

# Population screening for bladder cancer

An evidence map to outline the volume and type of evidence related to population screening for bladder cancer for the UK National Screening Committee

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**The UK National Screening Committee secretariat is hosted by the Department of Health and Social Care**

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# About the UK National Screening Committee (UK NSC)

The UK NSC advises ministers and the NHS in the 4 UK countries about all aspects of [population screening](#) and supports implementation of screening programmes.

Conditions are reviewed against [evidence review criteria](#) according to the UK NSC's [evidence review process](#).

Read a [complete list of UK NSC recommendations](#).

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[www.gov.uk/uknsc](http://www.gov.uk/uknsc)

Blog: <https://nationalscreening.blog.gov.uk/>

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Published May 2026

# Summary

This document discusses the findings of the evidence map on screening for bladder cancer.

Evidence maps are a way of scanning published literature to look at the volume and type of evidence in relation to a specific topic. They inform whether the evidence is sufficient to commission a more sustained analysis on the topic under consideration.

Based on the findings of this evidence map, no further evidence synthesis work on population screening for bladder cancer should be commissioned at the present time.

The UK National Screening Committee (UK NSC) will reconsider screening for bladder cancer in 3-years' time.

# Introduction and approach

## Background and objectives

The UK National Screening Committee (UK NSC) external reviews (also known as evidence summaries or evidence reviews) are developed in keeping with the UK NSC evidence review process to ensure that each topic is addressed in the most appropriate and proportionate manner. Further information on the evidence review process can be accessed [online](#).

Bladder cancer is a complex disease requiring effective diagnostic and monitoring strategies. Early detection plays a crucial role in the prognosis and treatment of the disease, with various bladder cancer biomarkers appearing to be instrumental in diagnosing and monitoring. In the United Kingdom (UK), there are 10,470 new cases of bladder cancer each year with a 46% survival rate for 10 or more years. Of the total cases of bladder cancer 49% are preventable.<sup>1</sup>

The main preventable risk factor for bladder cancer is smoking, which is thought to account for 45% of the cases of bladder cancer each year in the UK. About 6% of bladder cancer cases in the UK are linked to occupational exposure to certain chemicals and about 2% of cases are linked to radiation exposure.<sup>2</sup>

Most bladder cancers (75 to 80%) do not grow deeper than the lining or connective tissue of the bladder and do not involve the muscle wall of the bladder. Such cancers can be treated by telescopic removal of the cancer (transurethral resection of bladder tumour [TURBT]). This is often followed by instillation of chemotherapy or vaccine-based therapy into the bladder, with prolonged telescopic checking of the bladder (cystoscopy) as follow-up. Some people with bladder cancer in this group who are at higher risk are treated with major surgery to remove the bladder (cystectomy).<sup>3</sup>

When bladder cancer grows into the muscle wall of the bladder, it is called 'muscle-invasive' bladder cancer, and can spread to other areas of the body. Bladder cancer that has spread to other parts of the body in this way is called 'locally advanced' or 'metastatic' bladder cancer. People with cancer in or through the bladder muscle wall may be treated with intent to cure using chemotherapy, cystectomy or radiotherapy, and those who have cancer too advanced to cure may have radiotherapy and chemotherapy to manage the condition.

In around 20% of cases, the cancer has invaded the muscle wall at presentation. In these cases, the cancer can spread rapidly and even with optimal treatment, five-year survival is only 50%.<sup>4</sup>

The tumour/ node/ metastasis (TNM) classification of bladder cancer is based on the depth of tissue invasion and involvement of lymph nodes or metastases. Tumour grade and stage is a strong predictor of future disease progression and prognosis.<sup>3</sup> The stage describes how deeply a cancer has grown, while the grade gives an idea of how fast the cancer cells are growing.

High-grade muscle invasive bladder cancers (T2 and above) are aggressive and have the worst prognosis. The 2010 NSC review noted that for a bladder cancer screening programme to be effective in reducing mortality, any screening test must be able to detect cancers that are destined to become muscle-invading, but before they have done so.<sup>5</sup>

The current evidence map has been developed in order to assess whether further work on screening for bladder cancer is justified and to identify current guidelines in the area both nationally and internationally.

Screening for bladder cancer is a topic currently due for an update external review.

## Previous review on screening for bladder cancer

review carried out by Solutions for Public Health. The UK NSC did not recommend screening because there was no safe, precise and valid screening test for bladder cancer.<sup>6</sup>

The last UK NSC review of this condition was an Evidence Map produced in July 2020 which recommended that a rapid review on screening for bladder cancer should not be commissioned at the present time and that the UK National Screening Committee (UK NSC) would return to consider screening for bladder cancer in 3-years' time.<sup>7</sup>

## Aims of the evidence map

Evidence maps are rapid evidence products which aim to gauge the volume and type of evidence relating to a specific topic.

This evidence map has been developed to assess whether a more sustained review on screening for bladder cancer should be commissioned and to evaluate the volume and type of evidence relevant to general population screening for bladder cancer in adults.

The aim was to address the following questions:

1. What are the diagnostic accuracies of screening tests which identify pre-muscle invading bladder cancer?
2. Are there any national or international guidelines or recommendations on population screening for bladder cancer?

The findings of this evidence map will provide the basis for discussion to support decision making on whether there is sufficient evidence to justify commissioning a more sustained review of the evidence on the whole population screening for bladder cancer.

The aim of this document is to present the information necessary for the UK NSC to decide this.

# Search methods

In order to gauge the volume and type of evidence on the diagnostic accuracy of screening tests for bladder cancer (research question 1), a focused search of the following key resources was conducted on 2 July 2025:

- MEDLINE (including Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions) (Ovid): 1946 to July 01, 2025
- Embase (Ovid): 1974 to 2025 July 01
- Cochrane Central Register of Controlled Trials (Cochrane Library): Issue 6 of 12, June 2025
- Cochrane Database of Systematic Reviews (Cochrane Library): Issue 7 of 12, July 2025
- KSR Evidence (<https://ksrevidence.com/>): to 2.7.25

National and international guidelines on population screening for bladder cancer (research question 2) were identified using the following resources:

- Trip Database (<https://www.tripdatabase.com/>): to 2.7.25
- NICE Guidance (<https://www.nice.org.uk/guidance/>): to 2.7.25
- International HTA Database (<https://database.inahta.org/>): to 2.7.25

Guidelines included in the previous Evidence Map were checked for recent updates<sup>7</sup>.

The search strategies used relevant search terms, comprising a combination of indexed keywords (e.g., from medical subject headings and the Embase thesaurus Emtree) and free-text terms appearing in the titles and/or abstracts of database records. Searches were limited by date to identify references published since the searches conducted in 2019 and by language (for research question 1) to identify only references published in English. Conference proceedings were excluded where possible.

Full strategies for all searches conducted as well as the tables outlining the specific Inclusion/Exclusion criteria used are provided in Appendix 1.

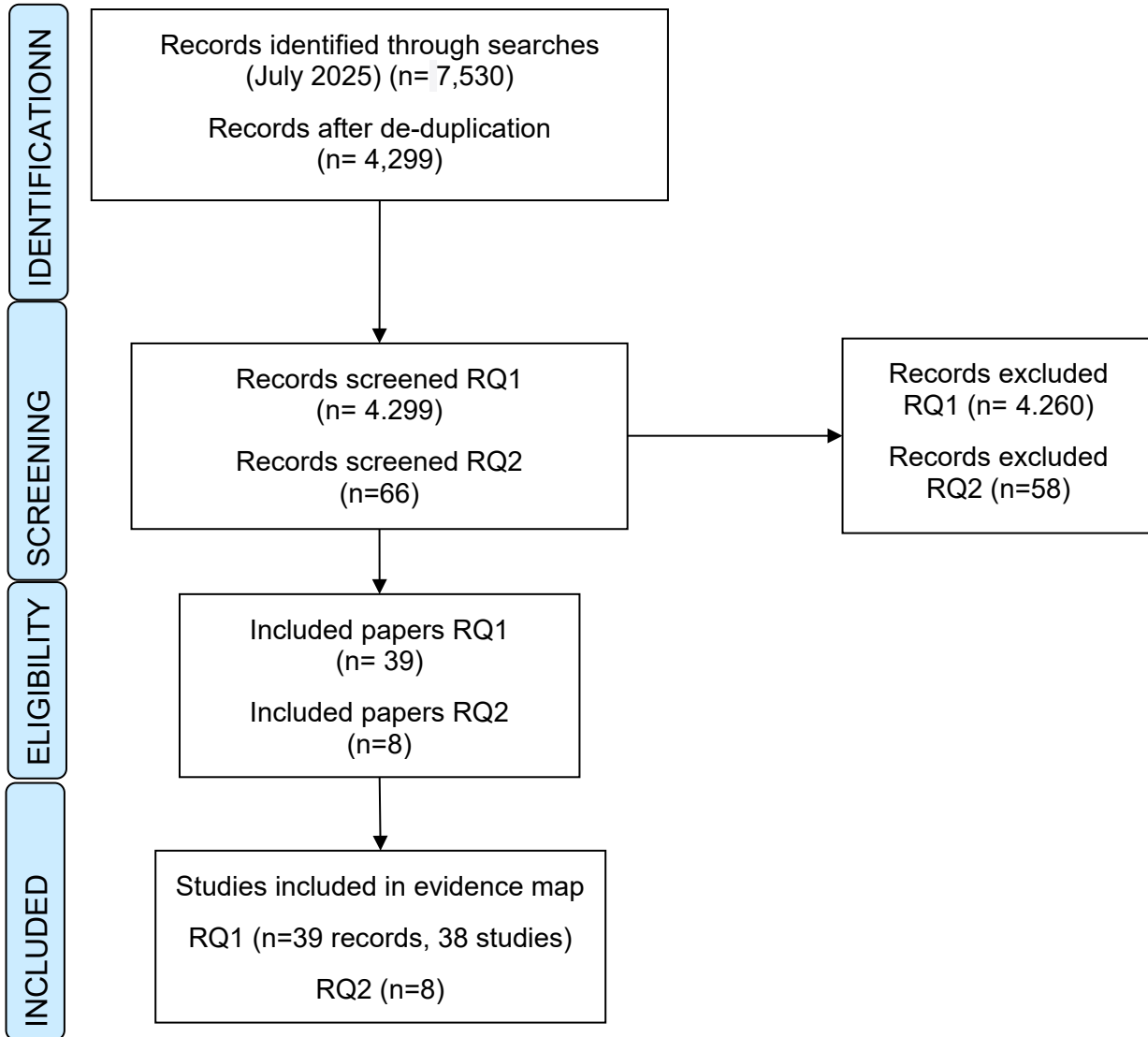
## Handling of citations

Identified references from the bibliographic database searches were downloaded into EndNote bibliographic management software for further assessment and handling. Individual records within the EndNote libraries were tagged with searching information, such as searcher, date searched, database host, database searched, strategy name and iteration, theme or search question. This enabled the information specialist to track the origin of each individual database record, and its progress through the screening and review process.

For all searches undertaken by the Kleijnen Systematic Reviews Information team, the main Embase strategy was independently peer reviewed by a second KSR Information Specialist. Strategy peer review was informed by items based on the CDA (Canada's Drug Agency) PRESS checklist (<https://www.cda-amc.ca/press-peer-review-electronic-search-strategies>).

# Summary of findings

As detailed in Appendix 1, searches were conducted on 02 July 2025. A total of 7,530 references were identified. After de-duplication, 4,299 references remained for screening. After screening, 47 papers were included (39 and 8 for research questions 1 and 2, respectively). Please see the PRISMA flow diagram below for a more detailed overview.



One reviewer screened all titles and abstracts, a second reviewer screened the references using ASReview, an open-source AI for screening references (<https://asreview.nl/>). All references were reviewed at abstract level, though in three cases full texts were reviewed to clarify uncertain pieces of information. A formal quality appraisal of the evidence was not required, given the remit of the evidence map.

Tables summarising the identified evidence are available in Appendix 2.

## Question 1: What are the diagnostic accuracies of screening tests which identify pre-muscle invading bladder cancer?

The reviewers identified an exceedingly high number of potentially relevant studies reporting on a wide range of tests for various biomarkers (>100 potentially relevant references).

Given the high volume of primary studies potentially fulfilling the inclusion criteria for question 1, 38 systematic reviews (reported in 39 records) of relevant biomarkers were identified.<sup>8-46</sup> These were typically considered in a diagnostic context but will give some indication of the applicability of available tests for population screening for bladder cancer. Key characteristics of these systematic reviews are reported in Appendix 2.

The most studied biomarkers were microRNAs, including for survivin.<sup>9, 12, 13, 17, 21, 28, 35, 39</sup> A few systematic reviews assessed the diagnostic performance of commercially available urinary biomarker tests.<sup>18, 19, 22, 25, 29, 34, 40</sup> The remaining systematic reviews assessed a range of biomarkers, as detailed in Appendix 2.

Some of those have the potential to be used in non-invasive diagnosis of bladder cancer:

- A systematic review, including 771 participants (417 bladder cancer patients and 354 controls), reported a sensitivity and specificity of 90.7% and 90%, respectively, for urinary apolipoprotein A1 (ApoA-1).<sup>24</sup>
- A systematic review, including 2,031 participants (1252 bladder cancer patients and 779 controls), reported a sensitivity and specificity of 84% and 91%, respectively, for Urothelial Carcinoma-Associated 1 (UCA1) in the early detection of bladder cancer.<sup>15</sup> Another systematic review, including 1,436 participants (954 bladder cancer and 482 non-bladder cancer patients), reported similar results (sensitivity 83% and specificity 86%) for lncRNA-UCA1 to diagnose bladder cancer.<sup>37</sup>
- A systematic review including 40 studies (no details on included participants) reported a pooled specificity and pooled sensitivity of survivin mRNA of 95% and 94%, respectively. The pooled specificity and pooled sensitivity of survivin protein was reported as 95% and 87%, respectively.<sup>13</sup> Another systematic review, including 15 studies and 1,624 participants, reported pooled sensitivity and specificity values for the detection of urinary survivin mRNA expression in the diagnosis of bladder cancer of 86% and 95%, respectively.<sup>28</sup>
- A network meta-analysis, including 58 studies and 12,038 participants, concluded that “HYAL-1 and survivin are suitable urine biomarkers for bladder cancer diagnosis”.<sup>33</sup>
- A systematic review, including 28 studies (no details on included participants), studied the performance “of five urine-based biomarker tests in the setting hematuria workup” and concluded that “while these tests may provide some clinical utility, none of the assays have thus far demonstrated objective evidence to supplant the gold diagnostic standard” (cystoscopy).<sup>18</sup> This was confirmed by another systematic review concluding that “as of now, none of these markers presented evidences so as to be accepted by international guidelines for diagnosis of BC” (bladder cancer).<sup>25</sup>
- A systematic review, including 44 studies which reported on 112 biomarkers and combinations, identified “some promising novel biomarkers and biomarker combinations (N < 3 studies for each biomarker/combination) with negative predictive values of ≥90%. These biomarkers have potential for use as a triage tool in community and primary care settings for reducing unnecessary specialist referrals”.<sup>20</sup>

It should be noted that a few of the systematic reviews suggested combining different tests to improve the diagnostic performance.<sup>9, 23, 32</sup>

A significant number of systematic reviews noted the need for further studies to confirm the findings of the review.<sup>10, 13-16, 19, 20, 22, 23, 27, 29, 30, 34, 39, 40, 42, 43, 45, 46</sup>

Further studies, including randomised studies conducted in the UK, are being conducted and will be able to provide further clarity on the feasibility of these biomarkers for the detection of bladder cancer in asymptomatic people.<sup>47</sup> YORKSURE (ISRCTN34273159), expected to run to October 2028, is a “tiered, randomised, multicohort study to test the feasibility of a large BCa screening randomised controlled trial. In three parallel cohorts, participants will self-test urine (at home)” and primary outcomes are “recruitment and randomisation, rates of positive test and acceptability of the design”.

In summary, the identified evidence highlighted some biomarkers that might have suitable diagnostic accuracy for confirming or ruling out suspected cases of bladder cancer. However, there is an insufficient volume of evidence for the population screening of asymptomatic people for bladder cancer to justify an evidence summary. The type of evidence identified is unlikely to lead to a change in the UK NSC’s current position. This conclusion is in line with the findings in relation to question 2, discussed below.

## Question 2: Are there any national guidelines or recommendations on population screening for bladder cancer?

The evidence map identified three updates for the five guidelines identified for the 2020 evidence map as well as three additional guidelines and two overviews of guidelines.

None of these recommended general population screening of asymptomatic adults, see Appendix 2 for details.

# Conclusions

The findings of this evidence map are unlikely to impact on current recommendations on screening for bladder cancer as no new evidence was identified that would change those conclusions.

# Recommendations

On the basis of this evidence map, there is an insufficient volume of evidence for the population screening of asymptomatic people for bladder cancer to justify an evidence summary because most studies did not include relevant populations. This topic should ideally be re-considered in 3-years' time.

# Appendix 1 — Search strategy for the evidence map

## Databases and platforms searched

Resource	Host	Date range	Date searched	Records found before deduplication	Records found after deduplication
MEDLINE	Ovid	1946 - 1.7.25	2.7.25	3578	3521
Embase	Ovid	1974 - 1.7.25	2.7.25	3606	665
CENTRAL	Cochrane	Iss 6/12, Jun 2025	2.7.25	83	18
CDSR	Cochrane	Iss 7/12, Jul 2025	2.7.25	1	1
KSR Evidence	<a href="https://ksrevidence.com/">https://ksrevidence.com/</a>	to 2.7.25	2.7.25	185	28
Trip Database	<a href="https://www.tripdatabase.com/">https://www.tripdatabase.com/</a>	to 2.7.25	2.7.25	26	25
NICE Guidance	<a href="https://www.nice.org.uk/guidance">https://www.nice.org.uk/guidance</a>	to 2.7.25	2.7.25	11	10
HTA Database	<a href="https://database.inahta.org/">https://database.inahta.org/</a>	to 2.7.25	2.7.25	37	28
Update check of previous guidelines			2.7.25	3	3
<b>TOTAL</b>				<b>7530</b>	<b>4299</b>

## Search strategies

**MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions (Ovid): 1946 to July 01, 2025**

**Date searched: 2.7.25**

**Records found: 3578**

- 1 exp Urinary Bladder Neoplasms/ 67196
- 2 Urologic Neoplasms/ 6574
- 3 (Carcinoma, Transitional Cell/ or Carcinoma, Papillary/) and bladder\$.ti,ab. 15411
- 4 (bladder\$ adj3 (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or adenocarcinoma\$)).ti,ab,ot. 69731
- 5 ((urinary tract or urologic) adj3 (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or adenocarcinoma\$)).ti,ab,ot. 5970
- 6 ((transitional cell or transitional cancer cell or tcc or papillary) and bladder\$).ti,ab,ot. 10487

7 or/1-6 96638  
8 Mass Screening/ 121959  
9 "Early Detection of Cancer"/ 44630  
10 early diagnosis/ 32124  
11 Urinalysis/ or diagnostic techniques, urological/ 10627  
12 biomarkers/ur or exp biomarkers, tumor/ur 19431  
13 Hematuria/di [Diagnosis] 2247  
14 (screen\$ or (early adj3 (diagnos\$ or detect\$))).ti,ab,ot. 1372341  
15 (urinalysis or urinalysis).ti,ab,ot. 9888  
16 (urin\$ adj5 (test\$ or screen\$ or analys\$ or cytolog\$ or strip or strips or stick or sticks or culture)).ti,ab,ot. 60228  
17 (dipstick\$ or "dip stick\$").ti,ab,ot. 4677  
18 ((hematuria or haematuria or blood) adj5 (microscopic or nonvisible or non-visible)).ti,ab,ot. 4707  
19 (microhematuria or microhaematuria).ti,ab,ot. 1117  
20 (((haemoglobin or hemoglobin) adj5 (screen or screened or screening or test or tests or tested or testing)) and urin\$).ti,ab,ot. 271  
21 (biomarker\$ or marker\$).ti. 286238  
22 (urin\$ adj5 (biomarker\$ or marker\$)).ti,ab,ot. 15282  
23 (((cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or adenocarcinoma\$) adj5 (biomarker\$ or marker\$)) and urin\$).ti,ab,ot. 4905  
24 (((cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or adenocarcinoma\$) adj5 (biomarker\$ or marker\$)) and screen\$).ti,ab,ot. 12186  
25 (minichromosom\$ maintenance complex or mini-chromosom\$ maintenance complex or "mmc5" or "mmc-5").ti,ab,ot. 430  
26 (nuclear matrix protein\$ or "nmp22" or "nmp-22").ti,ab,ot. 1229  
27 (adxbladder or adx bladder or immunocyt or immuno cyt or cxbladder or "cx bladder" or "urna2" or "urna-2").ti,ab,ot. 102  
28 (UroVysion or BTA test\$ or BTA STAT or BTASTAT or BTA TRAK or bladder tumo?r anti-gen\$ or CFHrp or BladderChek).ti,ab,ot. 486  
29 (Hyaluronic acid or Hyaluronidase or survivin or telomerase or DD23 or microsatellite analysis or UBC Rapid test or UBC rapid VISUAL or UBC ELISA or XPERT BC Monitor or XPERT bladder cancer or "BC UroMark" or TaqMan Arrays or soluble FAS or sFAS or bladder tumor fibronectin or IGF2 or "MAGE-A3").ti,ab,ot. 74557  
30 or/8-29 1816383  
31 7 and 30 12733  
32 exp animals/ not (exp animals/ and humans/) 5352689  
33 31 not 32 12456  
34 (201909\$ or 201910\$ or 201911\$ or 201912\$ or 2020\$ or 2021\$ or 2022\$ or 2023\$ or 2024\$ or 2025\$).dt. 9133941  
35 33 and 34 3880  
36 limit 35 to english language 3775  
37 (comment or editorial or letter or news).pt. or case report.ti,ab. 3013484  
**38 36 not 37 3578**

**Embase (Ovid): 1974 to 2025 July 01**

**Date searched: 2.7.25**

**Records found: 3185**

1 exp \*bladder cancer/ or \*bladder papilloma/ or exp \*bladder tumor/ 75293  
2 \*urinary tract cancer/ 3818  
3 \*Urinary tract tumor/765  
4 (bladder\$ adj3 (cancer\$ or neoplas\$ or carcinoma\$ or tumor\$r\$ or malignan\$ or adenocarcinoma\$)).ti,ab,ot. 99080  
5 ((urinary tract or urologic) adj3 (cancer\$ or neoplas\$ or carcinoma\$ or tumor\$r\$ or malignan\$ or adenocarcinoma\$)).ti,ab,ot. 8698  
6 ((transitional cell or transitional cancer cell or tcc or papillary) and bladder\$).ti,ab,ot. 14366  
7 or/1-6 120720  
8 \*mass screening/ or \*cancer screening/ or \*screening/ or \*screening test/ 127714  
9 \*Diagnostic Accuracy/ 24484  
10 \*early diagnosis/ or \*early cancer diagnosis/ 22310  
11 \*urinalysis/ 14535  
12 \*urine cytology/ 1607  
13 \*test strip/ or \*urine test strip/ 2008  
14 (\*marker/ or \*biological marker/ or exp \*tumor marker/) and (\*urine/ or \*bladder/) 795  
15 \*hematuria/di 1446  
16 (screen\$ or (early adj3 (diagnos\$ or detect\$))).ti,ab,ot. 1970197  
17 (urinalysis or urinalysis).ti,ab,ot. 20384  
18 (urin\$ adj5 (test\$ or screen\$ or analys\$ or cytolog\$ or strip or strips or stick or sticks or culture)).ti,ab,ot. 100889  
19 (dipstick\$ or "dip stick\$").ti,ab,ot. 7488  
20 ((hematuria or haematuria or blood) adj5 (microscopic or nonvisible or non-visible)).ti,ab,ot. 7690  
21 (microhematuria or microhaematuria).ti,ab,ot. 1802  
22 (((haemoglobin or hemoglobin) adj5 (screen or screened or screening or test or tests or tested or testing)) and urin\$).ti,ab,ot. 637  
23 (biomarker\$ or marker\$).ti. 405870  
24 (urin\$ adj5 (biomarker\$ or marker\$)).ti,ab,ot. 23645  
25 (((cancer\$ or neoplas\$ or carcinoma\$ or tumor\$r\$ or malignan\$ or adenocarcinoma\$) adj5 (biomarker\$ or marker\$)) and urin\$).ti,ab,ot. 7573  
26 (((cancer\$ or neoplas\$ or carcinoma\$ or tumor\$r\$ or malignan\$ or adenocarcinoma\$) adj5 (biomarker\$ or marker\$)) and screen\$).ti,ab,ot. 18705  
27 (minichromosom\$ maintenance complex or mini-chromosom\$ maintenance complex or "mmc5" or "mmc-5").ti,ab,ot. 511  
28 (nuclear matrix protein\$ or "nmp22" or "nmp-22").ti,ab,ot. 1492  
29 (adxbladder or adx bladder or immunocyt or immuno cyt or cxbladder or "cx bladder" or "urna2" or "urna-2").ti,ab,ot. 158  
30 (UroVysion or BTA test\$ or BTA STAT or BTASTAT or BTA TRAK or bladder tumor\$r antigen\$ or CFHrp or BladderChek).ti,ab,ot. 779  
31 (Hyaluronic acid or Hyaluronidase or survivin or telomerase or DD23 or microsatellite analysis or UBC Rapid test or UBC rapid VISUAL or UBC ELISA or XPERT BC Monitor or XPERT bladder cancer or "BC UroMark" or TaqMan Arrays or soluble FAS or sFAS or bladder tumor fibronectin or IGF2 or "MAGE-A3").ti,ab,ot. 94292  
32 or/8-31 2557281  
33 7 and 32 18030  
34 ("conference abstract" or "conference review").pt. or conference\$.so,st. 5573126  
35 clinicaltrials.gov.jn. 533511  
36 33 not (34 or 35) 12230

37 animal/ 1716434  
38 animal experiment/ 3347425  
39 (rat or rats or mouse or mice or murine or rodent or rodents or hamster or hamsters or pig or pigs or porcine or rabbit or rabbits or animal or animals or dogs or dog or cats or cow or bovine or sheep or ovine or monkey or monkeys).ti,ab,ot,hw. 8218003  
40 or/37-39 8218003  
41 exp human/ 28674713  
42 human experiment/ 719694  
43 or/41-42 28678057  
44 40 not (40 and 43) 6059361  
45 36 not 44 11870  
46 (201909\$ or 201910\$ or 201911\$ or 201912\$ or 2020\$ or 2021\$ or 2022\$ or 2023\$ or 2024\$ or 2025\$).dd. 12391875  
47 45 and 46 3952  
48 (comment or editorial or letter or news).pt. or case report.ti,ab. 2824601  
49 47 not 48 3771  
**50 limit 49 to English language 3606**

## The Cochrane Library

<https://www.cochranelibrary.com/>

Date searched: 2.7.25

Records found:

**Cochrane Database of Systematic Reviews (Issue 7 of 12, July 2025): 1**

**Cochrane Central Register of Controlled Trials (Issue 6 of 12, June 2025): 83**

#1 MeSH descriptor: [Urinary Bladder Neoplasms] explode all trees 2439  
#2 MeSH descriptor: [Urologic Neoplasms] this term only 191  
#3 MeSH descriptor: [Carcinoma, Transitional Cell] this term only 893  
#4 MeSH descriptor: [Carcinoma, Papillary] this term only 198  
#5 bladder\*.ti,ab 17238  
#6 (#3 or #4) and #5 652  
#7 (bladder\* near/3 (cancer\* or neoplas\* or carcinoma\* or tumo?\* or malignan\* or adenocarcinoma\*)):ti,ab 4653  
#8 (("urinary tract" or urologic) near/3 (cancer\* or neoplas\* or carcinoma\* or tumo?\* or malignan\* or adenocarcinoma\*)):ti,ab 258  
#9 (("transitional cell" or "transitional cancer cell" or tcc or papillary) and bladder\*):ti,ab 715  
#10 #1 or #2 or #6 or #7 or #8 or #9 5451  
#11 MeSH descriptor: [Mass Screening] this term only 5177  
#12 MeSH descriptor: [Early Detection of Cancer] this term only 2676  
#13 MeSH descriptor: [Early Diagnosis] this term only 789  
#14 MeSH descriptor: [Urinalysis] this term only 329  
#15 MeSH descriptor: [Diagnostic Techniques, Urological] this term only 51  
#16 MeSH descriptor: [Hematuria] this term only and with qualifier(s): [diagnosis - DI] 22  
#17 MeSH descriptor: [Biomarkers] this term only and with qualifier(s): [urine - UR] 1236

- #18 MeSH descriptor: [Biomarkers, Tumor] explode all trees and with qualifier(s): [urine - UR] 104
- #19 (screen\* or (early near/3 (diagnos\* or detect\*))) :ti,ab 115032
- #20 (urinalysis or urinalysis):ti,ab 3967
- #21 (urin\* near/5 (test\* or screen\* or analys\* or cytolog\* or strip or strips or stick or sticks or culture)) :ti,ab 13704
- #22 (dipstick\* or "dip stick" or "dip sticks") :ti,ab 605
- #23 ((hematuria or haematuria or blood) near/5 (microscopic or nonvisible or "non-visible")) :ti,ab 168
- #24 (microhematuria or microhaematuria):ti,ab 58
- #25 (((haemoglobin or hemoglobin) near/5 (screen or screened or screening or test or tests or tested or testing)) and urin\*) :ti,ab 195
- #26 (biomarker\* or marker\*) :ti 20113
- #27 (urin\* near/5 (biomarker\* or marker\*)) :ti,ab 2568
- #28 (((cancer\* or neoplas\* or carcinoma\* or tumo?r\* or malignan\* or adenocarcinoma\*) near/5 (biomarker\* or marker\*)) and urin\*) :ti,ab 313
- #29 (((cancer\* or neoplas\* or carcinoma\* or tumo?r\* or malignan\* or adenocarcinoma\*) near/5 (biomarker\* or marker\*)) and screen\*) :ti,ab 514
- #30 ("minichromosome maintenance complex" or "mini-chromosome maintenance complex" or "mmc5" or "mmc-5") :ti,ab 40
- #31 ("nuclear matrix protein" or "nmp22" or "nmp-22") :ti,ab 20
- #32 (adxb bladder or adx bladder or immunocyt or immuno cyt or cx bladder or "cx bladder" or "urna2" or "urna-2") :ti,ab 11
- #33 (UroVysion or (BTA next test\*) or "BTA STAT" or BTastat or "BTA TRAK" or (bladder next tumo?r next antigen\*) or CFHrp or BladderChek) :ti,ab 23
- #34 ("Hyaluronic acid" or Hyaluronidase or survivin or telomerase or DD23 or "microsatellite analysis" or "UBC Rapid test" or "UBC rapid VISUAL" or "UBC ELISA" or "XPert BC Monitor" or "XPert bladder cancer" or "BC UroMark" or "TaqMan Arrays" or "soluble FAS" or sFAS or "bladder tumor fibronectin" or IGF2 or "MAGE-A3") :ti,ab 5258
- #35 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 152925
- #36 #10 and #35 690
- #37 #36 with Cochrane Library publication date Between Jan 2020 and Jun 2025, in Cochrane Reviews 1
- #38 #36 with Publication Year from 2020 to 2025, in Trials 268
- #39 (trial registry record or Clinical trial protocol):pt 575303
- #40 (conference or congress):ti,so,pt 271599
- #41 #38 not (#39 or #40) 83**

## KSR Evidence: to 2.7.25

<https://ksrevidence.com/>

Date searched: 2.7.25

Records found: 185

- 1 (bladder\* near/3 (cancer\* or neoplas\* or carcinoma\* or tumo?r\* or malignan\* or adenocarcinoma\*)) in Title or Abstract 1246 results
- 2 (("urinary tract" or urologic) near/3 (cancer\* or neoplas\* or carcinoma\* or tumo?r\* or malignan\* or adenocarcinoma\*)) in Title or Abstract 161 results

3 ("transitional cell" or "transitional cancer cell" or tcc or papillary) and bladder\*) in Title or Abstract 27 results

4 #1 or #2 or #3 in All text 1338 results

5 (screen\* or (early near/3 (diagnos\* or detect\*))) in Title or Abstract 50527 results

6 (urinalysis or urinalysis) in Title or Abstract 40 results

7 (urin\* near/5 (test\* or screen\* or analys\* or cytolog\* or strip or strips or stick or sticks or culture)) in Title or Abstract 746 results

8 (dipstick\* or "dip stick" or "dip sticks") in Title or Abstract 47 results

9 ((hematuria or haematuria or blood) near/5 (microscopic or nonvisible or "non-visible")) in Title or Abstract 23 results

10 (microhematuria or microhaematuria) in Title or Abstract 5 results

11 (((haemoglobin or hemoglobin) near/5 (screen or screened or screening or test or tests or tested or testing)) and urin\*) in Title or Abstract 1 result

12 biomarker\* or marker\* in Title 5074 results

13 (urin\* near/5 (biomarker\* or marker\*)) in Title or Abstract 281 results

14 (((cancer\* or neoplas\* or carcinoma\* or tumo?r\* or malignan\* or adenocarcinoma\*) near/5 (biomarker\* or marker\*)) and urin\*) in Title or Abstract 110 results

15 (((cancer\* or neoplas\* or carcinoma\* or tumo?r\* or malignan\* or adenocarcinoma\*) near/5 (biomarker\* or marker\*)) and screen\*) in Title or Abstract 406 results

16 ("minichromosome maintenance complex" or "mini-chromosome maintenance complex" or "mmc5" or "mmc-5") in Title or Abstract 2 results

17 ("nuclear matrix protein" or "nmp22" or "nmp-22") in Title or Abstract 14 results

18 (adxbladder or adx bladder or immunocyt or immuno cyt or cxbladder or "cx bladder" or "urna2" or "urna-2") in Title or Abstract 9 results

19 (UroVysion or (BTA next test\*) or "BTA STAT" or BTAsat or "BTA TRAK" or (bladder next tumo?r next antigen\*) or CFHrp or BladderChek) in Title or Abstract 10 results

20 ("Hyaluronic acid" or Hyaluronidase or survivin or telomerase or DD23 or "microsatellite analysis" or "UBC Rapid test" or "UBC rapid VISUAL" or "UBC ELISA" or "XPRT BC Monitor" or "XPRT bladder cancer" or "BC UroMark" or "TaqMan Arrays" or "soluble FAS" or sFAS or "bladder tumor fibronectin" or IGF2 or "MAGE-A3") in Title or Abstract 800 results

21 #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 in All text 55745 results

**22 #21 and #4 in All text Date published: 2020 - 2025 185 results**

**Trip Database: to 2.7.25**

**<https://www.tripdatabase.com/>**

**Date searched: 2.7.25**

**Records found: Guidelines – 25**

**Regulatory Guidance - 1**

Limits:

Guidelines/Regulatory Guidance

2020-2025

# 5 ((title:"urinary tract neoplasms") OR (title:"bladder neoplasms") OR (title:"urinary tract cancer") OR (title:"bladder cancer")) 9310  
# 4 (title:"urinary tract neoplasms") 3  
# 3 (title:"bladder neoplasms") 12  
# 2 (title:"urinary tract cancer") 115  
# 1 (title:"bladder cancer") 9183

**NICE Guidance: to 2.7.25**

<https://www.nice.org.uk/guidance>

**Date searched:**

**Records found: 11**

Limits:

Type: Guidance

Status: Published

Year: 2019-2025

Browse – Bladder Cancer

**HTA Database: to 2.7.25**

<https://database.inahta.org/>

**Date searched: 2.7.25**

**Records found: 37**

Limits:

Year: 2020-2025

Project Status: Completed

6	#5 OR #4 OR #3 OR #2 OR #1	101
5	"urinary tract neoplasms"	0
4	"bladder neoplasms"	1
3	"urinary tract cancer"	0
2	"bladder cancer"	65
1	"Urinary Bladder Neoplasms"[mhe]	82

## Inclusion/Exclusion Criteria

### Question 1 (Diagnostic accuracies for screening tests identifying per-muscle invading bladder cancer)

Item	Included	Excluded
<b>Population</b>	<ul style="list-style-type: none"> <li>Asymptomatic adults aged <math>\geq 18</math> years</li> </ul>	<ul style="list-style-type: none"> <li>Paediatric populations (age <math>&lt; 18</math> years)</li> </ul>
<b>Index Tests</b>	<ul style="list-style-type: none"> <li>Dipstick markers for microscopic haematuria, if offered in combination with other markers</li> <li>Urinary biomarkers such as:               <ul style="list-style-type: none"> <li>Protein- and cell-based biomarkers: BTAstat® (BTA), Nuclear matrix protein (NMP22), ImmunoCyt™, MCM5</li> <li>Gene-based biomarkers, UroVysion® (FISH) and Cxbladder (uRNA-2)</li> </ul> </li> <li>Urinary cytology</li> </ul>	NA
<b>Reference standard</b>	<ul style="list-style-type: none"> <li>Cystoscopy</li> <li>Biopsy</li> </ul>	
<b>Comparator</b>	<ul style="list-style-type: none"> <li>Any or none</li> </ul>	NA
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>Any harms (e.g. overdiagnosis, overtreatment)</li> <li>Sensitivity</li> <li>Specificity</li> <li>Positive &amp; negative predictive values</li> <li>Likelihood ratios</li> <li>Area under the curve</li> <li>Test failures</li> <li>Other accuracy/validity outcomes</li> </ul>	<ul style="list-style-type: none"> <li>Studies which do not report the outlined outcomes</li> </ul>
<b>Study designs</b>	<ul style="list-style-type: none"> <li>Consecutively enrolled or randomly assigned populations will be prioritised</li> <li>Other study designs to be reported if no studies of the previous type are available.</li> </ul>	<ul style="list-style-type: none"> <li>Case series</li> <li>Single arm studies</li> <li>Editorials</li> </ul>
<b>Timeframe &amp; Language</b>	<ul style="list-style-type: none"> <li>Published between 2020 and 2025 in English</li> </ul>	<ul style="list-style-type: none"> <li>Published prior to 2020</li> <li>Not in English</li> </ul>
<b>Geographical scope</b>	<ul style="list-style-type: none"> <li>UK studies will be prioritised but in the absence of studies-comparable countries will be reported</li> </ul>	<ul style="list-style-type: none"> <li>Studies from countries that their health system is not comparable</li> </ul>
BTA = Bladder Tumour Antigen; NA = not applicable; NMP = Nuclear matrix protein; UK = United Kingdom; UroVysion® (FISH) = Fluorescence in situ hybridization		

### Question 2 (Current national/international guidelines/recommendations on population screening for bladder cancer)

Item	Included	Excluded
<b>Population</b>	<ul style="list-style-type: none"> <li>Asymptomatic adults aged <math>\geq 18</math> years</li> </ul>	Paediatric populations (age $< 18$ years)
<b>Intervention</b>	<ul style="list-style-type: none"> <li>National or international guidelines, recommendations or consensus statements from professional organisations, royal colleges or equivalent, national departments of health or national screening organisations</li> </ul>	<ul style="list-style-type: none"> <li>Informal opinion papers, non-comprehensive consensus guidelines, or grey literature lacking validation.</li> </ul>

Item	Included	Excluded
	<ul style="list-style-type: none"> <li>Clinical practice Guidelines (CPGs) issued by professional bodies (e.g. NICE, EAU, ESMO) for any type of formal screening.</li> </ul>	<ul style="list-style-type: none"> <li>Reports from unrecognised or informal organisations without expert validation.</li> </ul>
<b>Comparator</b>	NA	NA
<b>Outcomes</b>	NA	NA
<b>Study design</b>	<ul style="list-style-type: none"> <li>National or international guidelines, recommendations or consensus statements from professional organisations, royal colleges or equivalent, national departments of health or national screening organisations</li> </ul>	<ul style="list-style-type: none"> <li>Informal opinion papers, non-comprehensive consensus guidelines, or grey literature lacking validation.</li> </ul> <p>Reports from unrecognised or informal organisations without expert validation.</p>
<b>Timeframe &amp; Language</b>	<ul style="list-style-type: none"> <li>Published between 2020 and 2025</li> <li>Published in English</li> </ul>	<ul style="list-style-type: none"> <li>Published prior to 2020</li> <li>Not Published in English</li> </ul>
<b>Geographical scope</b>	<ul style="list-style-type: none"> <li>No restrictions-guidelines from both the UK and internationally</li> </ul>	Not applicable
<p>CPG = clinical practice guideline; EAU = European Association of Urology; ESMO = European Society for Medical Oncology; NA = not applicable; NICE = National Institute for Health and Care Excellence; UK = United Kingdom</p>		

## Appendix 2 – Identified evidence

### Question 1

Searches for this evidence map identified 38 systematic reviews of relevant biomarkers. Key characteristics are presented in the Table below.

Reference	Inclusion	Biomarker/ Test	Conclusion
Aalami 2021 <sup>36</sup>	Databases: 6 Search: Oct 2020 Studies: 4 Participants: 656 (417 bladder cancer, 239 controls)	Angiogenin	“This meta-analysis showed that ANG could be a fair biomarker for the diagnosis of BCa patients”
Aalami 2024 <sup>11</sup>	Databases: NR Search: Mar 2024 Studies: 7 Participants: 1051 (576 bladder cancer, 481 controls)	Angiogenin/ ribonuclease 5	“Our meta-analysis confirms ANG/RNase 5 as a reliable biomarker for early bladder cancer detection, showing strong diagnostic accuracy and no publication bias”
Aveta 2023 <sup>17</sup>	Databases: NR Search: NR Studies: 60 (convenient sample) Participants: NR	MicroRNAs	“Several umiRNAs have been identified as diagnostic biomarkers of urothelial carcinoma and bladder cancer (BC), allowing us to discriminate malignant from nonmalignant forms of hematuria”
Cui 2021 <sup>35</sup>	Databases: 3 Search: NR Studies: 11 Participants: 1220 (bladder cancer, Asian population)	MicroRNAs	“Urinary miRNAs show good performance in diagnosing BC in Asia, and, therefore, can serve as effective biomarkers for early clinical screening and auxiliary diagnosis of BC”
Dardeer 2021 <sup>24</sup>	Databases: 3 Search: Mar 2020 Studies: 4 Participants: 771 (417 bladder cancer, 354 controls)	Apolipoprotein A1	“ApoA-1 showed high sensitivity and specificity, so it could be a useful biomarker in diagnosis of bladder cancer”
De Sousa Neto <sup>9</sup>	Databases: 1 Search: July 2022 Studies: 21	MicroRNAs	“There is a trend to cluster the expressed miRNAs to build diagnostic panels or use them in association with other diagnostic

Reference	Inclusion	Biomarker/ Test	Conclusion
	Participants: NR		methods to achieve reasonable accuracy”
Ding 2021 <sup>37</sup>	Databases: >6 Search: Dec 2019 Studies: 7 Participants: 1436 (954 bladder cancer, 482 non-bladder cancer)	lncRNA-UCA1	“lncRNA-UCA1 has a high value of clinical auxiliary diagnosis for bladder cancer, and it can be further promoted and applied clinically”
Dong 2021 <sup>33</sup>	Databases: 3 Search: NR Studies: 58 Participants: 12038	Urinary biomarkers	“HYAL-1 and survivin are suitable urine biomarkers for bladder cancer diagnosis”
Fu 2020 <sup>28</sup>	Databases: 4 Search: NR Studies: 15 Participants: 1624	Urinary survivin mRNA expression detected by RT-PCR	“Compared with traditional urine cytology, urinary survivin mRNA detection using reverse transcription-PCR was identified to be more effective in the diagnosis of early bladder cancer”
Grimaldi 2022 <sup>21</sup>	Databases: 2 Search: NR Studies: 25 Participants: 4054	MicroRNAs	“We did not identify a univocal consensus for a specific diagnostic miRNA signature but only isolated the signatures, some of them with better diagnostic power compared to the others”
He 2024 <sup>15</sup>	Databases: 6 Search: July 2023 Studies: 12 Participants: 2031 (1252 bladder cancer, 779 controls)	UCA1	“UCA1 could serve as a potential biomarker for BCa detection with good diagnostic performance. Besides, compared to UCA1 in blood, urine and tissue UCA1 exhibited higher diagnostic value. Further prospective clinical research is needed to corroborate the conclusion”
Heard 2024 <sup>18</sup>	Databases: NR Search: NR Studies: 28 Participants: NR	NMP22, BTA, UroVysion, ImmunoCyt/uCyt, CxBladder, and Bladder EpiCheck	“Our analysis finds that while these tests may provide some clinical utility, none of the assays have thus far demonstrated objective evidence to supplant the gold diagnostic standard”
Hentschel 2021 <sup>41</sup>	Databases: 3 Search: Oct 2019 Studies: 25 Participants: NR	Mutation analysis	“We observed substantial differences in diagnostic accuracy of urinary BC mutation markers among publications. To translate the data summarised in the present review to future clinical practice, heterogeneity in research design, BC population, mutation analysis technique and urinary DNA should be considered. Eventual clinical implementation of urinary BC mutation markers can only be

Reference	Inclusion	Biomarker/ Test	Conclusion
			achieved by collecting more and stronger evidence”
Herranz 2021 <sup>26</sup>	Databases: NR Search: NR Studies: NR Participants: NR	Cell-free DNA	“We have summarized the up-to-date studies evaluating the value of cfDNA as potential diagnostic, prognostic, or monitoring biomarker for BC in several biofluids”
Kravchuk 2024 <sup>19</sup>	Databases: 6 Search: Nov 2023 Studies: 4 Tests: 1190 (bladder cancer prevalence 14.9%)	Uromonitor R	“This systematic review supports the use of Uromonitor R considering its favorable diagnostic performance (...) Due to currently limited aggregated data from only four studies with heterogeneous quality, confirmatory studies are needed”
Laukhtina 2021 <sup>22, 34</sup>	Databases: 3 Search: Apr 2021 Studies: 21 Participants: 7330	Urinary biomarkers	“Our analyses support high diagnostic accuracy of the studied novel UBTs, supporting their utility in the NMIBC surveillance setting. All of these might potentially help prevent unnecessary cystoscopies safely. There are not enough data to reliably assess their use in the primary diagnostic setting. These results have to be confirmed in a larger cohort as well as in head-to-head comparative studies. Nevertheless, our study might help policymakers and stakeholders evaluate the clinical and social impact of the implementation of these tests into daily practice”
Li 2024 <sup>12</sup>	Databases: 4 Search: NR Studies: 6 Participants: NR	miRNA-143	“miRNA-143 may serve as a promising noninvasive tool for the early detection of BCa”
Liu 2021 <sup>39</sup>	Databases: 4 Search: Oct 2020 Studies: 8 Participants: NR	mRNAs	“Xpert Bladder Cancer presents high accuracy and specificity in monitoring bladder cancer compared with cystoscopy. More researches are still required to further confirm this conclusion”
Long 2024 <sup>10</sup>	Databases: 5 Search: NR Studies: 21 Participants: 3348	Urine-derived exosomes	“Urine-derived exosomes have significant diagnostic prospects in the diagnosis of BC. Nevertheless, their application in clinical settings still demands a considerable number of clinical trials to confirm their clinical feasibility and practicability”
Morozov 2021 <sup>38</sup>	Databases: 2 Search: NR Studies: NR Participants: NR	hTERT, hTR and TERT promoter mutation	“Although telomerase subunits showed clinically relevant values in genitourinary cancers, developing fast and cost-effective methods is required before contemplating routine use”

Reference	Inclusion	Biomarker/ Test	Conclusion
Muham-mad 2024 <sup>43</sup>	Databases: 4 Search: NR Studies: NR Participants: NR	Molecular biomarkers	“The study highlights the potential of various gene and protein biomarkers for the detection of bladder cancer. Further research is necessary to validate these biomarkers' diagnostic and prognostic potential in identifying bladder cancer in suspected cases”
Papavasil-iou 2023 <sup>20</sup>	Databases: 2 Search: May 22 Studies: 44 Biomarkers: 112	Biomarkers which might be suitable for use in community and primary care settings	“We identified some promising novel biomarkers and biomarker combinations (N < 3 studies for each biomarker/combination) with negative predictive values of ≥90%. These biomarkers have potential for use as a triage tool in community and primary care settings for reducing unnecessary specialist referrals. Despite promising emerging evidence, further validation studies in the general population are required at different stages within the diagnostic pathway”
Peng 2020 <sup>27</sup>	Databases: 3 Search: June 2019 Studies: 22 Participants: 2867	Telomerase Activity	“TA can be used as a potential biomarker for the diagnosis of bladder cancer with its high specificity. Rigorous and high-quality prospective studies are required to verify our conclusion”
Sciarra 2021 <sup>25</sup>	Databases: 2 Search: Jan 2019 Studies: NR Participants: NR	Urinary tests	“Most of the proposed molecular markers were able to improve the sensitivity with similar or lower specificity when compared to UC. However, variability of results among the different studies was strong. Thus, as of now, none of these markers presented evidences so as to be accepted by international guidelines for diagnosis of BC”
Sharma 2022 <sup>31</sup>	Databases: NR Search: NR Studies: 8 Participants: 5114	MCM5	“MCM5 has an overall moderate diagnostic accuracy for detecting BC. Sub-group analysis revealed good diagnostic performance in patients with high-grade tumors and primary diagnosis of symptomatic patients”
Silva-Ferreira 2024 <sup>8</sup>	Databases: 3 Search: Dec 2022 Studies: 68 Participants: 12696 (5557 bladder cancer)	Urinary DNA Methylation-based Biomarkers	“DNA methylation biomarkers disclose high accuracy for bladder cancer detection in urine. Nonetheless, validation studies in different clinical settings are scarce, hampering clinical use. The identified biomarkers should be prioritized in future validation studies”
Soorobjebally 2023 <sup>29</sup>	Databases: 1 Search: Mar 2021 Studies: NR	VisioCyt R, Xpert RBladder, BTA stat R, BTA TRAK TM, NMP22 BC R, NMP22 R BladderChek R Test, ImmunoCyt TM/uCyt1+ TM,	“Urinary biomarkers might have a complementary place in bladder cancer diagnosis and NMIBC surveillance. However, their clinical benefit remains to be confirmed”

Reference	Inclusion	Biomarker/ Test	Conclusion
	Participants: NR	UroVysion Bladder Cancer Kit R, Cxbladder, ADXBLADDER, Urodiag R	
Su 2021 <sup>23</sup>	Databases: 3 Search: May 2021 Studies: 23 Participants: 3604 (1883 bladder cancer, 1721 controls)	Exosome-Derived Long Non-Coding RNAs	“Exosome-derived lncRNAs hold great promise as non-invasive diagnostic biomarkers of bladder cancer. However, their clinical value needs to be examined in further comprehensive prospective studies”
Wang 2020 <sup>42</sup>	Databases: 3 Search: NR Studies: 15 Participants: 6582 (3370 bladder cancer, 3212 controls)	Non-invasive biomarkers	“lncRNAs in urine and blood may serve as noninvasive diagnostic biomarkers with great promise for bladder cancer, while their clinical values need to be examined through further synthetic forward-looking studies”
Wang 2022 <sup>32</sup>	Databases: NR Search: NR Studies: 12 Participants: 2456	NMP22	“NMP22 has moderate diagnostic efficiency for bladder cancer. Its sensitivity is greater than UC, but its specificity is significantly lower than that of UC. At present, it cannot replace traditional cystoscopy and UC, but it can be combined to detect bladder tumors. It plays a major role in screening, postoperative monitoring and follow-up”
Wen 2021 <sup>46</sup>	Databases: NR Search: NR Studies: 13 Participants: 1266	Volatile organic compound	“Urinary VOC analysis has shown promising performance for non-invasive diagnosis of cancer. However, limitations in study design have resulted in inconsistencies between studies. These limitations are summarised and discussed in order to support future studies”
Wolfs 2021 <sup>40</sup>	Databases: NR Search: NR Studies: NR Participants: NR	NMP22, BTA, UroVysion, ImmunoCyt ADXBLADDER and bladder EpiCheck	NB: Non-systematic review included range of relevant biomarkers “The clinical implementation of these biomarkers in the follow up of NMIBC has to be further investigated in prospective randomized trials for low as well as high grade tumors”
Xu 2021 <sup>45</sup>	Databases: 5 Search: Apr 2021 Studies: 16 Participants: 3324	Urinary Exosomes	“Urinary exosomes may serve as novel non-invasive biomarkers for urological cancer detection. Future clinical trial designs must validate and explore their utility in treatment decision-making”
Ye 2022 <sup>30</sup>	Databases: NR Search: NR Studies: 45	microRNAs	“Urine and blood-based miRNAs may potentially be promising biomarkers for non-invasive early detection of bladder tumor. The diagnostic accuracy of blood-based

Reference	Inclusion	Biomarker/ Test	Conclusion
	Participants: 7540		miRNAs would be better than those of urine-based ones, and multiple miRNA panels yielded more accurate results than single-miRNA assay. Besides, miR-143 is a promising candidate biomarker for diagnosing BCa. More prospective and standardized studies are required to confirm the future findings”
Zhang 2023 <sup>16</sup>	Databases: 7 Search: Jul 2023 Studies: 12 Participants: 1186 (728 bladder cancer, 458 controls)	MUC7	“MUC7 might be a potential biomarker for diagnosing BC. However, more large sample and multicenter studies are needed to prove whether it can be used in clinical diagnosis”
Zhao 2024 <sup>14</sup>	Databases: 3 Search: NR Studies: 46 Participants: 5637 (3015 bladder cancer, 2622 controls)	Non-coding RNAs	“Exosomal ncRNAs in blood and urine may play a vital role in diagnosing bladder cancer as prospective noninvasive biomarkers; nonetheless, their clinical performance needs to be confirmed by further massive proactive researches”
Zhou 2024 <sup>13</sup>	Databases: 7 Search: NR Studies: 40 Participants: NR	Survivin	“Survivin takes on great significance in diagnosing bladder cancer. However, due to some limitations in the number and quality of covered studies, this conclusion should be validated through additional higher quality clinical studies”
Zhu 2022 <sup>44</sup>	Databases: 4 Search: NR Studies: 28 Participants: NR	Cytokeratin 19	“CYFRA21-1 has a high diagnostic efficiency for bladder cancer”

## Question 2

### Previously identified guidelines

The 2020 version of the Evidence Map identified 5 guidelines for population screening (references 6 to 10 of the document).<sup>7</sup>

For three of these guidelines, updates have been identified:

1. US Preventive Services Task Force. Bladder Cancer in Adults, August 2011 (update statement April 2019)<sup>48</sup> concluding that “the current evidence is insufficient to assess the balance of benefits and harms of screening for bladder cancer in asymptomatic adults”

Update July 2024: “Literature scans conducted in July 2024 in the MEDLINE and PubMed databases and the Cochrane Library showed a lack of new evidence to support an updated systematic review on the topic at this time”.<sup>49</sup>

2. European Association of Urology (EAU). Non-muscle-invasive Bladder Cancer, 2019,<sup>50</sup> concluding that due to the “low incidence of [bladder cancer] in the general population and the short lead-time impair feasibility and cost-effectiveness (...) routine screening for [bladder cancer] is not recommended”

In line with standard procedure for EAU guidelines, an annual assessment of newly published literature is conducted. Subsequent updates (most recently 2025) did not identify any changes.<sup>51</sup>

3. European Society for Medical Oncology (ESMO). Practice Guidelines for diagnosis, treatment and follow-up. These guidelines, published in 2014, stated that “current evidence suggests that screening for bladder cancer on a population level is not helpful for improving survival”.<sup>52</sup>

A later version of the guideline, published in 2022, made no reference to screening.<sup>53</sup>

### Newly identified guidelines

Another three guidelines were identified for the evidence map:

1. American Urological Association (AUA), last amendment in 2024.<sup>54</sup>

The guideline describes a “limited role for urinary biomarkers to replace cystoscopic surveillance in NMIBC”, no recommendation regarding a whole population screening is given.

2. Association française d’urologie (AFU), last update in 2024 for period 2024 to 2026.<sup>55</sup>

For a “population at risk of BC that is linked to previous occupational exposure (in particular to aromatic amines, polycyclic aromatic hydrocarbons (PAHs), nitrosamines, and chlorinated solvents such as perchloroethylene)”, the guideline recommends targeted screening to be carried out 20 years after the onset of exposure but does not give a recommendation regarding a whole population screening.

3. Canadian Urological Association guideline on the management of non-muscle-invasive bladder cancer, published in 2021<sup>56</sup>

No recommendation regarding a whole population screening is given.

In addition, two overviews of guidelines were identified, including 16 clinical practice guidelines for bladder cancer and four guidelines for non-muscle-invasive bladder cancer, respectively.<sup>57, 58</sup>

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