Guidelines for screening with urinary dipsticks differ substantially – a systematic review

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ABSTRACT

INTRODUCTION: Urinary dipsticks are frequently used for screening as part of health checks and at hospital admission, but the benefits and harms of this are unknown.

METHODS: Health authorities and a selection of specialist societies in nine countries were identified through internet searches. Recommendations on dipstick screening at health checks or hospital admission were sought on websites as well as by email contact. Other relevant organisations encountered were also included. Recommendations were summarised narratively.

RESULTS: A total of 67 organisations were included. No positive or negative recommendations were found regarding screening with combined dipsticks. Screening for bacteriuria in non-pregnant persons was discouraged, while guidance on screening with dipsticks for haemoglobin, glucose and protein was uncommon and often unclear.

CONCLUSION: Useful guidance was rare. Practitioners are largely left to themselves when deciding whether or not to offer screening with urinary dipsticks. This situation needs to be remedied as benefit has not been shown and because screening with dipsticks can cause harm.

SYSTEMATIC REVIEW

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A frequently used component of general health checks is analysis of the urine [1, 2], which is often performed as a urinary dipstick test [3]. Patients admitted to hospital are also often routinely screened with a urinary dipstick, but the prevalence of this practice is unknown and likely varies between countries and regions. Use of urinary dipsticks may lead to detection of a wide array of serious conditions, e.g. urological cancers or glomerulonephritis. Early detection through screening could lead to improved prognosis, but it could also lead to unnecessary follow-up investigations such as kidney biopsies, cystoscopies, unnecessary antibiotic treatment, long-term follow-up of inconsequential abnormalities and psychological stress in healthy persons.

Dipsticks frequently combines testing for multiple substances, e.g. protein, glucose, blood, nitrite and leukocytes, which complicates the assessment of such testing. Screening for protein or albumin has been recommended for persons with certain risk factors [4-6] and is common in some countries, although there have been no trials on this [7]. In Japan, the general population has been systematically screened for proteinuria and haematuria with dipsticks for decades [8]. Enthusiasm for screening for asymptomatic microscopic haematuria has declined [9, 10], although not entirely [11, 12]. Screening asymptomatic non-pregnant persons for leukocytes, nitrite and glucose in the urine has fallen out of favour and it is unclear how often dipsticks are used for that purpose. However, it can be difficult to avoid as leukocytes and nitrite are frequently included in commonly used combined dipsticks.

There are no trials on screening for haemoglobin or protein in the urine [7, 10] and probably none on screening for glucose, leukocytes and nitrite. In other types of screening, trials have sometimes shown the benefits to be smaller than expected [13-16], and the harms greater [13, 14, 16]. In light of this lack of robust evidence, it is puzzling why screening with dipsticks is prevalent. One possible explanation may be that they are easy to use and are perceived as harmless. Furthermore, the idea that any early detection of disease is beneficial is widespread among clinicians and patients alike, despite evidence of over-diagnosis and other harms with several forms of screening [17].

It is the task of health authorities to provide recommendations on which interventions to use, both in sick and healthy people. Specialist societies also provide recommendations. The purpose of the present study was to find and describe existing recommendations on screening with urinary dipsticks, focusing on two types of screening: general health checks and routine screening of patients admitted to hospital.

METHODS

The search strategy was defined a priori, with the aim of limiting the workload while increasing the chance of finding the most important recommendations.

Six types of organisations were pre-specified: the main national health authority issuing guidance to health professionals and national professional societies for nephrology, urology, clinical biochemistry, general internal medicine, and general practice/family practice. Nine countries were pre-specified, based on the official language and on the likelihood of finding recommendations: Australia, Canada, Denmark, Ireland, New Zealand, Norway, Sweden, the United Kingdom and USA.

The internet was searched with Google to identify

the relevant organisations. When two organisations of the same kind from one country appeared equally important, they were both included. When online collections of guidelines were found, e.g. the National Guideline Clearinghouse (USA) or Helsebiblioteket (Norway), these were searched, too. Other organisations were also included when judged to be important, e.g. international organisations or charities, without first looking at the contents of their website.

The website of each included organisation was browsed for guidelines or recommendations on the topic and searched using relevant pre-specified keywords, when possible. The search terms were: urinary dipstick, dipstick, urinalysis, urine strip test, urine screening, routine urinalysis, routine dipstick, routine testing, routine admission testing, admission testing, bladder cancer AND screening, (haematuria OR haematuria) AND screening, kidney disease AND screening, renal disease AND screening, proteinuria AND screening, glomerulonephritis, diabetes AND screening, bacteriuria AND screening, cystitis AND screening, health check, health evaluation, health examination, albumin. The terms were modified to suit the individual search engines and were translated when needed.

Longer documents that might have contained guidance were also searched, e.g. health technology assessments. Finally, all included organisations were e-mailed and asked whether they knew of relevant guidelines, also guidelines issued by other organisations. Recommendations were sought regarding screening with combined dipsticks and common individual components: haemoglobin, protein or albumin, leukocytes and nitrite and glucose. Recommendations for screening of specific risk groups, e.g. people with diabetes or pregnant women, were not specifically sought out. When guidance on population-based screening programmes was found, it was included as such recommendations have relevance for screening in health checks.

Relevant text, including the reference, was copied into an Excel sheet. Information on whether the included websites linked to guidelines from other organisations was also recorded along with an indication of whether the organisation explicitly endorsed that guideline. The data collection was done in November and December 2010, and in January 2013 the websites were revisited to check for new guidelines and updates.

The results were summarised in tables and in narrative. No statistics were used.

RESULTS

A total of 67 organisations were included (**Figure 1**, **Table 1**). In six cases, more than one type of organisation from a country was included, in one case two websites from the same organisation were included, and in four cases two countries shared a specialist society. Three international specialist organisations, three charities and one guideline-producing network were also included because they appeared to be important sources of guidance. Of these, five were in nephrology, one in urology and one was general.

Health checks

Combined dipsticks

No recommendations were found on screening with combined dipsticks.

Haemoglobin

Only one organisation, the UK National Screening Committee, gave a recommendation regarding screening with dipsticks for haemoglobin, recommending against using them (**Table 2**) [18]. Nephrological and urological societies from the UK had a joint statement recommending against testing for haematuria in the absence of identifiable clinical reasons, but did not explicitly mention dipsticks [19].

Other organisations mentioned the topic without giving recommendations. Two stated that the evidence behind screening for bladder cancer was insufficient to determine the balance between benefits and harms [20, 21], two urological societies discussed the course of action when asymptomatic microscopic haematuria had been identified [22, 23], and a list of policy positions from one public authority stated “No policy” under screening for bladder cancer, while at the same time noting that it is “very common in general practice and often part of a routine medical examination” [24].

Leukocytes/nitrite

No organisations explicitly mentioned screening with dipsticks for leukocytes or nitrite, but four organisations

FIGURE 1

Overview of process. See Table 1 for names of included organisations and website addresses.

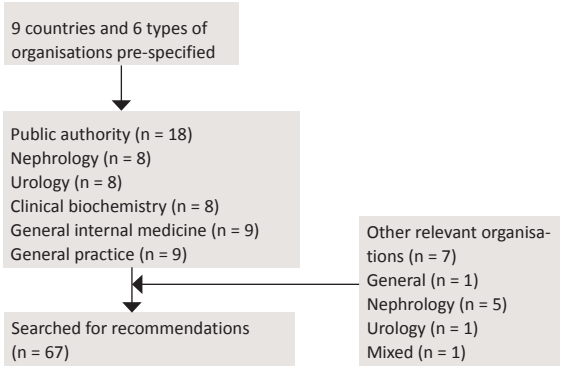

TABLE 1

List of organisations searched for recommendations.

Country	Organisation
Public authority	
Denmark	National Board of Health (www.sst.dk)
Sweden	Socialstyrelsen (www.socialstyrelsen.se), Statens Beredning för medicinsk Utvärdering (www.sbu.se)
Norway	The Norwegian Knowledge Centre for the Health Services, (Kunnskapssenteret, www.kunnskapssenteret.no/ and www.helsebiblioteket.no/ Retningslinjer)
UK	UK National Screening Committee (www.screening.nhs.uk), National Institute for Health and Clinical Excellence (www.nice.org.uk)
Ireland	Health Service Executive (www.hse.ie)
USA	United States Preventive Services Task Force (www.uspreventiveservicestaskforce.org/), Agency for Healthcare Research and Quality (www.ahrq.gov), National Guideline Clearinghouse (www.guideline.gov)
Canada	Canadian Task Force on Preventive Health Care (www.canadiantaskforce.ca), Public Health Agency of Canada (www.phac-aspc.gc.ca)
Australia	National Health and Medical Research Council (www.nhmrc.gov.au), Clinical Practice Guidelines Portal (www.clinicalguidelines.gov.au)
New Zealand	National Screening Unit (www.nsu.nz) (under the National Health Board), Ministry of Health (www.health.govt.nz/), New Zealand Guidelines Group (www.health.govt.nz/about-ministry/ministry-health-websites/new-zealand-guidelines-group)
Nephrology	
Denmark	Dansk Nefrologisk Selskab (www. nephrology.dk)
Sweden	Svensk Njurmedicinsk Förening (www.njur.se)
Norway	Norsk Nyremedisinsk Forening (www.nephro.no)
UK	The Renal Association (www.renal.org)
Ireland	Irish Nephrology Society (www.nephrology.ie)
USA	American Society of Nephrology (www.asn-online.org)
Canada	Canadian Society of Nephrology (www.csnscn.ca)
Australia	Australian and New Zealand Society of Nephrology (www.nephrology.edu.au)
New Zealand	Australian and New Zealand Society of Nephrology (www.nephrology.edu.au)
Urology	
Denmark	Dansk Urologisk Selskab (www.urologi.dk)
Sweden	Svensk Urologisk Förening (www.urologi.org)
Norway	Norsk Urologisk Forening (www.legeforeningen.no/nuf)
UK	British Association of Urological Surgeons (www.baus.org.uk)
Ireland	Irish Society of Urology (at the website of the Royal College of Surgeons in Ireland, www.rcsi.ie)
USA	American Urological Association (www.auanet.org)
Canada	Canadian Urological Association (www.cua.org)
Australia	Urological Society of Australia and New Zealand (www.usanz.org.au)
New Zealand	Urological Society of Australia and New Zealand (www.usanz.org.au)
Clinical biochemistry	
Denmark	Dansk Selskab for Klinisk Biokemi (www.dskb.dk)
Sweden	Svensk Förening för Klinisk kemi (www.kliniskkemi.org)
Norway	Norsk Forening for Medisinsk Biokjemi (legeforeningen.no/Fagmed/Norsk-forening-for-medisinsk-biokjemi)
UK	Association for Clinical Biochemistry (www.acb.org.uk)
Ireland	Association of Clinical Biochemists in Ireland (www.acbi.ie)
USA	American Association for Clinical Chemistry (www.aacc.org)
Canada	Canadian Society of Clinical Chemists (www.cscc.ca)
Australia	Australasian Association of Clinical Biochemists (www.aacb.asn.au)
New Zealand	Australasian Association of Clinical Biochemists (www.aacb.asn.au)
General internal medicine	
Denmark	Dansk Selskab for Intern Medicin (www.dsim.dk)
Sweden	Svensk Internmedicinsk Förening (www.sim.nu/sv)
Norway	Norsk Indremedisinsk Forening (legeforeningen.no/Fagmed/Norsk-indremedisinsk-forening)
UK	The Royal College of Physicians in London. (www.rcplondon.ac.uk)
Ireland	Irish Association of Internal Medicine (www.internalmedicine.ie)
USA	American College of Physicians (www.acponline.org), Society of General Internal Medicine (www.sgim.org)
Canada	Canadian Society of Internal Medicine (www.csimonline.com)
Australia	Internal Medicine Society of Australia and New Zealand (www.imsanz.org.au)
New Zealand	Internal Medicine Society of Australia and New Zealand (www.imsanz.org.au)
General practice	
Denmark	Dansk Selskab for Almen Medicin (www.dsam.dk)
Sweden	Svensk Förening för Allmänmedicin (www.sfam.se)
Norway	Norsk Forening for Allmennmedisin (www.legeforeningen.no/Fagmed/Norsk-forening-for-allmennmedisin)
UK	Royal College of General Practitioners (www.rcgp.org.uk)
Ireland	Irish College of General Practitioners (www.icgp.ie)
USA	American Academy of Family Physicians (www.aafp.org)
Canada	The College of Family Physicians of Canada (www.cfpc.ca)
Australia	The Royal Australian College of General Practitioners (www.racgp.org.au)
New Zealand	The Royal New Zealand College of General Practitioners (www.rnzcgp.org.nz)
Other	National Kidney Foundation (www.kidney.org/professionals/kdoqi), Kidney Disease: Improving Global Outcomes (www.kdigo.org), International Society of Nephrology (www.theisn.org), European Association of Urology (www.uroweb.org), Caring for Australasians with Renal Impairment (www.cari.org.au), Scottish Intercollegiate Guidelines Network (www.sign.ac.uk). European Renal Association – European Dialysis and Transplant Association (www.european-renal-best-practice.org)

TABLE 2

Summary of relevant identified content.

	Recommendation on dipsticks	Other relevant content
Combined	None	None
Haemoglobin	*The UK National Screening Committee [18]* "Screening for bladder cancer should not be offered" "Screening by urine dipstick testing for protein and blood is not recommended and should no longer take place" *Joint Statement by the Renal Association (UK) and the British Association of Urological Surgeons' joint statement [19]* "Urine testing for haematuria should only be performed for identifiable clinical reasons; there is currently no evidence to support opportunistic screening of the general population"	*The United States Preventive Services Task Force [20]* Concluded that the evidence is insufficient to determine the balance of benefits and harms of screening for bladder cancer in asymptomatic adults. *American Academy of family physicians [21]* "The AAFP concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for bladder cancer in asymptomatic adults" *American Urological Association [22]* Guideline on management on asymptomatic microscopic haematuria mentions that there is limited evidence behind screening for haematuria, but does not recommend against screening *Danish Urological Society [23]* In a guideline on bladder cancer, it is discussed what should be done if asymptomatic microscopic haematuria is identified. No recommendations about screening *The New Zealand National Screening Unit [24]* In an overview of policy positions, screening for bladder cancer is listed as "No policy"
Leukocytes/nitrite	*European Association of Urology [25]* Recommends that screening for asymptomatic bacteriuria should only be done in pregnant women and before invasive genitourinary procedures *United States Preventive Services Task Force [26]* "The available evidence continues to support screening for asymptomatic bacteriuria in pregnant women, but not in other groups of adults" *American Academy of Family Physicians [27]* "The AAFP recommends against screening for asymptomatic bacteriuria in men and nonpregnant women" *Royal Australian College of General Practitioners [28]* "Identifying and treating non-pregnant adults with asymptomatic bacteriuria does not improve outcomes and may increase antibiotic resistance"	None
Glucose	*Danish Health and Medicines Authority [29]* "Examination of the possible use of urine test strips for screening has not been included in this HTA report as it is regarded as an obsolete analysis in this connection"	*UK National Screening Committee [30]* "Policy position: General population screening should not be offered. Whole population screening has been assessed against the UK NSC criteria and does not meet a number of the criteria" "The UK National Screening Committee has identified the need for a Vascular Risk Management Programme, however, which includes diabetes." This refers to the NHS Health Check programme, which does not use dipsticks for glucose. *Joint statement from the Danish Society for Clinical Biochemistry, Danish College of General Practitioners and Danish Endocrinological Society [31]* "The working group recommends an intensified effort in detecting persons with unrecognised diabetes, but does not recommend general screening." No specific mention of dipsticks, but the rejection of general screening must also encompass dipsticks
Protein/albumin	*UK National Screening Committee [32]* "Policy position: A national screening programme for kidney disease is not recommended" "Screening by urine dip stick testing for protein and blood is not recommended and should no longer take place." (Found on website relating to screening for bladder cancer [18]) *Canadian Society of Nephrology [33]* Recommends against mass screening with dipsticks, but recommends screening high-risk groups using ACR or PCR	*The Royal Australian College of General Practitioners [28]* Recommends screening high risk people with BP, ACR and eGFR. "Dipstick urine test is not adequate to identify microalbuminuria" *Kidney Disease: Improving Global Outcomes (KDIGO) [34]* No recommendation, but makes a note that there appears to be no evidence supporting screening unselected populations *Scottish Intercollegiate Guidelines Network [35]* "Dipstick proteinuria (≥ 1+) can be used to identify patients at risk of subsequent end-stage renal disease and cardiovascular disease" "Urine dipstick testing cannot be used reliably in isolation to diagnose the presence or absence of proteinuria" *New Zealand National Screening Advisory Committee [36]* States that current policy is "Opportunistic screening and self-testing using a urine dip-stick" *U.S. Preventive Services Task Force [46]* "Concludes that the evidence is insufficient to assess the balance of benefits and harms of routine screening for chronic kidney disease (CKD) in asymptomatic adults. Mentions urine testing for albuminuria" *American Academy of Family Physicians [47]* "The AAFP concludes that the evidence is insufficient to assess the balance of benefits and harms for routine screening for chronic kidney disease (CKD) in asymptomatic adults. Common tests considered for CKD screening include creatinine-derived estimates of glomerular filtration rate (GFR) and urine testing for albumin"

ACR = albumin-creatinine ratio; BP = blood pressure; eGFR = estimated glomerular filtration rate; HTA = Health Technology Assessment; NHS = National Health Service; NSC = National Screening Committee; PCR = protein-creatinine ratio.

offered guidance on screening of healthy people for asymptomatic bacteriuria. All recommendations went against screening of non-pregnant asymptomatic persons [25-28].

Glucose

The only mention of screening for glucose with urinary dipsticks was in a health technology assessment report which noted that this technique was considered obsolete and would not be included in the report [29]. The UK National Screening Committee and a joint statement from three Danish specialist societies recommended that population screening for diabetes be avoided, without mentioning dipsticks, but both highlighted a need for increased detection of unrecognised diabetes [30, 31].

Protein/albumin

Two organisations unequivocally recommended avoiding screening with dipsticks for protein. One of these was the UK National Screening Committee, but the recommendation was found on the web page relating to screening for bladder cancer [18], while the page about screening for kidney disease did not mention dipsticks [32]. A 2008 guideline from the Canadian Society of Nephrology also recommended against mass screening with dipsticks for protein [33].

Other organisations touched on the subject without giving relevant recommendations. Kidney Disease: Improving Global Outcomes noted that there appears to be no evidence for screening unselected populations with reagent strips [34].

The Scottish Intercollegiate Guidelines Network noted that dipstick testing can be used to identify persons at risk of subsequent end-stage renal disease and cardiovascular disease, but also noted that "urine dipstick testing cannot be used reliably in isolation to diagnose the presence or absence of proteinuria" [35].
A New Zealand public authority gave its policy regarding screening for chronic kidney disease as "opportunistic screening and self-testing using a urinary dipstick" [36].

Several other organisations, including the influential National Kidney Foundation K/DOQI guideline, gave no recommendations for or against general screening, but recommended screening high-risk groups for chronic kidney disease, with varying definitions of what constituted high risk [37-42]. The recommended tests were typically measurement of the albumin-creatinine ratio (ACR) or an albumin-specific dipstick in combination with the estimated glomerular filtration rate. The topic of ACR dipsticks was mentioned by the National Institute of Health and Clinical Excellence [37], stating that dipsticks should only be used if they are capable of measuring albumin at low concentrations and of expressing the results as an ACR.

Admission to hospital

No recommendations were found on any kind of routine dipstick screening on admission to hospital.

DISCUSSION

Recommendations on the use of urinary dipsticks for screening purposes were scarce and often unclear. Despite a thorough search of websites from health authorities and medical societies in nine countries, no recommendations were found on the use of combined dipsticks in health checks or at admission to hospital.

Only one clear statement was found on screening for microscopic haematuria with dipsticks, recommending against their use. Surprisingly, only one urological society gave clear guidance on screening for microscopic haematuria, recommending against, but did not mention dipsticks. Other organisations discussed the topic without giving recommendations. The scarcity of clear guidance may be related to the fact that the literature seems to be in a stalemate, with some observational studies hinting at a possibly important beneficial effect [8, 11], but with no trials to confirm or refute this.

No clear recommendations were found on screening for urinary glucose with dipsticks, but, as was stated in one health technology assessment report, this technique is considered obsolete. It is likely that some experts consider it self-evident that it should not be used, but it is unlikely that all practitioners – including nurses who perform the tests in hospitals – know this.

Regarding screening for bacteriuria, only four recommendations were found, and they all clearly discouraged this practice, except in pregnant women. However, none of the recommendations specifically mentioned dipsticks as the screening method.

Screening for chronic kidney disease was frequently mentioned, and some organisations discussed limitations of dipstick testing for protein, but clear recommendations were scant. As with glucose, it is possible that some experts simply consider dipstick screening for proteinuria an obsolete technique not worth recommending against in guidelines. Assessing the albumin-creatinine ratio in high-risk persons was often recommended, but although this is a better measure than proteinuria, and although a high-risk only strategy likely reduces over-diagnosis and overtreatment, it is still not clear whether screening is beneficial or not. Albumin-creatinine ratio and dipstick proteinuria are predictors for total and cardiovascular mortality [43], but ACR only adds minimally to traditional cardiovascular risk prediction methods [44]. Treatment with angiotensin-converting enzyme inhibitors appears to reduce end-stage renal

disease in persons with chronic kidney disease, macroalbuminuria and diabetes [7], but has not been proven effective for non-diabetic chronic kidney disease stage 1-3, which constitute the majority of cases [45]. Screening trials have not been conducted and information on the harms of diagnosis, treatment, and follow-up is scarce [7].

The comprehensive and systematic search used in this study far exceeds what can be expected from a clinician looking for guidance. However, it is possible that some guidance has been overlooked or misinterpreted. The language limitations and the selection of certain medical fields probably reduced the number of recommendations found. Also, the choice of not searching regional and local authorities may mean that some guidance has been missed. However, such guidance, if it exists, will not necessarily reflect any national or international consensus. Four hospitals were contacted and none of them had any policy on the topic.

The combined dipsticks in common use in health checks and at admission to hospital have a potential to do harm, as do all medical interventions. Even when used for non-screening purposes, they give redundant information that may initiate a diagnostic cascade, and from this viewpoint their existence can be questioned. Using them for screening purposes without solid knowledge from randomised trials that the benefits exceed the harms is unethical, and guidance from authorities and specialist societies should reflect this. There is a need for clear and pragmatic "Do not use" lists regarding tests, helping practitioners avoid subjecting their patients to possibly useless and potentially harmful tests.

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Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	separate abstract file
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2 (mentioned that several things were pre-specified)
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2-3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	NA
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	NA
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	NA
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	NA

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	NA (but table 1 shows

			information on organisations)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	4-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	7-8
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	9
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Abstract

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