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BMJ uncertainties paper

Uncertainties: Monitoring type 2 diabetes, chronic kidney disease and hypertension in primary care. Are the guidelines evidence based?

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Box 1: What you need to know

1. Current UK guidelines for monitoring type 2 diabetes, chronic kidney disease and hypertension are largely based on expert opinion; robust evidence for optimal monitoring strategies and testing intervals is lacking.
2. Unnecessary testing in primary care can lead to false positives and false negatives, increase workload for clinicians, and increase costs for the health service.
3. Patients and healthcare professionals should be aware of these uncertainties, when making shared decisions about chronic disease monitoring.

Pathology tests have a unique place in chronic disease management. They are used to guide disease management, assess risk and compliance, enable early detection of adverse events, complications and development of secondary diseases. Primary care clinicians rely on guidelines for common chronic diseases such as type 2 diabetes, chronic kidney disease (CKD) and hypertension, to inform which tests they recommend to their patients and how frequently they should be done. With rates of pathology tests rising – at an estimated annual cost of £1.8bn to primary care in the UK¹ - and the potential for harm from overtesting, it is important to consider the evidence base for these recommendations. In this article, we review monitoring strategies in current UK guidelines for patients with type 2 diabetes, CKD, and hypertension, highlighting the uncertainties in these guidelines and the need for further research.

What is the evidence of uncertainty?

Box 2: Search strategy and guideline selection

We searched for published UK guidelines for the management of patients with type 2 diabetes, CKD1-3*, or hypertension using the following sources:

- National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guidelines Network (SIGN)
- Royal Colleges of Pathologists (RCPATH), Physicians, and General Practitioners
- Quality Outcomes Framework (QOF)

The following guidelines are included in this review:

- SIGN 116 Management of diabetes (2017)
- NICE CG127 Hypertension, the clinical management of primary hypertension in adults (2011)
- NICE CG182 Chronic Kidney disease (partial update) (2014)
- NICE NG28 Type 2 diabetes in adults (2015)
- NICE PH38 Evidence reviews (Type 2 diabetes: prevention in people at high risk) (2017)
- RCPATH: National minimum retesting intervals in pathology (2015)

We extracted any guidance on the use of laboratory tests for disease monitoring, the recommended frequency of testing, as well as the level of evidence on which the guidance was based. Tests recommended specifically in relation to medication monitoring are not included. The main limitation of this search strategy is that we did not search the primary literature itself. As a consequence, we may have missed evidence that is not picked up by the guidelines or was published after the guideline was written.

*CKD4 and 5 are generally monitored in secondary care and are therefore not included in our analysis.

Tests recommended by guidelines

For the chronic diseases reviewed the recommended tests are similar across guidelines. For instance, in type 2 diabetes, the monitoring tests recommended across guidelines are glycated haemoglobin (HbA1c), plasma glucose profile, and renal function tests such as estimated glomerular filtration rate (eGFR) and urine albumin:creatinine ratio (ACR) (Figure 1). Surprisingly, there is no clear recommendation in the SIGN 116 diabetes guideline to routinely measure HbA1c.² In CKD1-3, guidelines recommend testing for eGFR and ACR routinely, but not for serum calcium, phosphate, parathyroid hormone, and vitamin D (Figure 2). For hypertension, recommended monitoring tests are urine ACR, haematuria, electrolytes and creatinine, total and HDL cholesterol, renal profile, Hba1c, lipid profile, blood glucose, and eGFR (Figure 3).

Testing recommendations are scattered across most guidelines with no specific sections on monitoring. Consequently, clinicians need to read an entire guideline to get an overview of all recommended tests. An overview of monitoring recommendations from several guidelines is provided by the RCPATH national minimal retesting intervals report, but this document refers to outdated guidelines and awaits updating.³ We recommend that future guidelines include a summary section on monitoring.

Retesting intervals in guidelines are often missing or unclear

Recommended frequency of testing varies between guidelines or are sometimes not specified at all. For example, SIGN recommends annual testing of renal function in patients with diabetes,² whereas NICE suggest that test intervals should be determined by previous renal function results.⁴ NICE recommends that individual needs are taken into account when determining the frequency of monitoring, although it is not specified how testing intervals should be adjusted.⁵ 'Blood glucose' should be tested *routinely* in patients with hypertension to screen for diabetes according to NICE, but without stating the frequency.⁶

Robust evidence for optimal monitoring strategies and testing intervals is lacking

The majority of these recommendations are based on expert opinion, provided by the respective guideline development groups. None of the recommendations are solely based on evidence. Where evidence is cited it does not address the fundamental question of whether the test in question is necessary or beneficial. For instance, in support of ACR monitoring, SIGN diabetes guideline cites a meta-analysis of 10 diagnostic cohort studies in diabetic patients.²⁷ However, these studies investigate test performance of ACR, but not whether ACR monitoring has an impact on disease progression or mortality in diabetes patients. eGFR and ACR monitoring recommendations in the NICE CKD guideline are supported by 11 retrospective cohort studies.⁴ However, the evidence of these 11 studies could not be meta-analysed due to substantial variation in the reference groups used, and there was a lack of literature addressing optimal frequency of testing. Evidence was cited to justify a recommendation not to monitor a blood marker in one instance, namely parathyroid hormone monitoring in CKD.¹⁴ Four cross-sectional studies showed that parathyroid hormone increased in early stages of CKD, but because there was no consensus that patients with modestly elevated parathyroid hormone benefit from treatment, the NICE guideline development group recommends that parathyroid hormone should not be monitored in patients with stage 1, 2 and 3 CKD.

There is no evidence to support frequency of testing of any test, in any of the guidelines. Recommendations regarding frequency of testing are entirely based on expert opinion.

Is ongoing research likely to provide relevant evidence?

ClinicalTrials.gov, a clinical trial registry, was searched for studies addressing optimising chronic disease monitoring, using combinations of the following search terms: “type 2 diabetes”, “chronic kidney disease”, “hypertension”, “primary care”, “general practice”, “laboratory test”, and “monitoring”. No relevant ongoing studies were identified. There is a lack of scientific studies that address optimal monitoring of chronic diseases. Current studies focus of the diagnostic or prognostic accuracy of certain tests, but there is significant uncertainty about how to determine optimal testing frequency or how to evaluate whether monitoring is appropriate. Uncertainties as to which tests should be recommended to monitor people with chronic conditions, and how frequently they should be tested, can only be clarified if additional evidence can be generated.

Recommendations for future research

Research should address the following question: what is the optimal monitoring strategy for type 2 diabetes, CKD, and hypertension patients? This includes both ‘which tests should be used’, as well as ‘what is the optimal frequency of testing’. There is a gap in the evidence on the benefits of repeated testing on patient outcomes, i.e. disease progression, development of secondary diseases, quality of life, and mortality. Although an RCT would provide the highest level of evidence, this may not be feasible as a long follow-up will be needed to determine the effect on patient outcomes and randomising a group to a ‘no monitoring’ condition may be considered unethical. An observational study may be conducted instead. The large variation between regions in testing may allow comparison of patient outcomes with certain chronic diseases in ‘low’ and ‘high’ monitoring regions, although there would be important sources of bias and confounding to consider in such an analysis. The populations in ‘low’ and ‘high’ monitoring regions may be inherently different, for example with different sociodemographic or age profiles, and it can be challenging to account for all these differences.

Further research is required, and rigorous research methods should be developed to enable evidence-based monitoring of chronic diseases. This evidence should feed into guidance. When electronic testing panels are introduced in primary care, these should be flexible enough that they can be updated regularly as new evidence becomes available.

What should we do in the light of the uncertainty?

We recommend using the current guidelines where clear testing recommendations are given, as they are based on the best available evidence; these guideline recommendations should feed into, rather than over-ride, discussions with patients that incorporate their values and preferences. In the absence of clear evidence, it is all the more important that clinicians consider with their patients which tests are likely to influence disease management. GPs should ensure that there is a clear clinical rationale for each test that they perform. As chronic disease monitoring is often delegated to nursing staff or healthcare assistants, GPs should consider offering training about these uncertainties and potential harms of over-testing to the wider primary care team.

Shared decision making

Patients' values and preferences about monitoring should always be taken into account. Some patients may prefer more frequent testing, others will opt for less. Information about testing, including the uncertainties raised here, should be shared with patients to promote shared decision making (box 4). We recommend that clinicians explain to patients that testing is not always a good thing, and that there may be harms associated with over-testing.

Avoiding unnecessary testing

There may be a tendency in the light of uncertainty for GPs or other clinicians involved in chronic disease monitoring to err on the side of caution and request additional or more frequent tests 'just in case'. Another reason to do more tests than recommended is to 'make the most of a blood drawing', i.e. adding monitoring tests before they are due when taking blood for another reason. Unnecessary testing in a low prevalence setting such as primary care is more likely to lead to false positives, which in turn can lead to cascades of follow-up testing.^{8 11} This can generate anxiety for patients, increased workload for doctors, and increased costs for the health service.^{9 10} False negative results, on the other hand, may lead to false reassurances and delayed diagnosis.¹¹

A substantial proportion of pathology testing may be unnecessary, or even inappropriate. In one study of cholesterol testing rates in Oxfordshire, 42-79% of cholesterol tests were estimated as potentially unnecessary.¹² However, there is no consensus on what an 'inappropriate' test is and estimates of inappropriate test ordering vary substantially (0.2%–100%).¹³ Most studies examining inappropriate testing, compare testing rates to guideline recommendations, rather to robust evidence on what constitutes an "appropriate" or "inappropriate" test.

Developing ‘test groups’ for pathology test requests

Laboratory test software often allows users to create ‘test groups’ so that users can order a panel of tests for a given chronic disease with one click. Regional test groups may help reduce unwarranted variation in testing for monitoring chronic diseases and reduce overall testing rates.¹⁴ We are aware that practices often develop their own ‘test groups’ or ‘practice profiles’, and these may include other tests, such as full blood count, liver function tests, and lipid profiles, in addition to tests recommended by current guidelines. In the absence of a clear clinical rationale, any extra monitoring tests are essentially functioning as screening tests for occult disease. We recommend such screening should be avoided given the absence of clear benefits and significant risks of false positives.

Box 3: How patients were involved in the creation of this article

We held a discussion workshop with members of the CLAHRC West Health Systems Panel, which aims to discuss projects of general health relevance, to gather their views on testing for chronic conditions. Participants had chronic conditions requiring blood test monitoring, or family members with chronic conditions.

From a patient perspective which tests are done is rather 'hidden' and they felt that the GP did not always explain what the tests are. They were surprised that guidelines about monitoring are largely based on expert opinion (*"I thought the NHS was run on evidence", one participant said*) and acknowledged that there is an urgent need to fill this knowledge gap. There is a general expectation that tests results are always 100% accurate (*"they do thousands of these, it'll be accurate"*) and that overtesting can not cause any harms (*"Testing can't quite actually harm someone can it?"*). This feedback informed the information in the "what patients need to know" box.

Box 4: What patients need to know

In our view, more frequent testing is rarely helpful for patients, and tends to lead to unnecessary follow-up testing, which in turn can lead to unnecessary invasive investigations. We believe, as supported by our focus group, that patients are generally receptive to having these risks and uncertainties explained to them and value this honesty from their clinicians. At the moment it is not known what the optimal way of monitoring is to maximize patients' benefits. We believe that in light of the uncertainty decisions around testing should be shared with patients and patients' preferences and views should be taken into account.

Box 5: Education into practice

- When you order blood tests for your patients, is there always a clear rationale for each test? We recommend avoiding ‘just-in-case’ or ‘we-have-always-done’ tests unless there is a clear rationale for ordering them.
- How do you explain to patients which tests they are having and why? How do you discuss the limitations of blood tests with patients?
- Do you use local practice protocols for blood tests in patients with chronic diseases? Do these contain any extra tests in addition to those recommended by current guidelines?
- The frequency of testing is not evidence based, however recommendations for annual testing seem a reasonable practical choice until better evidence is available.
- Think about the last time you talked to a patient about blood test results, to what extent do you think the patient understood what the test results meant for them?

Competing interest statement

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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Contributorship statement

ME: Identifying relevant guidelines, data extraction, writing of the manuscript.

RP: Building data extraction database, checking data extraction, critically revising the manuscript.

JW: Clinical advice, writing of the manuscript.

PW: Conception of the work, critically revising the manuscript.

Figure 1: Guidelines and evidence for type 2 diabetes monitoring tests.

Tests are referred to by the same names as in each relevant guideline. See Box 2 for full names included guidelines. Abbreviations: ACR, albumin creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HbA1c, haemoglobin A1c; NICE, National Institute for Health and Care Excellence; RCPATH, Royal College of Pathologists; SIGN; Scotland Intercollegiate Guidelines Network.

Figure 2: Guidelines and evidence for chronic kidney disease 1-3 (CKD)

Tests are referred to by the same names as in each relevant guideline. See Box 2 for full names included guidelines. Abbreviations: ACR, albumin creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NICE, National Institute for Health and Care Excellence; PTH, Parathyroid hormone; RCPATH, Royal College of Pathologists; SIGN; Scotland Intercollegiate Guidelines Network.

Figure 3: Guidelines and evidence for hypertension

Tests are referred to by the same names as in each relevant guideline. See Box 2 for full names included guidelines. Abbreviations: ACR, albumin creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HbA1c, haemoglobin A1c; HDL, high -density-lipoprotein; NICE, National Institute for Health and Care Excellence; RCPATH, Royal College of Pathologists; SIGN; Scotland Intercollegiate Guidelines Network.

References

1. O'Sullivan JW, Stevens S, Hobbs FDR, et al. Temporal trends in use of tests in UK primary care, 2000-15: retrospective analysis of 250 million tests. *BMJ* 2018;363:k4666. doi: 10.1136/bmj.k4666 [published Online First: 2018/11/30]
2. Scottish Intercollegiate Guidelines Network (SIGN). 116 Management of diabetes. *A national clinical guideline* 2010
3. Lang T, Croal B. National minimum retesting intervals in pathology: A final report detailing consensus recommendations for minimum retesting intervals for use in pathology. *The Royal College of Pathologists* 2015
4. National Institute for Health and Care Excellence (NICE). Clinical Guideline 182. Chronic kidney disease (partial update). *National Clinical Guideline Centre* 2014
5. National Institute for Health and Care Excellence (NICE). Clinical Guideline Update (NG28). Type 2 diabetes in adults. *Internal Clinical Guidelines Team* 2015
6. National Institute for Health and Clinical Excellence (NICE). Clinical Guideline 127. Hypertension. *National Clinical Guideline Centre* 2011
7. Ewald B, Attia J. Which test to detect microalbuminuria in diabetic patients? A systematic review. *Aust Fam Physician* 2004;33(7):565-7, 71. [published Online First: 2004/08/11]
8. Deyo RA. Cascade effects of medical technology. *Annu Rev Public Health* 2002;23:23-44. doi: 10.1146/annurev.publhealth.23.092101.134534 [published Online First: 2002/03/23]
9. Hobbs FDR, Bankhead C, Mukhtar T, et al. Clinical workload in UK primary care: a retrospective analysis of 100 million consultations in England, 2007-14. *Lancet* 2016;387(10035):2323-30. doi: 10.1016/S0140-6736(16)00620-6 [published Online First: 2016/04/10]
10. Petrie KJ, Sherriff R. Normal diagnostic test results do not reassure patients. *Evid Based Med* 2014;19(1):14. doi: 10.1136/eb-2013-101393 [published Online First: 2013/07/13]
11. Bennett CM, Guo M, Dharmage SC. HbA(1c) as a screening tool for detection of Type 2 diabetes: a systematic review. *Diabet Med* 2007;24(4):333-43. doi: 10.1111/j.1464-5491.2007.02106.x [published Online First: 2007/03/21]
12. Doll H, Shine B, Kay J, et al. The rise of cholesterol testing: how much is unnecessary. *Br J Gen Pract* 2011;61(583):e81-8. doi: 10.3399/bjgp11X556245 [published Online First: 2011/02/01]
13. O'Sullivan JW, Albasri A, Nicholson BD, et al. Overtesting and undertesting in primary care: a systematic review and meta-analysis. *BMJ Open* 2018;8(2):e018557. doi: 10.1136/bmjopen-2017-018557 [published Online First: 2018/02/15]
14. Whiting D, Croker R, Watson J, et al. Optimising laboratory monitoring of chronic conditions in primary care: a quality improvement framework *BMJ Open Quality* 2019;8(e000349) doi: 10.1136/bmjopen-2018-000349