



PRACTICE

UNCERTAINTIES

Are guidelines for monitoring chronic disease in primary care evidence based?

Martha M C Elwenspoek *research associate*^{1,2}, Rita Patel *senior research associate*^{1,2}, Jessica C Watson *GP, doctoral research fellow*^{1,2}, Penny Whiting *senior lecturer, programme director of MSc in epidemiology*^{1,2}

¹National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care West (NIHR CLAHRC West), University Hospitals Bristol NHS Foundation Trust, Bristol, UK; ²Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK

What you need to know

- 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
- Unnecessary testing in primary care can lead to false positive and false negative results, increased workload for clinicians, and increased costs for the health service
- 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 management of chronic diseases. They are used to guide disease management; assess risk and compliance; and 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, and hypertension to inform them which tests they should recommend to their patients and how frequently these 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 over-testing, 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, chronic kidney disease, and hypertension (**box 1**), highlighting the uncertainties in these guidelines and the need for further research.

Box 1: Search strategy and guideline selection

We searched for published UK guidelines for the management of patients with type 2 diabetes, chronic kidney disease stages 1-3², 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)²
- NICE CG127 Hypertension, the clinical management of primary hypertension in adults (2011)³
- NICE CG182 Chronic kidney disease (partial update) (2014)⁴
- NICE NG28 Type 2 diabetes in adults (2015)⁵
- NICE PH38 Evidence reviews (Type 2 diabetes: prevention in people at high risk) (2017)⁵
- RCPath: National minimum retesting intervals in pathology (2015)⁷

We extracted any guidance on the use of laboratory tests for disease monitoring, the recommended frequency of testing, and 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.

*Chronic kidney disease stages 4 and 5 are generally monitored in secondary care and are therefore not included in our analysis.

What is the evidence of uncertainty?

Tests recommended by guidelines

For the chronic diseases reviewed, the recommended tests are similar across guidelines. In the case of type 2 diabetes the monitoring tests recommended across guidelines are glycated haemoglobin (HbA_{1c}), plasma glucose profile, and renal function

Correspondence to: M M C Elwenspoek martha.elwenspoek@bristol.ac.uk

This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. The series advisers are Sera Tort, clinical editor, Nai Ming Lai, clinical editor, and David Tovey, editor in chief, the Cochrane Library. To suggest a topic for this series, please email us at uncertainties@bmj.com

tests such as estimated glomerular filtration rate (eGFR) and urine albumin:creatinine ratio (ACR) (fig 1). Surprisingly, there is no clear recommendation in the SIGN 116 diabetes guideline to measure HbA_{1c} routinely.²

For chronic kidney disease (stages 1-3), guidelines recommend measuring eGFR and ACR routinely, but not serum calcium, phosphate, parathyroid hormone, or vitamin D (fig 2).

For hypertension, recommended monitoring tests are urine ACR, haematuria, electrolytes and creatinine, total and high density lipoprotein (HDL) cholesterol, renal profile, HbA_{1c}, lipid profile, blood glucose, and eGFR (fig 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.⁷ 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 is 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 the frequency of such routine testing is not stated.³

Robust evidence for optimal monitoring strategies and testing intervals is lacking

Most 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, the SIGN diabetes guideline cites a meta-analysis of 10 diagnostic cohort studies in patients with diabetes.⁸ However, these studies investigate test performance of ACR, not whether ACR monitoring has an impact on disease progression or mortality in patients with diabetes. The NICE chronic kidney disease guideline's recommendations for monitoring eGFR and ACR are supported by 11 retrospective cohort studies.⁴ However, the evidence from these 11 studies could not undergo meta-analysis because of substantial variation in the reference groups used, and there was a lack of data addressing optimal frequency of testing. Evidence to justify a recommendation not to monitor a blood marker was cited in one instance, namely parathyroid hormone monitoring in chronic kidney disease.⁹ Four cross-sectional studies showed that parathyroid hormone increased in early stages of chronic kidney disease. However, 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, or 3 of chronic kidney disease.

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?

We searched ClinicalTrials.gov, a clinical trial registry, 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.

Recommendations for future research

Research should address the following question: What is the optimal monitoring strategy for type 2 diabetes, chronic kidney disease, and hypertension? This includes the question of 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 (that is, disease progression, development of secondary diseases, quality of life, and mortality). Although a randomised controlled trial 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 no monitoring 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 monitoring" 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 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 override, 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 the 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 discussed with patients to promote shared decision making (box 2). 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.

Box 2: What patients need to know about monitoring chronic diseases

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. Patients are generally receptive to having these risks and uncertainties explained to them and value this honesty from their clinicians.

At present, it is not known what the optimal way of monitoring is to maximise patients' benefits. In light of this uncertainty, we believe that decisions around testing should be shared with patients and that patients' preferences and views should be taken into account.

Avoiding unnecessary testing

There may be a tendency in the light of these uncertainties 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"—that is, 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.^{10,11} This can generate anxiety for patients, increased workload for doctors, and increased costs for the health service.^{12,13} 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.¹⁴ However, there is no consensus on what an inappropriate test is, and estimates of inappropriate test ordering vary substantially (0.2%–100%).¹⁵ Most studies examining inappropriate testing compare testing rates to guideline recommendations rather than 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.⁹ We are aware that general 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.

Education into practice

- When you order blood tests for your patients, is there always a clear rationale for each test?
- 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 unnecessary extra tests in addition to those recommended by current guidelines?
- 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?

How patients were involved in the creation of this article

We held a discussion workshop with members of the CLAHRC West Health Systems Panel to gather their views on testing for chronic conditions. Participants had chronic conditions requiring blood test monitoring or had family members with chronic conditions. Participants told us that which tests are done is rather "hidden" and they felt that their GPs did not always explain what the tests are. They were surprised that guidelines about monitoring are largely based on expert opinion and acknowledged that there is an urgent need to fill this knowledge gap. There was a general expectation that tests results are always 100% accurate and that over-testing could not cause any harms. This feedback informed the content of the "What patients need to know" box.

Contributors: MMCE identified relevant guidelines, performed data extraction, and helped write the manuscript. RP built the data extraction database, checked data extraction, and critically revised the manuscript. JCW provided clinical advice and helped write the manuscript. PW conceived of the work and critically revised the manuscript.

Competing interests: We have read and understood BMJ policy on declaration of interests and have no relevant interests to declare.

Funding: The research is supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care West (CLAHRC West) at University Hospitals Bristol NHS Foundation Trust. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health and Social Care. JCW is funded by a Doctoral Research Fellowship from the National Institute for Health Research (NIHR-2016-09-034).

Provenance and peer review: Commissioned, based on an idea from the authors; externally peer reviewed.

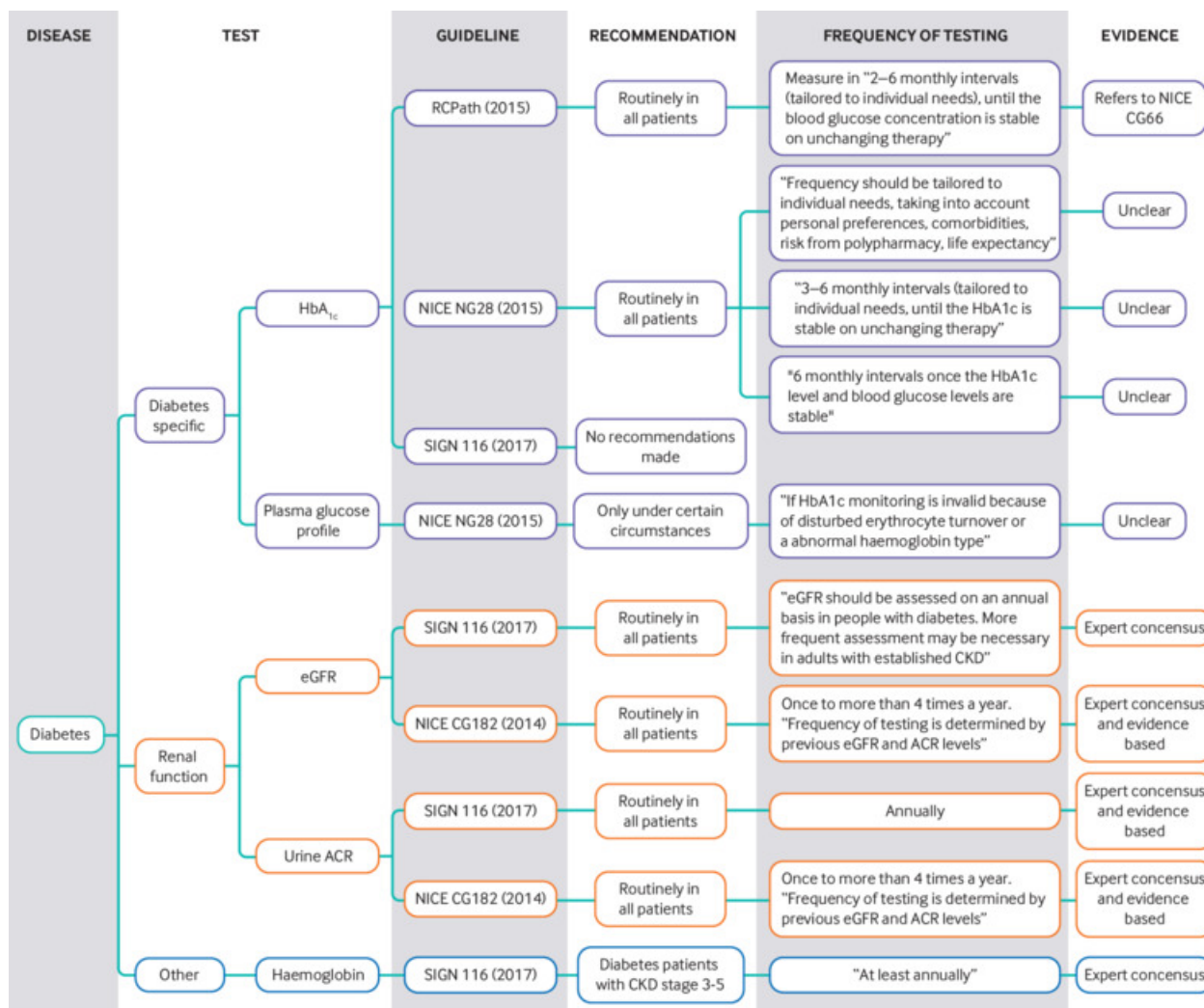
- 1 O'Sullivan JW, Stevens S, Hobbs FDR, et al. Temporal trends in use of tests in UK primary care, 2000-15: retrospective analysis of 250 million tests. *BMJ* 2018;363:k4666. 10.1136/bmj.k4666 30487169
- 2 Scottish Intercollegiate Guidelines Network (SIGN). *116 Management of diabetes: A national clinical guideline*. 2010. www.sign.ac.uk/assets/sign116.pdf.
- 3 National Institute for Health and Clinical Excellence. Hypertension in adults: diagnosis and management (clinical guideline CG127). 2011, updated 2016. www.nice.org.uk/guidance/cg127.
- 4 National Institute for Health and Care Excellence. Chronic kidney disease in adults: assessment and management (Clinical Guideline CG182). 2014, updated 2015. www.nice.org.uk/guidance/cg182.
- 5 National Institute for Health and Care Excellence. Type 2 diabetes in adults: management (NICE guideline NG28). 2015, updated 2017. www.nice.org.uk/guidance/ng28.
- 6 National Institute for Health and Clinical Excellence. Type 2 diabetes: prevention in people at high risk (public health guideline PH38). 2012, updated 2017. www.nice.org.uk/guidance/ph38.
- 7 Lang T, Croal B. National minimum retesting intervals in pathology: A final report detailing consensus recommendations for minimum retesting intervals for use in pathology. Royal College of Pathologists, 2015. www.rcpath.org/uploads/assets/uploaded/10558323-8ee4-4a39-84b53cb5dd0ec61b.pdf.
- 8 Ewald B, Attia J. Which test to detect microalbuminuria in diabetic patients? A systematic review. *Aust Fam Physician* 2004;33:565-7. 571.15301181
- 9 Whiting D, Croker R, Watson J, Brogan A, Walker AJ, Lewis T. Optimising laboratory monitoring of chronic conditions in primary care: a quality improvement framework. *BMJ Open* 2019;8:e000349. 10.1136/bmjopen-2018-000349 30997410
- 10 Deyo RA. Cascade effects of medical technology. *Annu Rev Public Health* 2002;23:23-44. 10.1146/annurev.pubhealth.23.092101.134534 11910053
- 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;24:333-43. 10.1111/j.1464-5491.2007.02106.x 17367307
- 12 Hobbs FDR, Bankhead C, Mukhtar T, et al. National Institute for Health Research School for Primary Care Research. Clinical workload in UK primary care: a retrospective analysis of 100 million consultations in England, 2007-14. *Lancet* 2016;387:2323-30. 10.1016/S0140-6736(16)00620-6 27059888

- 13 Petrie KJ, Sherriff R. Normal diagnostic test results do not reassure patients. *Evid Based Med* 2014;19:14. 10.1136/eb-2013-101393 23846986
- 14 Doll H, Shine B, Kay J, James T, Glasziou P. The rise of cholesterol testing: how much is unnecessary. *Br J Gen Pract* 2011;61:e81-8. 10.3399/bjgp11X556245 21276328

- 15 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:e018557. 10.1136/bmjopen-2017-018557 29440142

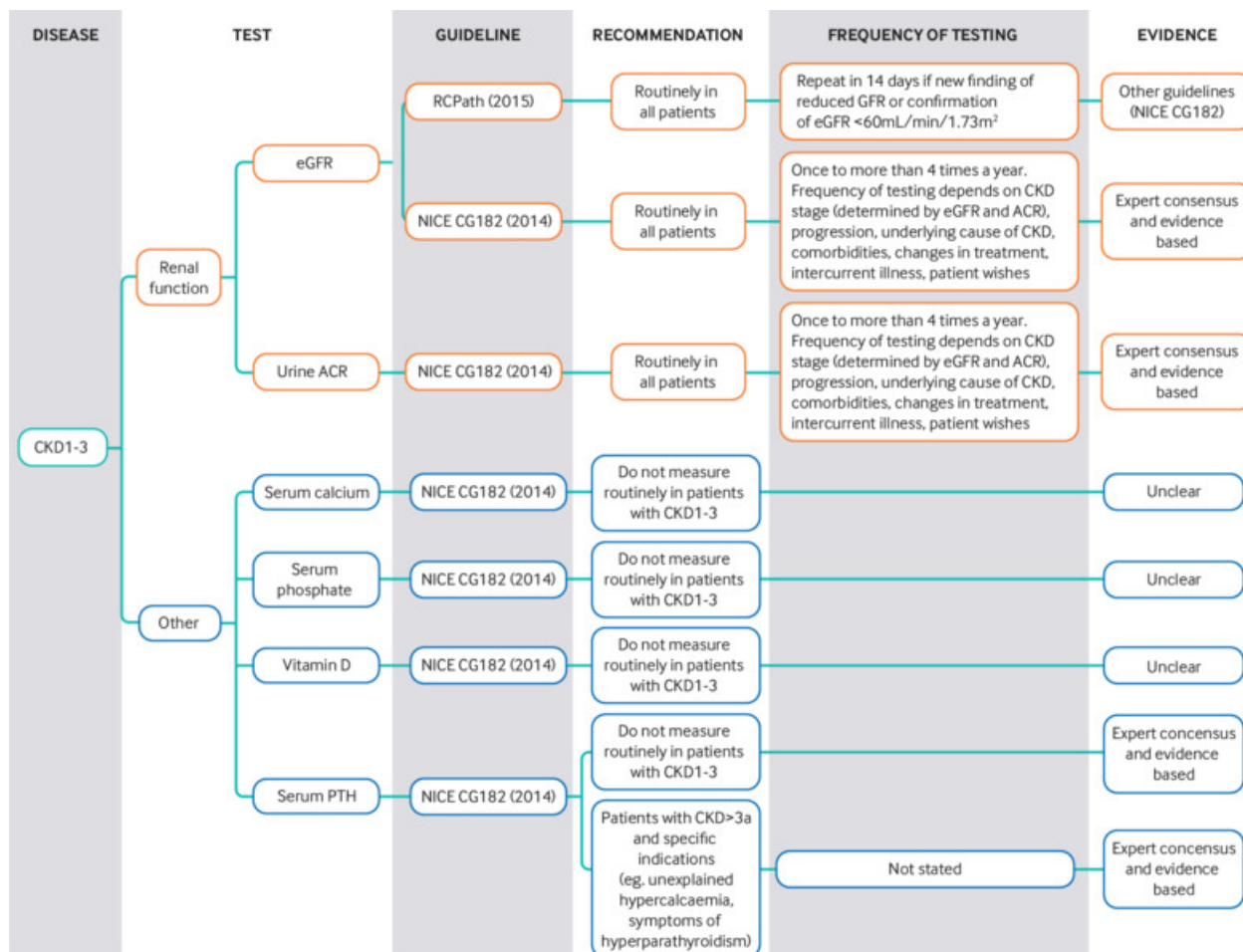
Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to <http://group.bmj.com/group/rights-licensing/permissions>

Figures



ACR = albumin:creatinine ratio; eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; RCPATH = Royal Colleges of Pathologists; NICE = National Institute for Health and Care Excellence; SIGN = Scottish Intercollegiate Guidelines Network

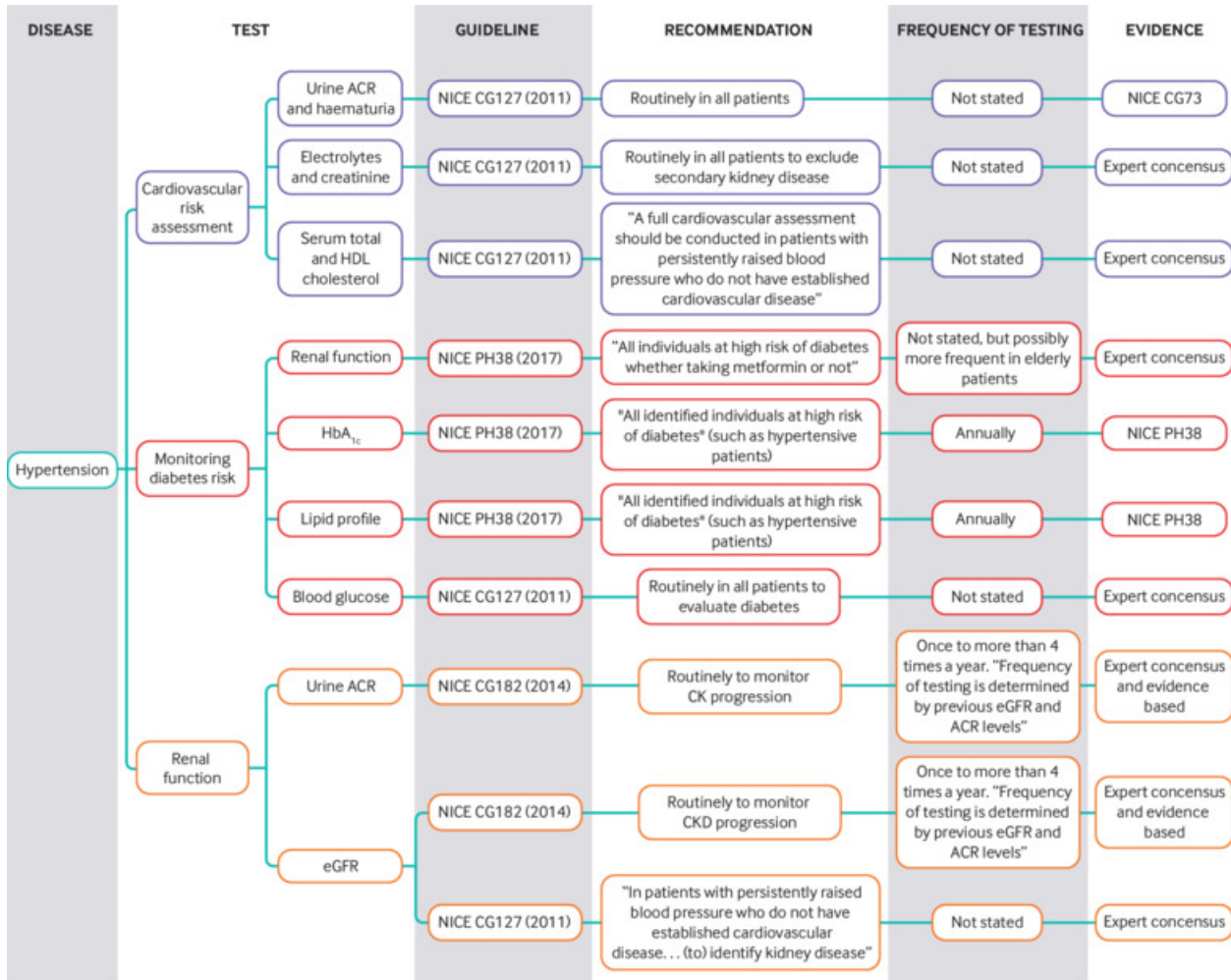
Fig 1 Guidelines and evidence for tests to monitor type 2 diabetes. Tests are referred to by the same names as in each relevant guideline. See [box 1](#) for details of included guidelines



CKD 1-3 = chronic kidney disease stages 1 to 3; ACR = albumin:creatinine ratio; PTH = parathyroid hormone; eGFR = estimated glomerular filtration rate; RCPATH = Royal Colleges of Pathologists; NICE = National Institute for Health and Care Excellence

Fig 2 Guidelines and evidence for tests to monitor chronic kidney disease (CKD) stages 1-3. Tests are referred to by the same names as in each relevant guideline. See [box 1](#) for details of included guidelines

BMJ: first published as 10.1136/bmj.l2319 on 13 June 2019. Downloaded from <http://www.bmj.com/> on 3 July 2019 by Richard Alan Pearson. Protected by copyright.



ACR = albumin:creatinine ratio; HDL = high density lipoprotein; eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; NICE = National Institute for Health and Care Excellence

Fig 3 Guidelines and evidence for tests to monitor hypertension. Tests are referred to by the same names as in each relevant guideline. See [box 1](#) for details of included guidelines