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# Utilising artificial intelligence for bladder cancer detection during cystoscopy and its impact on clinical outcomes: a systematic review and meta-analysis

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Keywords:	Artificial Intelligence, UROLOGY, Diagnostic Imaging



2 3 4	1	Utilising artificial intelligence for bladder cancer detection during cystoscopy
5 6	2	and its impact on clinical outcomes: a systematic review and meta-analysis
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42 43	18	
44 45 46	19	Ethics: No ethical considerations apply
40 47 48	20	
49 50	21	Word count: 1754
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## 26 ABSTRACT

Introduction: Cystoscopy has revolutionised the process of diagnosing bladder cancer, leading to better categorization of risk levels and more precise treatment plans. Nonetheless, concerns arise about the lack of uniformity among observers in predicting tumour stage and grade. To address these concerns, artificial intelligence (AI) is being incorporated into clinical settings to aid in the analysis of diagnostic and therapeutic images. The subsequent report outlines a systematic review and metaanalysis protocol aimed at evaluating the effectiveness of AI in predicting bladder cancer based on cystoscopic images.

> Methods and Analysis: Our systematic search will utilise databases including Pubmed, MEDLINE, Embase, and Cochrane. The articles published between May 2015 and April 2024 will be eligible for inclusion. For articles to be considered, they must employ AI for analysis of cystoscopic images to identify bladder cancer, present original data and be written in English. The protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) 2015 checklist. Quality and bias risk across chosen studies will be evaluated using the QUADAS-2 score.

45 Ethics and dissemination: Ethical clearance won't be necessary for conducting this
46 systematic review since results will be disseminated through peer-reviewed
47 publications and presentations at both national and international conferences.

**PROSPERO registration number:** CRD42024528345

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5 6 7	52	Strengths and limitations of this study
, 8 9	53	This protocol adheres to PRISMA guidelines and will incorporate subgroup
10 11	54	and sensitivity analyses to further explore the variability among the studies
12 13	55	included.
14 15 16	56	Al-specific metrics like the F1-score and precision-recall AUC will be
17 18	57	utilised to address limitations inherent in traditional pooled analysis, such
19 20	58	as the impact of imbalanced classes.
21 22 23	59	Given the novelty of AI technology in cystoscopy, long-term data regarding
24 25	60	its impact on clinical outcomes may be scarce.
26 27	61	Limitations on language and the exclusive use of cystoscopy may result in
28 29 30	62	a limited number of eligible studies for inclusion
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# 76 BACKGROUND

Bladder cancer is the commonest cancer of the urinary tract, and ranks as the ninth most common cancer worldwide according to the World Health Organization's 2020 report(1,2). The gold standard for diagnosing bladder cancer remains cystoscopy, as advocated by both the National Institute for Health and Care Excellence (NICE) and the European Association of Urology (EAU) guidelines(3). While white light cystoscopy (WLC) is the conventional method widely employed, however it potentially overlooks up to 20% of lesions. Furthermore, a recent systematic review and meta-analysis demonstrated that conventional WLC exhibits low diagnostic sensitivity compared to alternative modalities like blue light cystoscopy (BLC)(4). Despite the superior detection rates of bladder cancer associated with these alternative methods recommended by EAU, their adoption remains limited, likely due to their higher initial costs and limited availability(4). Transurethral resection of bladder tumour (TURBT) with white light cystoscopy (WLC) remains fundamental for diagnosing and treating non-muscle invasive bladder cancer (NMIBC) which accounts for around 75% of bladder tumours at the time of diagnosis(5). 

Artificial intelligence (AI) now boasts a remarkable ability to accurately recognise images. Al offers a promising solution to improve the diagnosis of bladder cancer during cystoscopy(6). Artificial intelligence broadly describes the modelling of intelligent behaviour by use of a computer model(7). Deep learning is a subset of artificial intelligence which more specifically positions AI within the context of medical imaging(8). Augmented cystoscopy employing deep learning holds promise in also enhancing tumour localization, intraoperative navigation, and surgical resection of bladder cancer during TURBT(9).

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While Artificial intelligence shows promise in the diagnosis of bladder cancer using cystoscopy, several limitations to the deployment of this technology need to be addressed. Given the cystoscopy imaging data used, such as WLC and BLC, studies are strongly encouraged to follow the Checklist for Artificial Intelligence in Medical Imaging (CLAIM)(10). This is to encourage the reproducibility of AI-models in development and forwarding the collaboration of research groups in external validation of their models. The checklist also provide a focus on the use of radiomic features as well as computer-aided diagnosis of imaging data. In order to be better suited for clinical development, models should be explainable in their decision-making process which may be currently under reported(11,12).

Existing reviews on this topic have provided a robust summary to the feasibility of the
application of AI in cystoscopy(13,14). But further investigation of the reported studies
with a goal of clinical deployment should be conducted next. Therefore, this systematic
review and meta-analysis seeks to outline the precision of artificial intelligence (AI) in
forecasting bladder cancer based on cystoscopic images and evaluate its potential
influence on patient clinical outcomes.

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- 0 116
- <sup>2</sup> 117 **METHODS AND ANALYSIS:**

This systematic review protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist(15). This study has been prospectively registered with the PROSPERO review database (CRD42024528345), and all methodologies detailed herein have been established prior to implementation. The statistical analysis will focus on evaluating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and areaunder-the-curve (AUC) associated with the application of artificial intelligence (AI) in

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detecting bladder cancer during cystoscopy, along with its impact on clinical outcomes. These parameters will be derived through comprehensive analysis and thematic synthesis of included studies. Pooled sensitivities and specificities across the studies will be determined before calculating PPV and NPV values. Al-specific matrices such F1-scores will as and Precision-Recall AUC also be investigated. 

Search Methodology 

A comprehensive search will be conducted across multiple databases including PubMed, MEDLINE, Embase, and the Cochrane Library. The search strategy will incorporate medical subject heading (MeSH) terms and free text combined with appropriate Boolean operators. Articles from May 2015 to April 2024 will be included to ensure a thorough retrieval of relevant evidence. The search will encompass the "bladder", "cancer", "diagnosis", "cystoscopy", "cystoscopic following key terms: images", "artificial intelligence", and "deep learning". The complete search strategy is outlined in Supplementary file 1. To streamline the initial screening phase, we will be utilising Rayyan, a semi-automated tool crafted to enhance the efficiency and precision of systematic review (16). All eligible articles identified in the initial search will be imported into Rayyan. Additionally, a manual examination of references cited in all included articles will be conducted to uncover any additional pertinent literature not captured by the initial search strategy. In instances where data is lacking or unclear, corresponding authors will be contacted for clarification.

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#### 50 Study selection and data extraction

51 Two researchers, M.B. and M.A., will independently conduct the screening process. They will carefully review the titles and abstracts of eligible studies, eliminating any 52 53 irrelevant articles. Full-text versions of relevant articles will then be retrieved for further evaluation. In the event of any discrepancies between the researchers, a third reviewer 54 (Y.Z.) will be consulted, and a consensus will be reached through discussion. The 55 56 reasons for excluding articles will be meticulously documented and outlined in a 57 PRISMA flow diagram. Prior to commencing the screening process, calibration 58 exercises will be conducted to ensure consistency among the researchers, thereby 59 minimising potential inter-reviewer bias.

60

#### 61 Inclusion and exclusion criteria

62 This systematic review will include studies employing either fully automated or semiautomated artificial intelligence (AI) for analysing cystoscopic images to detect bladder 63 64 cancer. Both prospective and retrospective studies will be considered. The main 65 comparisons will focus on evaluating sensitivities, specificities, positive predictive values (PPVs), negative predictive values (NPVs), and area under the curve (AUC) 66 values. Patient cohorts may include individuals with suspected or confirmed bladder 67 68 cancer cases, with histological findings serving as reference standards.

69 Excluded from analysis will be correspondence papers, ongoing studies, case reports, 70 and conference abstracts. Additionally, non-English language articles, studies not utilising cystoscopy as the primary diagnostic modality, and those involving patients 71 72 with a history of previous bladder cancer treatment will be excluded.

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# 175 Data extraction (table of collection)

The data outlined in Table 1 will be gathered from all selected studies. Each researcher
will independently conduct data extraction, consolidating the obtained information into
a comprehensive datasheet. Any discrepancies in data extraction will be reviewed by
a third evaluator, with the aim of reaching consensus for resolution.

180 If accessible, pertinent figures such as true positives, true negatives, false positives, 181 false negatives, and their derived calculations will be extracted accordingly. If these 182 figures are not explicitly provided, efforts will be made to compute them from available 183 data. In cases where computation is unattainable, the authors of the respective paper 184 will be contacted to provide the required data.

# 186 Table 1. Data collection items

Item No.	Data Title	Data Type
1	Year of publication	Study
	.4	characteristic
2	Study authors	Study
		characteristic
3	Patient population	Demographics
4	Study size	Demographics
5	Cystoscopic images	Methodology
6	Histopathology results	Methodology
7	AI models utilised	Methodology

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3 4 5		8	Definition for significant clinical	Methodology			
6 7			disease				
8 9 10	187	Al: artificial intelligence.					
10 11 12	188						
13 14	189	Endpoints					
15 16	190	The main en	dpoint of analysis will be the statist	ically significant quantification of			
17 18 19	191	accuracy when employing AI in bladder cancer detection during cystoscopy, aiming to					
20 21	192	assess its potential impact on clinical outcomes. Additional outcomes will encompass					
22 23	193	various parameters examining patient demographics.					
24 25 26	194						
20 27 28	195	Meta-analysi	s				
29 30 31 32 33 34 25	196	Should an ample number of suitable studies be accessible, we will proceed with a					
	197	meta-analysis	to amalgamate a quantitative measu	re of AI performance in identifying			
	198	bladder cancer from cystoscopic images. Initially, sensitivity and specificity values will					
36 37	199	be retrieved from studies, or if not accessible, computed from clinical data or solicited					
38 39	200	from authors.	If a notable fraction of studies employ	alternative metrics like F1-score			
40 41	201	or precision-re	ecall AUC, these metrics will be acquir	ed and scrutinised independently.			
42 43 44	202	The distribution	ons of untransformed, logit, and double	e-arcsine transformed proportions			
45 46	203	will be compa	ared and evaluated for normality usin	g density plots and Shapiro-Wilk			
47 48	204	tests. The set	of ratios most resembling a normal dist	tribution will be selected for further			
49 50 51	205	analysis.					
52 53	206	Heterogeneity	/ and inter-study variation will be quar	ntified using I2, and if statistically			
54 55	207	significant, a random-effects model will be employed for estimating the summary					
56 57	208	estimate. Lea	ve-one-out analysis (LOO) and accor	mpanying diagnostic plots will be			
58 59 60	209	used to ident	ify influential studies after the model f	its all relevant studies. Summary			

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proportions will be re-estimated based on the remaining studies after each study is removed. Studies exerting a statistically significant influence on the model will be identified as outliers and excluded. After excluding these studies, the model will then be refitted with a summary estimate comprising the remaining studies will be calculated to estimate the accuracy using AI in cystoscopy for bladder cancer detection. All data analysis and visualisation will be conducted using the R statistical environment with the "mymeta" and "meta" packages.

20 <sup>217</sup> 22 218

**Risk of bias in individual studies** : This study will use the QUADAS-2 tool to assess the quality and the risk of bias within each of the included studies (17). The scoring system is split into four main sections: patient selection, index test, reference standard, and flow and timing. Within each section, signalling questions assessed the quality of the research methodology and results at the study level. As included studies utilises imaging data, the CLAIM-AI checklist will be used to assess imaging specific considerations such as the classification, image reconstruction, text analysis and workflow optimisation (10). Two reviewers (M.B. and M.A.) will independently engage in this procedure, with any discrepancies resolved through consensus. The bias assessment will analyse the appropriateness and dependability of the data utilised. This analysis will contribute to evidence synthesis and enhance transparency, potentially leading to the exclusion of articles of low quality or indicative of high bias levels. If included, relevant commentaries will be integrated into the discussion. 

# 233 Ethics and Dissemination

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234 The potential of AI to assist in diagnosing bladder cancer during cystoscopy remains 235 to be thoroughly assessed. Our aim is to consolidate available information to elucidate 236 Al's role in cystoscopy for bladder cancer diagnosis and outline its impact on clinical 237 practice.

238 However, it is crucial to acknowledge several limitations. Firstly, given the novelty of 239 Al in this domain, there may be a limited number of studies available for evaluation. 240 Additionally, issues related to the diversity of reporting protocols due to regional 241 variations may arise. Furthermore, the presence of different neural networks could 242 potentially act as confounders due to variations in training datasets, leading to discrepancies in reported outcomes. 243

244 We intend to disseminate our findings through publication in a peer-reviewed journal. 245 The synthesis of this data will contribute to a deeper understanding of current AI methodologies in bladder cancer diagnosis. Ultimately, this knowledge may facilitate 246 the enhancement of existing systems, both supervised and unsupervised, to refine 247 248 reporting protocols and improve bladder cancer diagnosis in the future.

- 250 Patient and public involvement
  - 251 There will be no patient or public involvement in this study.
- 252
- 253 **Trial status** 
  - 254 - Preliminary searches: Started
    - Piloting of the study selection process: Not started 255
  - 256 - Formal screening: Not started
- 59 257 - Data extraction: Not started 60

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3 4	258	<ul> <li>Risk of bias assessment: Not started</li> </ul>
5 6 7	259	<ul> <li>Data analysis: Not started</li> </ul>
8 9 10	260	
11 12	261	Author Affiliations
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40 41 42	274	Contributors The authors' contribution includes, but is not limited to, the following:
43 44	275	MB and MA wrote the manuscript. YZ created the study concept. LM, EB and RH
45 46	276	provided supervision and guidance, GB and OO checked the manuscript in its current
47 48 49	277	form. YZ and MB are the guarantors of this work.
50 51	278	
52 53	279	Funding Imperial College London Open Access Fund
54 55 56	280	Competing Interests None
57 58	281	Patient consent for publication Not required
59 60	282	Provenance and peer review Not commissioned; externally peer-reviewed

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Utilising artificial intelligence for bladder cancer detection during cystoscopy and its impact on clinical outcomes: a systematic review and meta-analysis

The search terms for this systematic review are as follows:

((artificial intelligence OR machine intelligence OR computational intelligence OR neural network OR deep learning OR machine learning OR reinforcement learning OR convolutional neural network OR artificial neural network OR recurrent neural network OR deep neural network OR intelligent model OR AI OR NN OR DL OR ML OR CNN OR ANN OR RNN OR DNN) AND ((Bladder AND (cancer OR malignant OR transitional cell or urothelial OR squamous cell OR adenocarcinoma OR papillary OR carcinoma in situ OR non muscle invasive OR lesions OR disease)) AND (Cystoscopy OR cystoscopic images OR flexible cystoscopy OR cystourethroscopy )) AND diagnosis).

Searches will be conducted on the following databases:

PubMed, MEDLINE, Embase, and Cochrane databases

# Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

# **Instructions to authors**

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	<u>#1a</u>	Identify the report as a protocol of a systematic review	1
Update	<u>#1b</u>	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration			
	<u>#2</u>	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors			
Contact	<u>#3a</u>	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1, 12
Contribution	<u>#3b</u>	Describe contributions of protocol authors and identify the guarantor of the review	12
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1 2	Amendments			
3 4 5 6		<u>#4</u>	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes: otherwise, state plan for documenting important	n/a
7 8 9			protocol amendments	
10 11 12	Support			
12 13 14	Sources	<u>#5a</u>	Indicate sources of financial or other support for the review	n/a
15 16	Sponsor	<u>#5b</u>	Provide name for the review funder and / or sponsor	n/a
17 10	Role of sponsor or	<u>#5c</u>	Describe roles of funder(s), sponsor(s), and / or	n/a
18 19 20	funder		institution(s), if any, in developing the protocol	
21 22	Introduction			
23 24 25 26	Rationale	<u>#6</u>	Describe the rationale for the review in the context of what is already known	2
27 28 29 30 31	Objectives	<u>#7</u>	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	2
32 33 34	Methods			
35 36 37 38 39 40	Eligibility criteria	<u>#8</u>	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	2
41 42	Information	#9	Describe all intended information sources (such as	5-6
43 44 45 46 47	sources	_	electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	
48 49 50 51 52	Search strategy	<u>#10</u>	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Supplementary file
53 54	Study records -	<u>#11a</u>	Describe the mechanism(s) that will be used to manage	7-8
55 56 57 58	data management		records and data throughout the review	
59 60		For pe	er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

-	Study records - selection process	<u>#11b</u>	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta- analysis)	7-8
0 1 2 3	Study records - data collection process	<u>#11c</u>	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6-8
4 5 6 7 8	Data items	<u>#12</u>	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6-8 copyright
)   <u>2</u>  }  }	Outcomes and prioritization	<u>#13</u>	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	9-10
25 26 27 28 29 30	Risk of bias in individual studies	<u>#14</u>	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	
	Data synthesis	<u>#15a</u>	Describe criteria under which study data will be quantitatively synthesised	8-10
	Data synthesis	<u>#15b</u>	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's $\tau$ )	8-10 g
	Data synthesis	<u>#15c</u>	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8-10
	Data synthesis	<u>#15d</u>	If quantitative synthesis is not appropriate, describe the type of summary planned	8-10
50 51 52 53 54	Meta-bias(es)	<u>#16</u>	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8-10
	Confidence in cumulative	<u>#17</u>	Describe how the strength of the body of evidence will be assessed (such as GRADE)	8-10
)	evidence	For pe	er review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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- https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

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# Utilising artificial intelligence for bladder cancer detection during cystoscopy and its impact on clinical outcomes: A protocol for a systematic review and meta-analysis

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<b>Primary Subject Heading</b> :	Urology
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Keywords:	Artificial Intelligence, UROLOGY, Diagnostic Imaging



2 3	1	Utilising artificial intelligence for bladder cancer detection during cystoscopy
4 5 6	2	and its impact on clinical outcomes: A Protocol for a systematic review and
7 8	3	meta-analysis
9 10 11	4	Mohamed Baana <sup>1</sup> , Murtada Arkwazi <sup>1</sup> , Yi Zhao <sup>2</sup> , Ojone Ofagbor <sup>3</sup> , Gaurika Bhardwaj <sup>4</sup> ,
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44 45 46	19	
47 48	20	Ethics: No ethical considerations apply
49 50	21	
51 52 53	22	Word count: 1754
54 55	23	
56 57	24	
58 59 60	25	

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## 26 ABSTRACT

Introduction: Cystoscopy has revolutionised the process of diagnosing bladder cancer, leading to better categorization of risk levels and more precise treatment plans. Nonetheless, concerns arise about the lack of uniformity among observers in predicting tumour stage and grade. To address these concerns, artificial intelligence (AI) is being incorporated into clinical settings to aid in the analysis of diagnostic and therapeutic images. The subsequent report outlines a systematic review and metaanalysis protocol aimed at evaluating the effectiveness of AI in predicting bladder cancer based on cystoscopic images.

> Methods and Analysis: Our systematic search will utilise databases including Pubmed, MEDLINE, Embase, and Cochrane. The articles published between May 2015 and April 2024 will be eligible for inclusion. For articles to be considered, they must employ AI for analysis of cystoscopic images to identify bladder cancer, present original data and be written in English. The protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) 2015 checklist. Quality and bias risk across chosen studies will be evaluated using the QUADAS-2 score.

45 Ethics and dissemination: Ethical clearance won't be necessary for conducting this
46 systematic review since results will be disseminated through peer-reviewed
47 publications and presentations at both national and international conferences.

**PROSPERO registration number:** CRD42024528345

2 3	<i>E</i> 1	
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5 6 7	52	Strengths and limitations of this study
, 8 9	53	This protocol adheres to PRISMA guidelines and will incorporate subgroup
10 11	54	and sensitivity analyses to further explore the variability among the studies
12 13	55	included.
15 16	56	Al-specific metrics like the F1-score and precision-recall AUC will be
17 18	57	utilised to address limitations inherent in traditional pooled analysis, such
19 20 21	58	as the impact of imbalanced classes.
22 23	59	Given the novelty of AI technology in cystoscopy, long-term data regarding
24 25	60	its impact on clinical outcomes may be scarce.
26 27 28	61	Limitations on language and the exclusive use of cystoscopy may result in
29 30	62	a limited number of eligible studies for inclusion
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33 34 35	64	
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#### 

# 76 BACKGROUND

Bladder cancer is the commonest cancer of the urinary tract, and ranks as the ninth most common cancer worldwide according to the World Health Organization's 2020 report(1,2). The gold standard for diagnosing bladder cancer remains cystoscopy, as advocated by both the National Institute for Health and Care Excellence (NICE) and the European Association of Urology (EAU) guidelines(3). While white light cystoscopy (WLC) is the conventional method widely employed, it potentially overlooks up to 20% of lesions. Furthermore, a recent systematic review and meta-analysis demonstrated that conventional WLC exhibits low diagnostic sensitivity compared to alternative modalities like blue light cystoscopy (BLC)(4). Despite the superior detection rates of bladder cancer associated with these alternative methods recommended by EAU, their adoption remains limited, likely due to their higher initial costs and limited availability(4). Transurethral resection of bladder tumour (TURBT) with WLC remains fundamental for diagnosing and treating non-muscle invasive bladder cancer (NMIBC) which accounts for around 75% of bladder tumours at the time of diagnosis(5).

Artificial intelligence (AI) now boasts a remarkable ability to accurately recognise images. Al offers a promising solution to improve the diagnosis of bladder cancer during cystoscopy(6). Artificial intelligence broadly describes the modelling of intelligent behaviour by use of a computer model(7). Deep learning is a subset of artificial intelligence which more specifically positions AI within the context of medical imaging(8). Augmented cystoscopy employing deep learning holds promise in also enhancing tumour localization, intraoperative navigation, and surgical resection of bladder cancer during TURBT(9).

 $\begin{array}{c} 6 \\ 7 \\ 7 \\ 9 \end{array}$  While Artificial intelligence shows promise in the diagnosis of bladder cancer using  $\begin{array}{c} 7 \\ 7 \\ 9 \end{array}$  100 cystoscopy, several limitations to the deployment of this technology need to be Page 5 of 15

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addressed. Given the cystoscopy imaging data used, such as WLC and BLC, studies are strongly encouraged to follow the Checklist for Artificial Intelligence in Medical Imaging (CLAIM)(10). This is to encourage the reproducibility of AI models in development and forwarding the collaboration of research groups in external validation of their models. The checklist also provides a focus on the use of radiomic features as well as computer-aided diagnosis of imaging data. In order to be better suited for clinical development, models should be explainable in their decision-making process which may be currently under reported(11,12).

Existing reviews on this topic have provided a robust summary to the feasibility of the application of AI in cystoscopy(13,14). But further investigation of the reported studies with a goal of clinical deployment should be conducted next. Therefore, this systematic review and meta-analysis seeks to outline the precision of artificial intelligence (AI) in forecasting bladder cancer based on cystoscopic images and evaluate its potential influence on patient clinical outcomes.

- **METHODS AND ANALYSIS:**

This systematic review protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist(15). This study has been prospectively registered with the PROSPERO review database (CRD42024528345), and all methodologies detailed herein have been established prior to implementation. The statistical analysis will focus on evaluating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area-under-the-curve (AUC) associated with the application of artificial intelligence (AI) in detecting bladder cancer during cystoscopy, along with its impact on clinical outcomes. These parameters will be derived through comprehensive analysis and thematic 

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synthesis of included studies. Pooled sensitivities and specificities across the studies will be determined before calculating PPV and NPV values. Al-specific matrices such as F1-scores and Precision-Recall AUC will also be investigated. 

#### Search Methodology

A comprehensive search will be conducted across multiple databases including PubMed, MEDLINE, Embase, and the Cochrane Library. The search strategy will incorporate medical subject heading (MeSH) terms and free text combined with appropriate Boolean operators. Articles from May 2015 to April 2024 will be included to ensure a thorough retrieval of relevant evidence. The search will encompass the following key terms: "bladder", "cancer", "diagnosis", "cystoscopy", "cystoscopic images", "artificial intelligence", and "deep learning". The complete search strategy is outlined in Supplementary file 1. To streamline the initial screening phase, we will be utilising Rayvan, a semi-automated tool crafted to enhance the efficiency and precision of systematic review (16). All eligible articles identified in the initial search will be imported into Rayyan. Additionally, a manual examination of references cited in all included articles will be conducted to uncover any additional pertinent literature not captured by the initial search strategy. In instances where data is lacking or unclear, corresponding authors will be contacted for clarification.

#### Study selection and data extraction

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Two researchers, M.B. and M.A., will independently conduct the screening process. They will carefully review the titles and abstracts of eligible studies, eliminating any irrelevant articles. Full-text versions of relevant articles will then be retrieved for further evaluation. In the event of any discrepancies between the researchers, a third reviewer (Y.Z.) will be consulted, and a consensus will be reached through discussion. The reasons for excluding articles will be meticulously documented and outlined in a PRISMA flow diagram. Prior to commencing the screening process, calibration exercises will be conducted to ensure consistency among the researchers, thereby minimising potential inter-reviewer bias.

#### Inclusion and exclusion criteria

This systematic review will include studies employing either fully automated or semi-automated artificial intelligence (AI) for analysing cystoscopic images to detect bladder cancer. Both prospective and retrospective studies will be considered. The main comparisons will focus on evaluating sensitivities, specificities, positive predictive values (PPVs), negative predictive values (NPVs), and area under the curve (AUC) values. Patient cohorts may include individuals with suspected or confirmed bladder cancer cases, with histological findings serving as reference standards.

Excluded from analysis will be correspondence papers, ongoing studies, case reports, and conference abstracts. Additionally, non-English language articles, studies not utilising cystoscopy as the primary diagnostic modality, and those involving patients with a history of previous bladder cancer treatment will be excluded.

#### Data extraction (table of collection)

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The data outlined in Table 1 will be gathered from all selected studies. Each researcher will independently conduct data extraction, consolidating the obtained information into a comprehensive datasheet. Any discrepancies in data extraction will be reviewed by a third evaluator, with the aim of reaching consensus for resolution.

If accessible, pertinent figures such as true positives, true negatives, false positives, false negatives, and their derived calculations will be extracted accordingly. If these figures are not explicitly provided, efforts will be made to compute them from available data. In cases where computation is unattainable, the authors of the respective paper will be contacted to provide the required data.

# 185 Table 1. Data collection items

Item No.	Data Title	Data Type
1	Year of publication	Study
	P	characteristic
2	Study authors	Study
		characteristic
3	Patient population	Demographics
4	Study size	Demographics
5	Cystoscopic images	Methodology
6	Histopathology results	Methodology
7	AI models utilised	Methodology

2						
3 4		8	Definition for significant clinical	Methodology		
5 6 7			disease			
8 9	186	AI: artificial i	ntelligence.			
10 11 12	187					
13 14	188	Endpoints				
15 16	189	The main e	ndpoint of analysis will be the statist	ically significant quantification of		
17 18	190	accuracy wh	en employing AI in bladder cancer dete	ction during cystoscopy, aiming to		
19 20 21	191	assess its potential impact on clinical outcomes. Additional outcomes will encompass				
22 23	192	various parameters examining patient demographics.				
24 25	193					
26 27 28	194	Meta-analys	is			
28 29 30	195	Should an ample number of suitable studies be accessible, we will proceed with a				
31 32	196	meta-analysis to amalgamate a quantitative measure of AI performance in identifying				
33 34	197	bladder cancer from cystoscopic images. Initially, sensitivity and specificity values will				
35 36 37	198	be retrieved from studies, or if not accessible, computed from clinical data or solicited				
37 38 39 40 41 42 43	199	from authors	. If a notable fraction of studies emplo	y alternative metrics like F1-score		
	200	or precision-	recall AUC, these metrics will be acquir	ed and scrutinised independently.		
	201	The distribut	ions of untransformed, logit, and doubl	e-arcsine transformed proportions		
45 46	202	will be compared and evaluated for normality using density plots and Shapiro-Wilk				
47 48	203	tests. The se	t of ratios most resembling a normal dis	tribution will be selected for further		
49 50	204	analysis.				
51 52 53	205	- Heterogeneity and inter-study variation will be quantified using I2, and if statistically				
54 55	206	significant, a random-effects model will be employed for estimating the summary				
56 57	207	estimate. Le	ave-one-out analysis (LOO) and acco	mpanying diagnostic plots will be		
58 59 60	208	used to iden	tify influential studies after the model	fits all relevant studies. Summary		

8	Definition for significant clinical	Methodology
	disease	

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proportions will be re-estimated based on the remaining studies after each study is removed. Studies exerting a statistically significant influence on the model will be identified as outliers and excluded. After excluding these studies, the model will then be refitted with a summary estimate comprising the remaining studies will be calculated to estimate the accuracy using AI in cystoscopy for bladder cancer detection. All data analysis and visualisation will be conducted using the R statistical environment with the "mvmeta" and "meta" packages.

**Risk of bias in individual studies** : This study will use the QUADAS-2 tool to assess the quality and the risk of bias within each of the included studies (17). The scoring system is split into four main sections: patient selection, index test, reference standard, and flow and timing. Within each section, signalling questions assessed the quality of the research methodology and results at the study level. As included studies utilises imaging data, the CLAIM-AI checklist will be used to assess imaging specific considerations such as the classification, image reconstruction, text analysis and workflow optimisation (10). Two reviewers (M.B. and M.A.) will independently engage in this procedure, with any discrepancies resolved through consensus. The bias assessment will analyse the appropriateness and dependability of the data utilised. This analysis will contribute to evidence synthesis and enhance transparency, potentially leading to the exclusion of articles of low quality or indicative of high bias levels. If included, relevant commentaries will be integrated into the discussion.

#### **Ethics and Dissemination**

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The potential of AI to assist in diagnosing bladder cancer during cystoscopy remains to be thoroughly assessed. Our aim is to consolidate available information to elucidate Al's role in cystoscopy for bladder cancer diagnosis and outline its impact on clinical practice.

However, it is crucial to acknowledge several limitations. Firstly, given the novelty of Al in this domain, there may be a limited number of studies available for evaluation. Additionally, issues related to the diversity of reporting protocols due to regional variations may arise. Furthermore, the presence of different neural networks could potentially act as confounders due to variations in training datasets, leading to discrepancies in reported outcomes. 

We intend to disseminate our findings through publication in a peer-reviewed journal. The synthesis of this data will contribute to a deeper understanding of current AI methodologies in bladder cancer diagnosis. Ultimately, this knowledge may facilitate the enhancement of existing systems, both supervised and unsupervised, to refine reporting protocols and improve bladder cancer diagnosis in the future.

There will be no patient or public involvement in this study.

- **Trial status**
- - Preliminary searches: Started

Patient and public involvement

- - Piloting of the study selection process: Not started
- - Formal screening: Not started
- - Data extraction: Not started

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1 2				
3 4	257	<ul> <li>Risk of bias assessment: Not started</li> </ul>		
5 6	258	<ul> <li>Data analysis: Not started</li> </ul>		
7 8 9	259			
10 11	260	Author Affiliations		
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14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42	262	<sup>2</sup> Imperial College London School of Medicine, London, UK		
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	272			
	273	Contributors The authors' contribution includes, but is not limited to, the following:		
43 44	274	MB and MA wrote the manuscript. YZ created the study concept. LM, EB and RH		
45 46	275	provided supervision and guidance, GB and OO checked the manuscript in its current		
47 48 49	276	form. YZ and MB are the guarantors of this work.		
50 51	277			
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54 55 56	279	Competing Interests None		
57 58	280	Patient consent for publication Not required		
59 60	281	Provenance and peer review Not commissioned; externally peer-reviewed		

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12 13	286	indication of whether changes were made. See						
14 15	287	https://creativecommons.org/licenses/by/4.0/.						
16 17 18	288							
19 20	289	ORCID IDs						
21 22 23 24 25 26 27 28 29 30 31 32	290	Mohamed Baana: <u>https://orcid.org/0009-0006-0384-9423</u>						
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37 38	297	<ul> <li>Rakesh Heer: <u>https://orcid.org/0000-0003-1952-7462</u></li> </ul>						
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Utilising artificial intelligence for bladder cancer detection during cystoscopy and its impact on clinical outcomes: A Protocol systematic review and meta-analysis

The search terms for this systematic review are as follows:

((artificial intelligence OR machine intelligence OR computational intelligence OR neural network OR deep learning OR machine learning OR reinforcement learning OR convolutional neural network OR artificial neural network OR recurrent neural network OR deep neural network OR intelligent model OR predictive model OR computational model OR algorithm OR AI OR NN OR DL OR ML OR CNN OR ANN OR RNN OR DNN) AND (random forests OR support vector machines OR nearest neighbours OR logistic regression) AND ((Bladder AND (cancer OR malignant OR transitional cell or urothelial OR squamous cell OR adenocarcinoma OR papillary OR carcinoma in situ OR non muscle invasive OR lesions OR disease)) AND (cystoscop\* OR cystoscop\* images OR flexible cystoscopy OR cystourethroscopy )) AND (diagnos\* OR detect\*)).

Searches will be conducted on the following databases:

PubMed, MEDLINE, Embase, and Cochrane databases

# Utilising artificial intelligence for bladder cancer detection during cystoscopy and its impact on clinical outcomes: A protocol for a systematic review and meta-analysis

Journal:	BMJ Open
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<b>Primary Subject Heading</b> :	Urology
Secondary Subject Heading:	Surgery
Keywords:	Artificial Intelligence, UROLOGY, Diagnostic Imaging



2 3	1	Utilising artificial intelligence for bladder cancer detection during cystoscopy
4 5 6	2	and its impact on clinical outcomes: A Protocol for a systematic review and
7 8	3	meta-analysis
9 10 11	4	Mohamed Baana <sup>1</sup> , Murtada Arkwazi <sup>1</sup> , Yi Zhao <sup>2</sup> , Ojone Ofagbor <sup>3</sup> , Gaurika Bhardwaj <sup>4</sup> ,
12 13	5	Mariam Lami <sup>4</sup> , Eva Bolton <sup>4</sup> , Rakesh Heer <sup>4</sup>
14 15 16	6	
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## 26 ABSTRACT

Introduction: Cystoscopy has revolutionised the process of diagnosing bladder cancer, leading to better categorization of risk levels and more precise treatment plans. Nonetheless, concerns arise about the lack of uniformity among observers in predicting tumour stage and grade. To address these concerns, artificial intelligence (AI) is being incorporated into clinical settings to aid in the analysis of diagnostic and therapeutic images. The subsequent report outlines a systematic review and metaanalysis protocol aimed at evaluating the effectiveness of AI in predicting bladder cancer based on cystoscopic images.

> Methods and Analysis: Our systematic search will utilise databases including Pubmed, MEDLINE, Embase, and Cochrane. The articles published between May 2015 and April 2024 will be eligible for inclusion. For articles to be considered, they must employ AI for analysis of cystoscopic images to identify bladder cancer, present original data and be written in English. The protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) 2015 checklist. Quality and bias risk across chosen studies will be evaluated using the QUADAS-2 score.

45 Ethics and dissemination: Ethical clearance won't be necessary for conducting this
46 systematic review since results will be disseminated through peer-reviewed
47 publications and presentations at both national and international conferences.

**PROSPERO registration number:** CRD42024528345

2 3	<i>E</i> 1	
4	51	
5 6 7	52	Strengths and limitations of this study
, 8 9	53	This protocol adheres to PRISMA guidelines and will incorporate subgroup
10 11	54	and sensitivity analyses to further explore the variability among the studies
12 13	55	included.
14 15 16	56	Al-specific metrics like the F1-score and precision-recall AUC will be
17 18	57	utilised to address limitations inherent in traditional pooled analysis, such
19 20 21	58	as the impact of imbalanced classes.
21 22 23	59	Given the novelty of AI technology in cystoscopy, long-term data regarding
24 25	60	its impact on clinical outcomes may be scarce.
26 27 28	61	Limitations on language and the exclusive use of cystoscopy may result in
28 29 30	62	a limited number of eligible studies for inclusion
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# 76 BACKGROUND

Bladder cancer is the commonest cancer of the urinary tract, and ranks as the ninth most common cancer worldwide according to the World Health Organization's 2020 report(1,2). The gold standard for diagnosing bladder cancer remains cystoscopy, as advocated by both the National Institute for Health and Care Excellence (NICE) and the European Association of Urology (EAU) guidelines(3). While white light cystoscopy (WLC) is the conventional method widely employed, it potentially overlooks up to 20% of lesions. Furthermore, a recent systematic review and meta-analysis demonstrated that conventional WLC exhibits low diagnostic sensitivity compared to alternative modalities like blue light cystoscopy (BLC)(4). Despite the superior detection rates of bladder cancer associated with these alternative methods recommended by EAU, their adoption remains limited, likely due to their higher initial costs and limited availability(4). Transurethral resection of bladder tumour (TURBT) with WLC remains fundamental for diagnosing and treating non-muscle invasive bladder cancer (NMIBC) which accounts for around 75% of bladder tumours at the time of diagnosis(5).

Artificial intelligence (AI) now boasts a remarkable ability to accurately recognise images. Al offers a promising solution to improve the diagnosis of bladder cancer during cystoscopy(6). Artificial intelligence broadly describes the modelling of intelligent behaviour by use of a computer model(7). Deep learning is a subset of artificial intelligence which more specifically positions AI within the context of medical imaging(8). Augmented cystoscopy employing deep learning holds promise in also enhancing tumour localisation, intraoperative navigation, and surgical resection of bladder cancer during TURBT(9).

 $\begin{array}{c} 6 \\ 7 \\ 7 \\ 9 \end{array}$  While Artificial intelligence shows promise in the diagnosis of bladder cancer using  $\begin{array}{c} 7 \\ 7 \\ 9 \end{array}$  100 cystoscopy, several limitations to the deployment of this technology need to be Page 5 of 15

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addressed. Given the cystoscopy imaging data used, such as WLC and BLC, studies are strongly encouraged to follow the Checklist for Artificial Intelligence in Medical Imaging (CLAIM)(10). This is to encourage the reproducibility of AI models in development and forwarding the collaboration of research groups in external validation of their models. The checklist also provides a focus on the use of radiomic features as well as computer-aided diagnosis of imaging data. In order to be better suited for clinical development, models should be explainable in their decision-making process which may be currently under reported(11,12).

Existing reviews on this topic have provided a robust summary to the feasibility of the application of AI in cystoscopy(13,14). But further investigation of the reported studies with a goal of clinical deployment should be conducted next. Therefore, this systematic review and meta-analysis seeks to outline the precision of artificial intelligence (AI) in forecasting bladder cancer based on cystoscopic images and evaluate its potential influence on patient clinical outcomes.

- **METHODS AND ANALYSIS:**

This systematic review protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist(15). This study has been prospectively registered with the PROSPERO review database (CRD42024528345), and all methodologies detailed herein have been established prior to implementation. The statistical analysis will focus on evaluating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area-under-the-curve (AUC) associated with the application of artificial intelligence (AI) in detecting bladder cancer during cystoscopy, along with its impact on clinical outcomes. These parameters will be derived through comprehensive analysis and thematic 

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synthesis of included studies. Pooled sensitivities and specificities across the studies
will be determined before calculating PPV and NPV values. Al-specific matrices such
as F1-scores and Precision-Recall AUC will also be investigated. This review intends
to start on the 1<sup>st</sup> October 2024 and end on the 30<sup>th</sup> April 2025.

2 130

# 131 Search Methodology

A comprehensive search will be conducted across multiple databases including PubMed, MEDLINE, Embase, and the Cochrane Library. The search strategy will incorporate medical subject heading (MeSH) terms and free text combined with appropriate Boolean operators. Articles from May 2015 to April 2024 will be included to ensure a thorough retrieval of relevant evidence. The search will encompass the following key terms: "bladder", "cancer", "diagnosis", "cystoscopy", "cystoscopic images", "artificial intelligence", and "deep learning". The complete search strategy is outlined in Supplementary file 1. To streamline the initial screening phase, we will be utilising Rayvan, a semi-automated tool crafted to enhance the efficiency and precision of systematic review (16). All eligible articles identified in the initial search will be imported into Rayyan. Additionally, a manual examination of references cited in all included articles will be conducted to uncover any additional pertinent literature not captured by the initial search strategy. In instances where data is lacking or unclear, corresponding authors will be contacted for clarification.

### 149 Study selection and data extraction

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Two researchers, M.B. and M.A., will independently conduct the screening process. They will carefully review the titles and abstracts of eligible studies, eliminating any irrelevant articles. Full-text versions of relevant articles will then be retrieved for further evaluation. In the event of any discrepancies between the researchers, a third reviewer (Y.Z.) will be consulted, and a consensus will be reached through discussion. The reasons for excluding articles will be meticulously documented and outlined in a PRISMA flow diagram. Prior to commencing the screening process, calibration exercises will be conducted to ensure consistency among the researchers, thereby minimising potential inter-reviewer bias.

#### Inclusion and exclusion criteria

This systematic review will include studies employing either fully automated or semi-automated artificial intelligence (AI) for analysing cystoscopic images to detect bladder cancer. Both prospective and retrospective studies will be considered. The main comparisons will focus on evaluating sensitivities, specificities, positive predictive values (PPVs), negative predictive values (NPVs), and area under the curve (AUC) values. Patient cohorts may include individuals with suspected or confirmed bladder cancer cases, with histological findings serving as reference standards.

Excluded from analysis will be correspondence papers, ongoing studies, case reports, and conference abstracts. Additionally, non-English language articles, studies not utilising cystoscopy as the primary diagnostic modality, and those involving patients with a history of previous bladder cancer treatment will be excluded.

#### Data extraction (table of collection)

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The data outlined in Table 1 will be gathered from all selected studies. Each researcher will independently conduct data extraction, consolidating the obtained information into a comprehensive datasheet. Any discrepancies in data extraction will be reviewed by a third evaluator, with the aim of reaching consensus for resolution.

If accessible, pertinent figures such as true positives, true negatives, false positives, false negatives, and their derived calculations will be extracted accordingly. If these figures are not explicitly provided, efforts will be made to compute them from available data. In cases where computation is unattainable, the authors of the respective paper will be contacted to provide the required data.

# 185 Table 1. Data collection items

Item No.	Data Title	Data Type
1	Year of publication	Study
	P	characteristic
2	Study authors	Study
		characteristic
3	Patient population	Demographics
4	Study size	Demographics
5	Cystoscopic images	Methodology
6	Histopathology results	Methodology
7	AI models utilised	Methodology

2					
3 4		8	Definition for significant clinical	Methodology	
5 6 7			disease		
8 9	186	AI: artificial i	ntelligence.		
10 11 12	187				
13 14	188	Endpoints			
15 16	189	The main e	ndpoint of analysis will be the statist	ically significant quantification of	
17 18	190	accuracy wh	en employing AI in bladder cancer dete	ction during cystoscopy, aiming to	
19 20 21	191	assess its po	otential impact on clinical outcomes. Ad	ditional outcomes will encompass	
22 23	192	various parameters examining patient demographics.			
24 25	193				
26 27 28	194	Meta-analys	is		
28 29 30	195	Should an a	mple number of suitable studies be a	ccessible, we will proceed with a	
31 32	196	meta-analys	s to amalgamate a quantitative measu	re of AI performance in identifying	
33 34 35 36 37 38 39 40 41	197	bladder cand	er from cystoscopic images. Initially, se	ensitivity and specificity values will	
	198	be retrieved	from studies, or if not accessible, comp	outed from clinical data or solicited	
	199	from authors	. If a notable fraction of studies emplo	y alternative metrics like F1-score	
	200	or precision-	recall AUC, these metrics will be acquir	ed and scrutinised independently.	
42 43	201	The distribut	ions of untransformed, logit, and doubl	e-arcsine transformed proportions	
45 46	202	will be comp	pared and evaluated for normality usir	g density plots and Shapiro-Wilk	
47 48	203	tests. The se	t of ratios most resembling a normal dis	tribution will be selected for further	
49 50	204	analysis.			
51 52 53	205	Heterogenei	y and inter-study variation will be qua	ntified using I2, and if statistically	
54 55	206	significant, a random-effects model will be employed for estimating the summary			
56 57	207	estimate. Le	ave-one-out analysis (LOO) and acco	mpanying diagnostic plots will be	
58 59 60	208	used to iden	tify influential studies after the model	fits all relevant studies. Summary	

8	Definition for significant clinical	Methodology
	disease	

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209 proportions will be re-estimated based on the remaining studies after each study is 210 removed. Studies exerting a statistically significant influence on the model will be 211 identified as outliers and excluded. After excluding these studies, the model will then 212 be refitted with a summary estimate comprising the remaining studies will be 213 calculated to estimate the accuracy using AI in cystoscopy for bladder cancer 214 detection. All data analysis and visualisation will be conducted using the R statistical 215 environment with the "mymeta" and "meta" packages.

Risk of bias in individual studies: This study will use the QUADAS-2 tool to assess the quality and the risk of bias within each of the included studies (17). The scoring system is split into four main sections: patient selection, index test, reference standard, and flow and timing. Within each section, signalling questions assessed the quality of the research methodology and results at the study level. As included studies utilises imaging data, the CLAIM-AI checklist will be used to assess imaging specific considerations such as the classification, image reconstruction, text analysis and workflow optimisation (10). Two reviewers (M.B. and M.A.) will independently engage in this procedure, with any discrepancies resolved through consensus. The bias assessment will analyse the appropriateness and dependability of the data utilised. This analysis will contribute to evidence synthesis and enhance transparency, potentially leading to the exclusion of articles of low quality or indicative of high bias levels. If included, relevant commentaries will be integrated into the discussion.

232 Ethics and Dissemination

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The potential of AI to assist in diagnosing bladder cancer during cystoscopy remains to be thoroughly assessed. Our aim is to consolidate available information to elucidate Al's role in cystoscopy for bladder cancer diagnosis and outline its impact on clinical practice.

However, it is crucial to acknowledge several limitations. Firstly, given the novelty of Al in this domain, there may be a limited number of studies available for evaluation. Additionally, issues related to the diversity of reporting protocols due to regional variations may arise. Furthermore, the presence of different neural networks could potentially act as confounders due to variations in training datasets, leading to discrepancies in reported outcomes. 

We intend to disseminate our findings through publication in a peer-reviewed journal. The synthesis of this data will contribute to a deeper understanding of current AI methodologies in bladder cancer diagnosis. Ultimately, this knowledge may facilitate the enhancement of existing systems, both supervised and unsupervised, to refine reporting protocols and improve bladder cancer diagnosis in the future.

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There will be no patient or public involvement in this study.

- **Trial status** 
  - - Preliminary searches: Started

Patient and public involvement

- - Piloting of the study selection process: Not started
- - Formal screening: Not started
- - Data extraction: Not started

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3 4 5 6 7	257	<ul> <li>Risk of bias assessment: Not started</li> </ul>	
	258	<ul> <li>Data analysis: Not started</li> </ul>	
7 8 9	259		
10 11	260	Author Affiliations	
12 13	261	<sup>1</sup> London North West University Healthcare NHS Trust, London, UK	
14 15 16	262	<sup>2</sup> Imperial College London School of Medicine, London, UK	
17 18 19 20 21	263	<sup>3</sup> Norfolk and Norwich University Hospital NHS Trust	
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22 23	265		
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	271		
	272		
	273	Contributors The authors' contribution includes, but is not limited to, the following:	
43 44	274	MB and MA wrote the manuscript. YZ created the study concept. LM, EB and RH	
45 46	275	provided supervision and guidance, GB and OO checked the manuscript in its current	
47 48 49	276	form. YZ and MB are the guarantors of this work.	
50 51	277		
52 53	278	Funding Imperial College London Open Access Fund	
54 55 56	279	Competing Interests None	
57 58	280	Patient consent for publication Not required	
59 60	281	Provenance and peer review Not commissioned; externally peer-reviewed	

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1 2 BMJ Open

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	286	indication of whether changes were made. See
14 15	287	https://creativecommons.org/licenses/by/4.0/.
16 17 19	288	
19         20         21         22         23         24         25         26         27         28         29         30         31         32         33         34         35         36         37         38         39         40         41         42	289	ORCID IDs
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