal antenatal visits (*10*). Regular home self-testing for proteinuria could improve the detection of pre-eclampsia by increasing screening whilst reducing the burden on primary care of more frequent testing. Self-testing could reduce the stress and inconvenience of frequent additional appointments in high risk women without compromising the ability to detect and monitor a potentially serious disease. It may also act to improve women's involvement in antenatal care and improve women's confidence in self-monitored results. Self-testing may also support a gradual move towards telehealth in the NHS as a means of reducing face to face visits and improving efficiency of care (*26*).

Previous Research:

We evaluated the literature comparing the accuracy and utility of standard proteinuria dipsticks used by a health professional to the same standard dipstick used by pregnant women themselves (self-testing). Three studies were identified, which are outlined below. A search of the clinical trials registry failed to find any on-going clinical trials into the self-testing of proteinuria in pregnancy. The reference standard for assessing proteinuria is a 24 hr laboratory measurement of protein excretion or urine protein-creatinine ratio (uPCR) (*7*). No reports were identified that directly compared self-testing for proteinuria to laboratory testing.

Accuracy compared to existing technology

A 2002 prospective observational study compared the accuracy of visually read dipstick self-testing for proteinuria by 209 pregnant women to the results of an experienced nurse using the same urine sample (*27*). All testing was carried out in an antenatal clinic and there was no comparison of the self-testing and nurse testing to 24 hr urine excretion or uPCR.

Women interpreting their dipstick analysis were found to have an equivalent false negative rate (8.6%) and higher false positive rate (35.9%) than of the nurse performing the same test There was significant difference ($p<0.001$) between the nurse's test and the women' results; however the majority (53%) of differences occurred between a negative protein result and a trace result, from a clinical viewpoint these changes were deemed insignificant. By considering a positive as 1+ or more and a negative defined as 0 or trace, a moderate, but significant difference remained between nurse test and self-test. The authors concluded that the pregnant women tended to overestimate their proteinuria (*27*).

This study suggests that women self-testing urine during the antenatal phase may be possible and implemented with verbal instructions during antenatal visits, with results being rechecked by a trained health professional if 1+ or more dipstick proteinuria reading was found. The tendency of the pregnant women to overestimate proteinuria could be at least partly addressed by further training; Bell *et al* (*28*) illustrated that overestimation of proteinuria largely occurred with the least experienced nursing staff, and that further training, particularly providing instructions to avoid rounding up results (If the colour appears between two categories to use the lower result) as you might expect reduced false positive rates. The authors also suggest that using a dipstick test only for protein (rather than one containing multiple different tests) may be less confusing.

Diagnostic tests for urinary albumin in pregnancy.

Urine albumin tests have been assessed in pregnancy with pooled estimates of sensitivity and specificity for pre-eclampsia have been calculated as follows; for albuminuria 62% (95% CI 23 to 90%) and 68% (95% CI 57 to 77%); albumin–creatinine ratio 19% (95% CI 12 to 28%) and 75% (95% CI 73 to 77%) (*29*). Furthermore preterm labour, preeclampsia, intrauterine growth restriction (IUGR),

preterm premature rupture of membranes (PPROM) were more common among women with albuminuria (*30*). This shows great promise for albumin levels to be used in the prediction of pre-eclampsia, however reports so far have been varied and further work is needed to evaluate the predictive power of this test and relationship between albuminuria and pregnancy outcome.(*8*) Dipsticks for albuminuria have been developed but are not currently part of clinical pathways and have not been tested in pregnancy in the home environment.

Impact compared to existing technology

There were no data presented on patient satisfaction or acceptability; however, no women declined to take part and many expressed 'disappointment' when the study concluded and the authors noted it would give women a sense of responsibility and control with their own care (*27*).

Our search identified a conference abstract outlining the results over a 10 year period during which the hospital issued pregnant women (over 26 weeks gestation) a prescription and guidance leaflet on self-testing of urine (*31*). A cohort of 100 prima gravida cases who developed pre-eclampsia were reviewed to determine the initial method of detection of pre-eclampsia. The article reported that 25% of women were self-referred to hospital, of which 20% were as a result of proteinuria detected on home urine dipstick. No further data was reported and the abstract concluded that the urine dipstick self-testing could be an affordable way of increased testing of proteinuria that could improve detection of disease by self-referral to midwifery staff in the community and in hospital. There is no full publication of this work to date.

A cost analysis study carried out in the U.S.A in 2006 involved 1140 women with gestational hypertension who performed a qualitative urine test twice daily alongside other biometric data (blood pressure, weight, foetal movement) (*18*). The accuracy of the urine self-testing was not analysed; however in comparison to a hypothetical control group, the admission rate and mean length of stay per patient reduced by 81% and 34%, respectively. Emphasis was placed on the need for at least once daily measurements to be taken, with increased patient education alongside ready access to healthcare providers, and the reliability of the individual.

In terms of efficacy, this study argued that due to the present technology and low rate of complications in asymptomatic mildly hypertensive patients, the essential monitoring required can be performed outside hospital, thereby reducing the need for prolonged hospital visits. Reducing the stress and inconvenience of hospital visits can result in pregnancy prolongation, decreasing short-term neonatal morbidity (*32*).

Self-monitoring of proteinuria in the general population

A number of studies examined the use of self-testing urine protein in the general population which provide useful insights into potential issues regarding feasibility and acceptability.

The Dutch Kidney Foundation began an albuminuria self-test program in September 2006, whereby adults, via a media campaign, were invited to order a free albuminuria self-test. Cross-sectional analysis indicated that of 71,741 participants, 21% individuals reported a positive result, however only 25% of these visited a GP after self-testing (*20*). Of the 3,983 participants who visited a GP, 183 individuals were diagnosed with new disease. A further study looked at the influence of this program upon detection of new disease before and after the program; the number of GP consultations increased by 5 per 10,000 in the year following the study, and 2.1 times more patients were diagnosed with urinary diseases, the increase being found particularly in patients with no previous risk factors (*33*). It is difficult to distinguish in this study the effects of the mass media campaign which may increase awareness generally within the population, from individuals self-testing specifically.

The number of false positives is a key concern regarding the impact of self-testing; three of the studies found (*20, 33, 34*), attempted to increase the diagnostic value of results by instructing individuals to carry out three self-tests within a week, or with five days in-between; and defining a positive test result as 2 positive tests out of three. However, an evaluation questionnaire study indicated that when a number of the tests were false positives this led to worries amongst patients; this could potentially lead to unnecessary use of health care/ medicalisation and unnecessary costs.

Guidelines and Recommendations

There is no mention of self-testing for proteinuria in NICE guidelines for pregnancy care or from NHS England *(5, 7).* However NICE indicate that further research is needed to determine the role of screening for proteinuria in healthy pregnancy and that there is a need for large, high-quality prospective studies comparing the various methods of measuring proteinuria (automated reagent-strip reading devices, urinary protein:creatinine ratio, urinary albumin:creatinine ratio, and 24-hour urine collection) in pregnant women with new-onset hypertension.

Cost-effectiveness and economic impact:

This simple and cheap test could improve the detection of a potentially serious disease (reducing further care due to early intervention), and could reduce additional appointments (*35*).

Research Questions:

1. What is the accuracy of self-testing of proteinuria by pregnant women in a home environment compared to nurse/midwife testing, automated readers or laboratory testing?
2. What is the acceptability of self-testing of proteinuria to women and health professionals in the UK?
3. Can self-testing of proteinuria improve detection of pre-eclampsia and/or enhance the decision making process regarding the need for additional or acute midwife appointments either alone or when combined self-monitored BP readings?
4. What is the effect of self-testing of proteinuria on the number of additional antenatal appointments required during pregnancy?
5. Is self-testing of proteinuria a cost effective method of measuring proteinuria in pregnancy? (How does the use of self-testing impact upon the rate of referral/ burden upon the NHS)
6. What is the accuracy of other proteinuria tests such as albuminuria reagent strips when used by pregnant women?

Suggested next step:

1. Studies evaluating acceptability of self-testing for proteinuria in pregnant women among health care professionals.
2. Pilot studies in pregnant women addressing accuracy, acceptability, utility and accuracy of self-testing.
3. Cost-effectiveness analysis of self-testing of proteinuria in primary care.

Expected outcomes:

Currently there is insufficient published evidence to draw firm conclusions about the clinical benefit of self-testing of proteinuria in pregnancy. The tendency of pregnant women to overestimate proteinuria combined with the current limitation of the technology in terms of specificity and sensitivity could result in an increased burden upon the healthcare system with minimal effects upon detection and outcome of pregnancies. Moreover, some countries have moved away from using urine proteinuria at all in prenatal care. However if proven to be sufficiently accurate and cost effective, the self-testing of proteinuria (or indeed albuminuria) has the potential to be a valuable method of screening for pre-eclampsia in pregnancy, and may result in earlier diagnosis of this condition than current practice, potentially leading to improved outcomes.

Table 1

Table of devices recommended for home testing

Device name/ manufacturer	Approval	Detection limit/range
Urincheck Health Screen 10 by Express Diagnostics	FDA cleared/ CLIA waived CE not stated	150-300mg/L
Uristix 4 by Siemens	FDA cleared/ CLIA waived CE marked	Not stated
Dirui –H series Reagent urinalysis by Dirui	FDA cleared/ CLIA waived CE marked	150-300mg/L
Medi-test Combi 2 by Machery Nagel	FDA cleared/CLIA waived	Not stated
URISPEC 11- way urine reagent test strips by Henry Schien	FDA cleared/ CLIA waived CE not stated.	Not stated
Combur 5HC test by Roche	FDA cleared/ CLIA waived (FDA approved for home use) CE marked	Not stated
Mission urinalysis reagent strips by Acon laboratories	FDA cleared- CLIA waived CE marked	75-150mg/L
Phinex 10 parameter urinalysis test reagent strips by Experian Health	FDA cleared/ CLIA waived	Not stated
Fisher brand10-SG urine reagent strips by Fisherbrand	FDA cleared/CLIA waived	Not stated
Urige- 3,5,8,9 urine reagent strips by syntron	FDA cleared /CLIA waived CE not marked	Not stated
Cybow urine reagent strips by DFI	FDA cleared/ CLIA waived CE marked	100-150mg/L
1 parameter protein test URS reagent strip by KIP diagnostics	FDA approved/CLIA waived CE marked	150-300mg/L

Tests recommended for professional use only

Device name/ manufacturer	Approval	Detection limit/range
Bayer **Multistix** 10SG by Siemens	FDA cleared/ CLIA waived CE marked	150 mg/L
Multistix pro by Siemens Bayer	FDA cleared/ CLIA waived	80-150 mg/L
Rapid response 11 Para URS Ultra (URS-1S69) by BTNX	FDA cleared/ CLIA waived CE marked	150 mg/L
Proadvantage urine reagent strips P080010 by NDC	FDA cleared/ CLIA waived CE not stated	Not stated
Diascreen 10 Urine test strips by Arkray Hypoguard	FDA cleared/ CLIA waived CE not stated	Not stated
Chemistrips by Roche diagnostics ->" unique design specifically for self-testing"	FDA cleared/ CLIA waived CE not stated	60 mg/L
Clarity Urocheck 10 SG / URS reagent stripstest strips by TECO diagnostics	FDA cleared/ CLIA waived CE	150 mg/L
Aimstick 10-SG reagent strips by Germaine Laboratories	FDA cleared/ CLIA waived CE mark not stated	150 mg/L
HealthMate 10 parameter GP/Professional urinalysis dipsticks UK urinalysis testing strips	FDA cleared/ CLIA waived CE marked	Not stated
Suresign professional urinalysis reagent strips by CIGA health care	FDA cleared- CLIA waived CE marked	Not stated
Valutest by Williams Medical Supplies	FDA cleared/ CLIA waived CE marked	Not stated
Medi-Lab performance urine reagent strips by Mckesson	FDA- CLIA waived CE not marked	Not stated
Meditest combi 10-SGL(also 5, 6,7,8,9) Urine test strips by Macherery Nagel	CE marked for professional use FDA – CLIA waived	100 mg/L
Clinistrip 10 –parameter urinalysis test strip	FDA- CLIA waived CE not marked	150 mg/L
URI-CHECK 10-SG urinalysis reagent strips	FDA-cleared/ CLIA waived CE marked	75-150 mg/L
10-LG parameter by IND diagnostics	FDA approved CLIA waived CE marked	150-300 mg/L
Accutest urine reagent strips by Jant Pharmaceutical	FDA approved CLIA waived CE mark not stated	100 mg/L
vCHEM urine chemistry strips by IRIS diagnostics	FDA approved / CLIA waived CE marked	Not stated
Combi- screen reagent test strip by Analyticon	FDA approved/CLIA waived CE marked	150 mg/L
New choice pro-professional urinalysis test reagent strips by NCI	FDA cleared/ CLIA waived CE marked	Not stated
Quickvue urinchek 10+ SG by Quidel	FDA cleared / CLIA waived CE marked	120 mg/L
Chemview-10 strip by Cenogenics Corporation	FDA cleared/ CLIA waived CE not marked	50-100 mg/L
Rediscreen urinalysis reagent strips -10 parameters by PerMaxim	FDA cleared/CLIA waived CE not marked	Not stated
Uritest 13G Urinalysis reagent strips by Uritest Medical Electronic Co.Ltd	FDA approved/ CLIA waived CE marked	100-300 mg/L
UROFAST 10 SG urine reagent strips by Biotron	FDA approved/CLIA waived	Not stated

References:

1. NHS. (2013) Pre-eclampsia *http://www.nhs.uk/conditions/Pre-eclampsia/Pages/Introduction.aspx*
2. Duley, L., Meher, S., and Abalos, E. (2006) Management of pre-eclampsia, *BMJ 332*, 463-468.
3. Douglas, K. A., and Redman, C. W. (1994) Eclampsia in the United Kingdom, *BMJ 309*, 1395-1400.
4. Cantwell, R., Clutton-Brock, T., Cooper, G., Dawson, A., Drife, J., Garrod, D., Harper, A., Hulbert, D., Lucas, S., McClure, J., Millward-Sadler, H., Neilson, J., Nelson-Piercy, C., Norman, J., O'Herlihy, C., Oates, M., Shakespeare, J., de Swiet, M., Williamson, C., Beale, V., Knight, M., Lennox, C., Miller, A., Parmar, D., Rogers, J., and Springett, A. (2011) Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom, *BJOG : an international journal of obstetrics and gynaecology 118 Suppl 1*, 1-203.
5. NICE. (2010) National Institute for Health and Care excellence CG62; Antenatal care In *NICE clinical guideline 62*.
6. Milne, F., Redman, C., Walker, J., Baker, P., Black, R., Blincowe, J., Cooper, C., Fletcher, G., Jokinen, M., Moran, P. A., Nelson-Piercy, C., Robson, S., Shennan, A., Tuffnell, A., and Waugh, J. (2009) Assessing the onset of pre-eclampsia in the hospital day unit: summary of the pre-eclampsia guideline (PRECOG II), *BMJ 339*, b3129.
7. NICE. (2010) National Institute for Health and Care excellence CG107; Hypertension in pregnancy: the management of hypertensive disorders during pregnancy In *NICE clinical guideline*.
8. Morris, R. K., Riley, R. D., Doug, M., Deeks, J. J., and Kilby, M. D. (2012) Diagnostic accuracy of spot urinary protein and albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients with suspected pre-eclampsia: systematic review and meta-analysis, *BMJ 345*, e4342.
9. Maybury, H., and Waugh, J. . (2005) Proteinuria in Pregnancy - Just What Is Significant?, *Fetal and Maternal Medicine Review 16*, 71-95.
10. HMSO. (1996) Report on Confidential Enquiries into Maternal Deaths in the United Kingtom 1991-1993.
11. Lu, J., Bu, R. F., Sun, Z. L., Lu, Q. S., Jin, H., Wang, Y., Wang, S. H., Li, L., Xie, Z. L., and Yang, B. Q. (2011) Comparable efficacy of self-monitoring of quantitative urine glucose with self-monitoring of blood glucose on glycaemic control in non-insulin-treated type 2 diabetes, *Diabetes research and clinical practice 93*, 179-186.
12. Piehlmeier, W., Renner, R., Schramm, W., Kimmerling, T., Garbe, S., Proetzsch, R., Fahn, J., Piwernetz, K., and Landgraf, R. (1999) Screening of diabetic patients for microalbuminuria in primary care--The PROSIT-Project. Proteinuria Screening and Intervention, *Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association 107*, 244-251.
13. Tomlinson, C., Marshall, J., and Ellis, J. E. (2008) Comparison of accuracy and certainty of results of six home pregnancy tests available over-the-counter, *Current medical research and opinion 24*, 1645-1649.
14. Voss, S. (1992) The usage of pregnancy tests in one health district, *British journal of obstetrics and gynaecology 99*, 1000-1003.
15. Anon. (1991) Self-monitoring to reduce the risk of preeclampsia, *Emergency Medicine 23*, 57, 61-52.
16. Barton, J. R., Istwan, N. B., Rhea, D., Collins, A., and Stanziano, G. J. (2006) Cost-savings analysis of an outpatient management program for women with pregnancy-related hypertensive conditions, *Disease Management 9*, 236-241.
17. Cartwright, W., Dalton, K. J., Swindells, H., Rushant, S., and Mooney, P. (1993) Home measurement of pregnancy hypertension, *Professional Care of Mother & Child 3*, 8-9.
18. Kennedy, S. (1991) Monitoring hypertension in pregnancy. Home self-testing of blood pressure levels, *Professional Nurse 6*, 566-568.
19. Heidland, A., Bahner, U., Deetjen, A., Gotz, R., Heidbreder, E., Schafer, R., and Teschner, M. (2009) Mass-screening for early detection of renal disease: benefits and limitations of self-testing for proteinuria, *Journal of nephrology 22*, 249-254.
20. Nielen, M. M., Schellevis, F. G., and Verheij, R. A. (2009) The usefulness of a free self-test for screening albuminuria in the general population: a cross-sectional survey, *BMC public health 9*, 381.
21. Peele, J. D., Jr., Gadsden, R. H., and Crews, R. (1977) Semi-automated vs. visual reading of urinalysis dipsticks, *Clinical chemistry 23*, 2242-2246.

22. Waugh, J. J., Clark, T. J., Divakaran, T. G., Khan, K. S., and Kilby, M. D. (2004) Accuracy of urinalysis dipstick techniques in predicting significant proteinuria in pregnancy, *Obstetrics and gynecology 103*, 769-777.
23. Phelan, L. K., Brown, M. A., Davis, G. K., and Mangos, G. (2004) A prospective study of the impact of automated dipstick urinalysis on the diagnosis of preeclampsia, *Hypertension in pregnancy : official journal of the International Society for the Study of Hypertension in Pregnancy 23*, 135-142.
24. Tuffnell, D. J., Jankowicz, D., Lindow, S. W., Lyons, G., Mason, G. C., Russell, I. F., and Walker, J. J. (2005) Outcomes of severe pre-eclampsia/eclampsia in Yorkshire 1999/2003, *BJOG : an international journal of obstetrics and gynaecology 112*, 875-880.
25. Pre-eclampsia, A. o. (2012) Your Questions Answered, *http://www.apec.org.uk/faq.html#2*.
26. Cottrell, E., McMillan, K., and Chambers, R. (2012) A cross-sectional survey and service evaluation of simple telehealth in primary care: what do patients think?, *BMJ open 2*.
27. Goh, J. T., and Krause, H. (2002) A prospective observational study on the accuracy of patient self-testing of urine at an antenatal clinic, *The Australian & New Zealand journal of obstetrics & gynaecology 42*, 67-68.
28. Bell, S. C., Halligan, A. W., Martin, A., Ashmore, J., Shennan, A. H., Lambert, P. C., and Taylor, D. J. (1999) The role of observer error in antenatal dipstick proteinuria analysis, *British journal of obstetrics and gynaecology 106*, 1177-1180.
29. Thangaratinam, S., Gallos, I. D., Meah, N., Usman, S., Ismail, K. M., and Khan, K. S. (2011) How accurate are maternal symptoms in predicting impending complications in women with preeclampsia? A systematic review and meta-analysis, *Acta obstetricia et gynecologica Scandinavica 90*, 564-573.
30. Bahasadri, S., Kashanian, M., and Khosravi, Z. (2011) Comparison of pregnancy outcome among nulliparas with and without microalbuminuria at the end of the second trimester, *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics 115*, 34-36.
31. McCauley, M., and Dornan, J. (2011) A cheap and efficient test to help with detection and monitoring of patients with pre-eclampsia *Irish journal of Medical science 180*, S141.
32. Jones, J. S., Istwan, N. B., Jacques, D., Coleman, S. K., and Stanziano, G. (2002) Is 34 weeks an acceptable goal for a complicated singleton pregnancy?, *Manag Care 11*, 42-47.
33. de Borst, J., Nielen, M. M., Verheij, R. A., and Schellevis, F. G. (2011) Increased incidence of kidney diseases in general practice after a nationwide albuminuria self-test program, *BMC family practice 12*, 81.
34. Piehlmeier, W., Renner, R., Kimmerling, T., Schramm, W., Garbe, S., Proetzsch, R., Fahn, J., Piwernetz, K., and Landgraf, R. (1998) Evaluation of the Micral-Test S, a qualitative immunologic patient self-test for microalbuminuria: the PROSIT project. Proteinuria Screening and Intervention, *Diabetic medicine : a journal of the British Diabetic Association 15*, 883-885.
35. Barton, J. R., and Sibai, B. M. (2008) Prediction and prevention of recurrent preeclampsia, *Obstetrics and gynecology 112*, 359-372.

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This report was prepared by the Primary Care Diagnostic Horizon Scanning Centre Oxford
Authors: Katherine Tucker*, Eleanor Brunt*, Matthew Thompson, Christopher P. Price, Richard J McManus, Carole Crawford, Carl Heneghan, Annette Plüddemann.
**These authors contributed equally.*
Contact details: Dr. Annette Plüddemann; Email: dec@phc.ox.ac.uk