

# BLADDER CANCER: AN ASSESSMENT OF INTERNATIONAL PRACTICE GUIDELINES





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- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
- **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.**
- **Finally, this report has been approved by common assent by the Executive Board.**



- Only the KCE is responsible for errors or omissions that could persist. The policy recommendations are also under the full responsibility of the KCE.
- The original NICE (National Institute for Health and Care Excellence) guideline to which this document refers, was produced by the British National Collaborating Centre for Cancer in 2015. It is available from <http://www.nice.org.uk/guidance/ng2>. NICE guidance is prepared for the National Health Service in England and Wales and does not necessarily apply to Belgium. NICE has not been involved in the development or adaptation of any guidance for use in Belgium.

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## ■ FOREWORD

As of today, no single medical doctor with a crowded practice would by any means be able to stay up to date by reading all good quality studies in his or her professional domain. Take for instance bladder cancer, the subject of the present publication: a PubMed search for reviews provides more than 5000 hits, each of them summarising a manifold of primary studies. The European Guidelines International Network (GIN) website presently provides access to 16 bladder cancer guidelines, while a search on the US National Guideline Clearinghouse yields as many as 100 guidelines.

Not all of these guidelines meet the highest quality standards. In some cases the search for evidence was insufficient, or the guideline development process was not documented in a transparent way. Other guidelines were fraught with conflicts of interest. But, before a guideline can really be considered trustworthy and, for that matter, useful to the clinician, each single step in its production process must satisfy all appropriate quality requirements. The correct appraisal of this level of quality doesn't come for free, though: it takes substantial time and asks for specific competences, neither of which being available in abundance in a normal clinical practice. As a consequence, the average practitioner is at risk of losing sight of the forest for the trees.

Time and again, KCE is confronted with the same difficult question: should we invest time and resources to add yet another guideline to the existing plethora? Sometimes, this seems to make sense, e.g. when the material out there doesn't pass the quality mark. It could also help to secure a good local acceptance of the recommendations. In the present case, however, we resolutely decided not to redo the work, for the good reason that we have a very recent comprehensive guideline from NICE in the UK, which, by all standards, is top quality! What we offer instead to the clinicians, is to separate the wheat from the chaff and to simply refer them to the best guideline that is currently around. Which makes for this rather atypical KCE product... but also allows us to orient our ever limited resources to other questions for which good answers lie not at hand yet.

Christian LÉONARD  
Deputy general director

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## ■ SCIENTIFIC REPORT

### 1 INTRODUCTION

#### 1.1 Background

The development of clinical care pathways is one of the main actions described in the Belgian National Cancer Plan 2008-2010 and one of the assignments of the College of Oncology. For many years the Belgian Health Care Knowledge Centre (KCE) has collaborated with the College of Oncology. More precisely, it has provided scientific support in the development of clinical practice guidelines. So far, this collaboration has resulted in the publication of clinical practice guidelines on breast cancer, colorectal cancer, testicular cancer, pancreatic cancer, upper gastrointestinal cancer, cervical cancer, prostate cancer and lung cancer.

Already in 2012 the College of Oncology submitted to the KCE a “Topic Proposal” on the diagnosis, management and follow-up of bladder cancer. Because of constraints in time and available human resources, the KCE decided to address this topic in 2014-2015.

#### 1.2 Overall objectives

In the scoping review of this project we found that some international groups performed an update of their bladder cancer guideline every year (European Association of Urology – EAU, and the US based National Comprehensive Cancer Network – NCCN). Furthermore, it appeared that the UK’s National Collaborating Centre for Cancer (NCC-C) was anticipating the publication of a guideline (GL) in February 2015, the draft of which became publicly available in June 2014 (the final document was published February 25, 2015).

For the sake of efficiency, we decided to critically appraise recently published GLs on bladder cancer before deciding if there was need for the production of one or more *de novo* Belgian recommendations. In the present document, we report the results of this critical appraisal.



### 1.3 Research question

Our aim was to identify a comprehensive high-quality practice guideline on the diagnosis, management and follow-up of both muscular-non-invasive and muscular-invasive bladder cancer (limited to urothelial carcinoma). Surgical and radiation therapy as well as adjuvant therapy were to be considered.

Ureteral, urethral and genital neoplasms were out of scope of the present report.

## 2 METHODOLOGY

### 2.1 Search strategy: databases and date limits

#### 2.1.1 Electronic medical databases

Electronic search for guidelines was performed following the procedure described in the KCE process book

(<https://kce.fgov.be/nl/content/wetenschappelijke-process-notes>).

The following databases were consulted in September 2014:

- Medline (<http://www.ncbi.nlm.nih.gov/pubmed>)
- Embase (<http://www.embase.com/>)
- The Cochrane Database of Systematic Reviews (<http://www.cochrane.org>)

##### 2.1.1.1 Medline @ Ovid

Date	2014-09-15		
Database	Medline (OVID)		
Search Strategy	#	Query	Results
1	exp Urinary Bladder Neoplasms/		<b>44404</b>
2	(tcc or transitional cell).mp.		<b>20272</b>
3	((bladder* or urin* or urotheli*) adj3 (cancer* or neoplasm* or tumo?r* or adenoma* or carcinoma* or adenocarcinom* or squamous* or malignan*)).mp.		<b>58897</b>
4	exp carcinoma, transitional cell/		<b>16020</b>
5	or/1-4		<b>64148</b>
6	limit 5 to systematic reviews		<b>886</b>
7	limit 6 to yr="2009 -Current"		<b>564</b>



## 2.1.1.2 Embase @ Embase.com

Date	2014-09-15		
Database	Embase (Embase.com)		
Search Strategy	#	Query	Results
(attention, for PubMed, check « Details »)	#1	'bladder cancer'/exp	45,658
	#2	tcc:ab,ti OR 'transitional cell':ab,ti	14,315
	#3	'bladder tumor'/exp	63,708
	#4	((bladder* OR urin* OR urotheli*) NEAR/3 (cancer* OR neoplas* OR tumor* OR tumour* OR carcinom* OR adenocarcinom* OR squamous* OR malignan*)):ab,ti	59,769
	#5	'transitional cell carcinoma'/exp	17,544
	#6	#1 OR #2 OR #3 OR #4 OR #5	85,488
	#7	[cochrane review]/lim OR 'systematic review' OR 'meta analyse' OR [meta analysis]/lim OR [systematic review]/lim OR 'meta analyses' OR 'meta analysis' OR 'guideline' OR 'guidelines'	588,690
	#8	#6 AND #7	2,580
	#9	[medline]/lim	21,349,079
	#10	#8 AND #9	1,644
	#11	#8 NOT #10	936
	#12	#11 AND (2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py)	804

## 2.1.1.3 Cochrane Database of Systematic Reviews

Date	2014-09-15		
Database	Cochrane		
Search Strategy	#	Query	Results
(attention, for PubMed, check « Details »)	#1	MeSH descriptor: [Urinary Bladder Neoplasms] explode all trees	1063
	#2	(tcc or "transitional cell"):ab,ti	398
	#3	((bladder* or urin* or urotheli*) near/3 (cancer* or carcinom* or adenocarcinom* or adenom* or squamous* or neoplas* or tumor* or tumour* or malignan*)):ab,ti	1679
	#4	MeSH descriptor: [Carcinoma, Renal Cell] explode all trees	491
	#5	#1 or #2 or #3 or #4	2425
	#6	#5 Publication Year from 2009 to 2014	709
Note	<b>CDSR: 23</b> <b>DARE: 121</b> <b>HTA database: 35</b> <b>CRD economic evaluations: 42</b>		



### 2.1.2 Handsearch on institutional websites

Since specific guidelines often can only be identified through local websites of scientific associations or government agencies, we complemented the abovementioned search in September 2014 with a search for existing guidelines published by other institutions after 01/01/2009 through the following websites:

- National Guideline Clearinghouse (NGC) (<http://www.guideline.gov/>): a US-based database of clinical practice guidelines primarily in the English language with free access
- International Guideline Library (G-I-N) (<http://www.g-i-n.net>): database of the Guideline International Network (KCE is member of GIN and has full access to the records)
- EBMPPracticeNet: DUODECIM guidelines, free access in Belgium, funded by RIZIV-INAMI, translation in Dutch and French
- National Institute for Health and Care Excellence (NICE) (<https://www.nice.org.uk/guidance>)
- Scottish Intercollegiate Guidelines Network (SIGN) (<http://www.sign.ac.uk/>)
- Nederlands Huisartsengenootschap (NHG) (<https://www.nhg.org/richtlijnen-praktijk>)
- Haute Autorité de Santé (HAS) [http://bfes.has-sante.fr/HTML/indexBFES\\_HAS.html](http://bfes.has-sante.fr/HTML/indexBFES_HAS.html)
- Canadian Medical Association (<https://www.cma.ca/En/Pages/clinical-practice-guidelines.aspx>)
- Diliguide (<http://www.diliguide.nl/>)
- European Association of Urology (EAU) (<http://uroweb.org/>)
- Australian clinical practice guidelines - National Health and Medical Research Council (NHMRC) <http://www.nhmrc.gov.au/>
- New Zealand Guidelines Group (NZGG) <http://www.nzgg.org.nz/>
- Google custom search

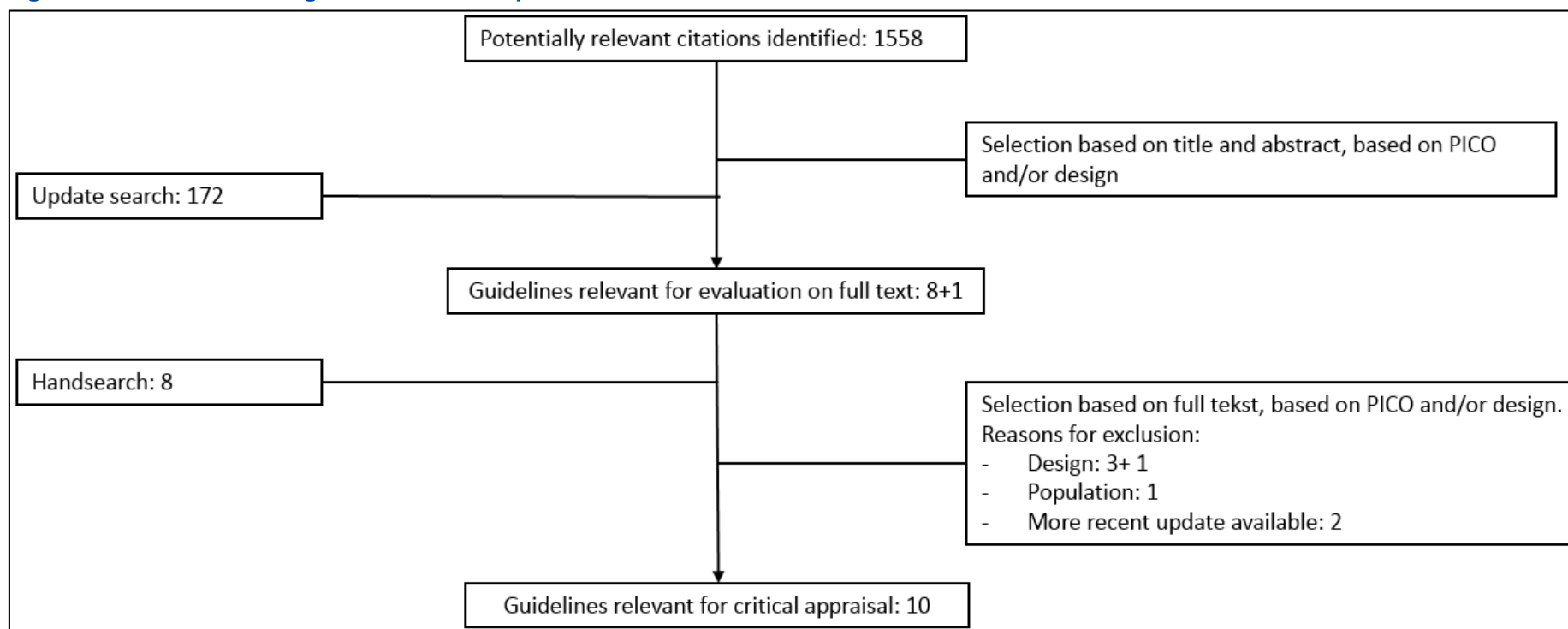
Guidelines published in Dutch, English, French or German were selected. Results are provided in Appendix. On January 8, 2015 an update of the searches was executed. It was decided to exclude guidelines published before Jan 1, 2010.

### 2.2 Search results and primary selection

The search strategy on electronic medical databases yielded 1558 hits. Selection on title and abstract based on research question and design, excluded 1550 references. The remaining 8 references were selected for full text evaluation (Figure 1).<sup>1-8</sup> On January 8, 2015 an update of the search strategy was performed. This update revealed 172 hits, from which 1 was selected for further evaluation.<sup>9</sup>



Figure 1 – Flowchart of the guideline selection process



The handsearch on institutional websites revealed 8 references (Alberta 2013, Alberta 2013, HAS 2010, EAU 2014, EAU 2014, NICE 2015, British Uro-oncology Group 2013 – documents available from websites - and Moretto<sup>10</sup>). References already found in the results from the electronic search strategy were not taken into account. After full text selection on research question and design, 5 references were excluded due to design (British Uro-oncology Group 2013) and population (Moretto<sup>10</sup>). Two references were rejected because of target condition (small cell carcinoma only).

On the 8<sup>th</sup> of January 2015, the handsearch was repeated but no new guidelines were identified. Overall, 10 guidelines were selected for further full critical appraisal.



### 2.3 The AGREE instrument

The Appraisal of Guidelines for REsearch & Evaluation (AGREE) Instrument is a tool that was developed to address the issue of variability in guideline quality. It assesses the methodological rigour and transparency in which a guideline is produced ([www.agreetrust.org](http://www.agreetrust.org)). The tool has gained international acceptance<sup>11, 12</sup> and it is also used in Belgium by CEBAM, the Centre for Evidence-Based Medicine, as the validation instrument of guidelines produced by national agencies. It is also used by the KCE as the standard for the critical appraisal of guidelines (<http://processbook.kce.fgov.be/>).

The AGREE-II instrument, which is an update of the original AGREE tool, comprises 23 items organised into 6 quality domains:

1. Scope and purpose:
    - a. The overall objective(s) of the guideline is (are) specifically described.
    - b. The health question(s) covered by the guideline is (are) specifically described.
    - c. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.
  2. Stakeholder involvement:
    - a. The guideline development group includes individuals from all relevant professional groups.
    - b. The views and preferences of the target population (patients, public, etc.) have been sought.
    - c. The target users of the guideline are clearly defined.
  3. Rigour of development:
    - a. Systematic methods were used to search for evidence.
    - b. The criteria for selecting the evidence are clearly described.
    - c. The strengths and limitations of the body of evidence are clearly described.
    - d. The methods for formulating the recommendations are clearly described.
    - e. The health benefits, side effects, and risks have been considered in formulating the recommendations.
    - f. There is an explicit link between the recommendations and the supporting evidence.
  4. Clarity of presentation:
    - a. The recommendations are specific and unambiguous.
    - b. The different options for management of the condition or health issue are clearly presented.
    - c. Key recommendations are easily identifiable
  5. Applicability:
    - a. The guideline describes facilitators and barriers to its application.
    - b. The guideline provides advice and/or tools on how the recommendations can be put into practice.
    - c. The potential resource implications of applying the recommendations have been considered.
    - d. The guideline presents monitoring and/or auditing criteria.
  6. Editorial independence:
    - a. The views of the funding body have not influenced the content of the guideline.
    - b. Competing interests of guideline development group members have been recorded and addressed.
- Each of the 23 items targets various aspects of practice guideline quality and can be scored on a scale from 1 (strongly disagree) to 7 (strongly agree). The global rating allows an overall assessment of the guideline's quality. Detailed scoring information is provided in the instrument that can be accessed on-line: [http://www.agreetrust.org/wp-content/uploads/2013/10/AGREE-II-Users-Manual-and-23-item-Instrument\\_2009\\_UPDATE\\_2013.pdf](http://www.agreetrust.org/wp-content/uploads/2013/10/AGREE-II-Users-Manual-and-23-item-Instrument_2009_UPDATE_2013.pdf). A final "Overall score" that may rank from 1 to 7 is provided at the end of the GL assessment. We used the AGREE-II instrument to evaluate the methodological quality of the selected 10 international guidelines. Each guideline was scored by two independent researchers (ADS, HVB) and discussed in case of disagreement.



### 3 CRITICAL APPRAISAL OF 10 RECENT GUIDELINES

A description of the assessment of each of the selected guidelines is provided below, in chronological order as they were published.

#### 3.1 Haute Autorité de Santé – 2010

This guideline (GL) is accessible from the HAS website ([http://www.has-sante.fr/portail/jcms/c\\_969326/fr/ald-n-30-cancer-de-la-vessie](http://www.has-sante.fr/portail/jcms/c_969326/fr/ald-n-30-cancer-de-la-vessie)).

**1: Scope and purpose.** The overall objective of this GL is adequately described. No explicit research questions were specified.

**2: Stakeholder involvement.** The GDG is composed of multidisciplinary group of medical experts. There is a strong involvement of the potential users and patient representatives (“groupe de lecture”).

**3: Rigour of development.** The evidence base for this GL is limited to other GLs and systematic reviews. Its bibliography includes only 29 references (all published before 2010). No search strategy nor criteria for selecting the evidence are provided. The methods for formulating the recommendations are described on the website (“80% agreement”). The document assigns no levels of evidence.

**4: Clarity of presentation.** Key recommendations are clearly summarised at the start.

**5: Applicability.** Facilitators and barriers to the application of the GL, potential resource implications or monitoring or auditing criteria are not considered.

**6: Editorial independence.** Not clearly mentioned.

**We attributed this GL an overall score of 2.0 in the AGREE-II instrument. Its major weakness is its inadequate search for evidence and the fact that it can no longer be considered up to date.**

**Up-to-dateness: search dates are not provided; the GL was validated in May 2010.**

#### 3.2 Italian Urological Association – 2010

This GL is accessible from the Italian Urological Association website (<http://www.uopro.it/pubblicazioni/new-italian-guidelines-on-bladder-cancer-based-on-the-world-health-organization-2004-classification.pdf>).<sup>7</sup> It focuses on the management of bladder cancer.

**1: Scope and purpose.** The overall objective of this GL is adequately described, but the research questions are not specified. The guideline aims to describe all management strategies in bladder cancer, so no further specification of the target population is provided.

**2: Stakeholder involvement.** The guideline development group consists of a multidisciplinary group composed of urologists, medical oncologists, radiotherapists, GPs, radiologists, epidemiologists and methodologists. In the list of authors the affiliation is mentioned, however their specific contribution in the development process is not mentioned. It is not mentioned whether the views and preference of the target population have been sought nor who the target users are.

**3: Rigour of development.** Within the item of systematic methods, the search date (2004-2008) and the searched database (Medline) are mentioned, but no information is provided on the search terms or the full search strategy. It is mentioned that selection criteria were applied for the in-and exclusion of the retrieved references, but we could not retrieve them. No formal quality assessment was performed to identify the strength and limitations of the body of evidence, however, every panellist assessed himself the internal and external validity of the retrieved studies. For the formulation of the recommendations the GRADE system was applied in combination with a consensus conference to discuss the discrepancies between the scientific evidence and the clinical practice. The explicit link between the recommendation and the evidence and the language use in the recommendations indicate the application of the GRADE system (e.g. it is advisable, it is recommended etc.). No information could be retrieved on the external review procedure or if an update of the guideline is foreseen.

**4: Clarity of presentation.** Each recommendation is followed by a description of its body of evidence. No schematic overview or text boxes with the key recommendations are provided.

**5: Applicability.** This guideline scored for all items of this domain very low due to the lack of information on potential facilitators and barriers to its





application and if potential resource implications have been considered. No monitoring and/or auditing criteria are reported.

**6: Editorial independence.** It is stated that no conflicts of interests were declared.

**We attributed this GL an overall score of 4.5 in the AGREE-II instrument. Its major strengths are the application of the GRADE system and the explicit link between the recommendations and the underlying evidence. The major weaknesses are the search date (until 2008), the rather brief description of the used search strategy and the lack of tools for clinical practice.**

**Up-to-dateness: the most recent search date is December 2008.**

### 3.3 International Bladder Cancer Group – 2011

This text in fact is a review of GLs for the management of non-muscle invasive bladder cancer.<sup>5</sup> It focuses on the definition of risk levels and postoperative chemotherapeutic instillation and BCG therapy. It is an update of a similar document that was published in 2008. For the present version, scientific literature as of April 2010 is included.

**1: Scope and purpose.** The overall objective is mentioned in the guideline but no clear details are provided on the health questions it considers.

**2: Stakeholder involvement.** The GDG is composed of an international committee of experts on bladder cancer management (“the international bladder cancer group”). There is no clear involvement of medical or paramedical disciplines other than urologists, nor of the potential users of the GL or patient representatives. It is not clear if any consultation process had taken place to capture patients/public’s views and preferences.

**3: Rigour of development.** For its review of GLs, this text only considers the GLs produced by the European Association of Urology (EAU), First International Consultation on Bladder Tumours, National Comprehensive Cancer Network and American Urological Association. It does not stipulate why those GLs were selected. Furthermore, it does not explain why it considered the EAU guidelines to represent best practice with regard to TURBT and the use of intra-vesical therapy, which it adopted as such. The present GL focuses on risk level definitions and management strategies. It

adapted the varying definitions that were used in existing GLs, but does not specify the supporting evidence for the new definitions.

The document does not assign levels of evidence. Description of side effects is not discussed.

**4: Clarity of presentation.** Key recommendations are clearly summarised in the results-section of the abstract. In the full text of the report, recommendations are adequately presented.

**5: Applicability.** A positive point is the inclusion of an algorithm for the treatment of non-invasive bladder cancer. Facilitators and barriers to the application of the GL, potential resource implications or monitoring or auditing criteria are not considered.

**6: Editorial independence.** It is not clear whether funding for the GL production was obtained. Conflicts of interests of the GDG members are provided.

**We attributed this GL an overall score of 3.0 in the AGREE-II instrument. In essence, this is rather a review of selected international GLs with an update of a few selected items.**

**Up-to-dateness: scientific evidence up to April 2010 included.**

### 3.4 French Urological Association Cancer Committee (CCAFU) – 2013

This is an update of a GL on non-invasive and invasive bladder cancer produced by the French Urological Association Cancer Committee (CCAFU).<sup>9</sup>

**1: Scope and purpose.** The overall objective is mentioned in the guideline but no further details are provided on the health questions and on the target population.

**2: Stakeholder involvement.** The low scores on the domain of stakeholder involvement can be explained by the lack of information on the professionals involved in the guideline development group and if any consultation process had taken place to capture patients/public’s views and preferences. There is no clear involvement of medical or paramedical disciplines other than urologists, nor of the potential users of the GL or patient representatives.





**3: Rigour of development.** The GL lacks a clear methodological section. There are no search terms provided and no criteria for selecting the evidence. Methods that were used to formulating the recommendations are not provided. The search strategy that was used is summarised in one single sentence: “A Medline search was performed between 2010 and 2013, as regards diagnosis, options of treatment and follow-up of bladder cancer”. This precludes a critical assessment of the search strategy. This guideline is an update of a previous version and this can explain the restricted time period searched (2010-2013). No information is provided on the selection criteria, the methods for formulating the recommendations, the external review procedure and the update procedure. These items were all scored with the lowest score (i.e. 1).

The document assigns levels of evidence (1 through 4) to its recommendations but it does not define the meaning of those levels, nor the potential range of levels.

Description of side effects is only provided for (adjuvant) medical treatment and not for surgery or radiotherapy.

**4: Clarity of presentation.** The formulation of the recommendations is clear but not specific and unambiguous enough to give a high AGREE score for this item, mainly due to the lack of information on the target population and the purposes of the recommendations (outcomes). This guideline aimed to cover the different diagnosis and management options in patients with bladder cancer, however, these options are mainly focused on the medical interventions. Some recommendations are summarised in a box but it is unclear if these recommendations are meant to be the key recommendations.

**5: Applicability.** A positive point is the inclusion of an algorithm for the treatment of non-invasive bladder cancer. However, other issues related to this domain are not considered: facilitators and barriers to the application of the GL, potential resource implications nor monitoring or auditing criteria.

**6: Editorial independence.** It is not clear whether funding for the GL production was obtained. Conflicts of interests of the GDG members are provided.

**We attributed this GL an overall score of 3.5 in the AGREE-II instrument. Its strengths are the clear presentation of the major recommendations and the inclusion of an algorithm for the treatment of non-invasive bladder cancer. Its major weaknesses are the apparent mono-disciplinary composition (urologists) of the GDG and the absence of stakeholder involvement.**

**Up-to-dateness: scientific evidence up to the year 2013 included.**

### 3.5 Alberta Provincial Genitourinary Tumour Team – 2013 (muscle-invasive cancer)

This GL is accessible from the Alberta Health Services website (<http://www.albertahealthservices.ca/cancerguidelines.asp>). It focuses on the staging and treatment of muscle invasive and locally advanced/metastatic bladder cancer.

**1: Scope and purpose.** The overall objective of this GL is adequately described. The research questions are in general reported, but no details are mentioned on the outcomes or comparators. The target population is described in a separate paragraph, but only focused on the cancer stage.

**2: Stakeholder involvement.** Notwithstanding the multidisciplinary composition of the GDG, this item received a lower score due to the lack of information on the names of the members, their affiliation and their role in the development of the guideline. Whether the views and preference of the target population have been sought, is not mentioned in the methodology section of this guideline. The target users are mentioned as “the clinicians”.

**3: Rigour of development.** This guideline scored for all items of this domain low. Some aspects of the methodology used are reported, but not enough details are provided to have a clear view on the development process (e.g. full search strategy, strengths and limitations of the body of evidence, etc.). The process for formulating the recommendations and if health benefits, side effects and risks have been considered is not reported. The information on the external review and the update procedure is rather vague: a formal review will be conducted at the Annual Provincial Meeting in 2015 and if critical new evidence is brought forward that time, the GDG will revise and update the document accordingly. The previous updates of this guidelines are well described. Via a link towards a methodology handbook more information could be found on the development process, but the information



is not specified for this specific guideline. The document assigns no levels of evidence nor strengths of recommendations.

**4: Clarity of presentation.** The recommendations give a concrete and precise answer to the research questions, also the different options for management are reported. In this guideline the recommendations are gathered per cancer stage, no key recommendations are indicated.

**5: Applicability.** This guideline scored for all items of this domain low due to the lack of information on potential facilitators and barriers to its application and if potential resource implications have been considered. Also no additional materials are provided to facilitate its dissemination and implementation into clinical practice. No monitoring and/or auditing criteria are reported.

**6: Editorial independence.** On the website of the National guidelines Clearinghouse is stated that “Some members of the Alberta Provincial Genitourinary Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner”. The conflicts of interests per authors are not listed.

**We attributed this GL an overall score of 4.5 in the AGREE-II instrument. Its major strengths are the adequate search for evidence and the clarity of presentation. The major weaknesses are the missing link between the retrieved body of evidence and the formulation of the recommendations.**

**Up-to-dateness: the most recent search date is up to March 2013.**

### 3.6 Alberta Provincial Genitourinary Tumour Team – 2013 (non-muscle-invasive cancer)

This GL is accessible from the Alberta Health Services website (<http://www.albertahealthservices.ca/cancerguidelines.asp>). It focuses on the staging and (surgical and adjuvant) treatment of non-muscle invasive bladder cancer.

**1: Scope and purpose.** The overall objective of this GL is adequately described. The research questions are in general reported, but no details are mentioned on the outcomes or comparators. The target population is described in a separate paragraph, mainly focused on the cancer stage.

**2: Stakeholder involvement.** Notwithstanding the multidisciplinary composition of the GDG, this item received a lower score due to the lack of information on the names of the members, their affiliation and their role in the development of the guideline. Whether the views and preference of the target population have been sought, is not mentioned in the methodology section of this guideline. The target users are mentioned as “the clinicians”.

**3: Rigour of development.** This guideline scored for all items of this domain quite low. Some aspects of the methodology used are reported, but not enough details are provided to have a clear view on the development process (e.g. full search strategy, strengths and limitations of the body of evidence, etc.). The search for literature consisted of two parts: an update of the original search strategy and a new literature search on bacillus Calmette-Guerin (BCG) therapy. The search strategy on BCG therapy is described in detail with search terms, in-and exclusion criteria, the number of selected citations and evidence tables. The process for formulating the recommendations and if health benefits, side effects and risks have been considered is not reported. The information on the external review and the update procedure is rather vague: a formal review will be conducted at the Alberta Genitourinary Tumour Team Annual Meeting in 2015 and if critical new evidence is brought forward that time, the GDG will revise and update the document accordingly. The previous updates of this guidelines are well described. Via a link towards a methodology handbook more information could be found on the development process, but the information is not specified for this specific guideline. The document assigns no levels of evidence nor strengths of recommendations.



**4: Clarity of presentation.** The recommendations give a concrete and precise answer to the research questions, also the different options for management are reported. In this guideline the recommendations are gathered per cancer stage, no key recommendations are indicated.

**5: Applicability.** This guideline scored for all items of this domain very low due to the lack of information on potential facilitators and barriers to its application and if potential resource implications have been considered. Also no additional materials are provided to facilitate its dissemination and implementation into clinical practice. No monitoring and/or auditing criteria are reported.

**6: Editorial independence.** On the website of the National guidelines Clearinghouse is stated that “Some members of the Alberta Provincial Genitourinary Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner”. The conflicts of interests per authors are not listed.

**We attributed this GL an overall score of 3.5 in the AGREE-II instrument. Its major strength is the clarity of presentation. The major weaknesses are the missing link between the retrieved body of evidence and the formulation of the recommendations. In fact this guideline strongly focuses on BCG and cannot be considered as a comprehensive bladder cancer guideline.**

**Up-to-dateness: the most recent search date is May 2013.**

### 3.7 European Association of Urology – 2014 (non-muscle-invasive cancer)

This GL is accessible from the European Association of Urology website (<http://uroweb.org/individual-guidelines/oncology-guidelines/>). It focuses on the diagnosis and treatment of non-muscle-invasive bladder cancer.

**1: Scope and purpose.** The overall objective of this GL is adequately described, but the research questions are not specified. The reader is unaware of the structure and the different sections in the guideline. The description of the target population is focused on the cancer stage.

**2: Stakeholder involvement.** In the introduction of the guideline is stated that the EAU Guidelines Panel consisted of an international multidisciplinary group of clinicians, including a pathologist and a statistician. On the EAU website all names of the collaborators could be retrieved, but their role in the development process is not specified. Whether the views and preference of the target population have been sought, is not mentioned in the methodology section of this guideline. The target users are not specified.

**3: Rigour of development.** The development process is only briefly mentioned, with a referral to the methodology handbook on the website, but the information in this handbook is not specified for this guideline. The full search strategy, the in-and exclusion criteria are lacking.

The introduction to the methodology section reads as follows: “*The recommendations provided in the current guidelines are based on literature searches performed by the expert panel members. A systemic literature search was performed for the systematic review of the role and extent of lymphadenectomy during radical cystectomy ...*” This wording suggests that only for a limited number of clinical questions a systematic review was performed.

Also the strengths and limitations of the body of evidence are not described. The level of evidence is assigned but the transparency between underlying evidence and the recommendation is insufficient. Next to the potential health benefits, also side effects and risks (such as treatment failure) have been considered per treatment strategy. Due to the lack of information on the grading of each outcome per treatment strategy, the explicit link between the evidence and the recommendations are less clear. The information on the external review and the update procedure is rather vague: while in the methodology handbook an external double-blind review with three validators is mentioned as a standard procedure in the development of a guideline, no information on this matter could be retrieved in this guideline. In the publication history can be retrieved all previous versions of this guideline and we could assume that this guideline will be updated regularly but it is not explicitly mentioned.

**4: Clarity of presentation.** Different algorithms and text boxes give a nice overview of the recommendations per treatment strategy.

**5: Applicability.** This guideline scored for most items of this domain low due to the lack of information on potential facilitators and barriers to its



application and if potential resource implications have been considered. No monitoring and/or auditing criteria are reported.

**6: Editorial independence.** On the EAU website the conflicts of interests of all authors are clearly mentioned. In the guideline it is also stated “that this guideline document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved.”

**We attributed this GL an overall score of 5.0 in the AGREE-II instrument. Its major strength is the clarity of presentation (text boxes and algorithms). The major weakness is the missing information on the process behind the formulation of the recommendations.**

**Up-to-dateness: the most recent search date is 2013.**

### 3.8 European Association of Urology – 2014 muscle-invasive cancer)

This GL is accessible from the European Association of Urology website (<http://uroweb.org/individual-guidelines/oncology-guidelines/>). It focuses on the diagnosis and treatment of muscle-invasive and metastatic bladder cancer.

**1: Scope and purpose.** The overall objective of this GL is adequately described, but the research questions are not specified. The reader is unaware of the structure and the different sections in the guideline. The description of the target population is focused on the cancer stage.

**2: Stakeholder involvement.** In the introduction of the guideline is stated that the EAU Guidelines Panel consisted of an international multidisciplinary group of experts from the field of urology, pathology, radiology and oncology. On the EAU website all names of the collaborators could be retrieved, but their role in the development process is not specified. Whether the views and preference of the target population have been sought, is not mentioned in the methodology section of this guideline. The target users are not specified.

**3: Rigour of development.** The development process is only very briefly mentioned, with a referral to the methodology handbook on the website, but the information in this handbook is not specified for this guideline. It is

unclear which search terms are used in which databases and until when is searched. Also the in-and exclusion criteria, the strengths and limitations of the body of evidence and the number of included citations are not reported. The level of evidence is assigned but the transparency between underlying evidence and the recommendation is insufficient. Next to the potential health benefits, also side effects and risks (such as treatment failure) have been considered per treatment strategy. An additional section is dedicated on quality of life. Due to the lack of information on the grading of each outcome per treatment strategy, the explicit link between the evidence and the recommendations are less clear. The information on the external review and the update procedure is rather vague: while in the methodology handbook an external double-blind review with three validators is mentioned as a standard procedure in the development of a guideline, no information on this matter could be retrieved in this guideline. In the publication history can be retrieved all previous versions of this guideline and we could assume that this guideline will be updated regularly but it is not explicitly mentioned.

**4: Clarity of presentation.** At the end of each section, an overview of the recommendations is presented. Also some flowcharts are provided to give an overview of the different management strategies in clinical practice.

**5: Applicability.** This guideline scored for most items of this domain low due to the lack of information on potential facilitators and barriers to its application and if potential resource implications have been considered. No monitoring and/or auditing criteria are reported.

**6: Editorial independence.** On the EAU website the conflicts of interests of all authors are clearly mentioned. In the guideline it is also stated “that this guideline document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved.”

**We attributed this GL an overall score of 4.0 in the AGREE-II instrument. Its major strength is the clarity of presentation (text boxes and flowcharts). The major weakness is the missing information on the development process of this guideline.**

**Up-to-dateness: the most recent search date is not clearly mentioned.**





### 3.9 National Comprehensive Cancer Network (NCCN) – 2015

During our initial search, we identified a NCCN GL that was published in 2013.<sup>6</sup> Upon further assessment of this GL, we accessed (March 1, 2015) the website of the NCCN (<http://www.nccn.org/default.aspx>) where a 2015 update of the Bladder Cancer GL was found, in addition to further information on the GL development process used by the NCCN. In March 2015, the discussion of the update was still in progress.

**1: Scope and purpose.** The overall objective of the NCCN guidelines are discussed on-line. No clear research questions related to bladder cancer were specified.

**2: Stakeholder involvement.** The GDG is composed of multidisciplinary group of medical experts on bladder cancer management. There is no clear involvement of paramedics, nor of the potential users of the GL or patient representatives. It is not clear if any consultation process had taken place to capture patients/public's views and preferences.

**3: Rigour of development.** This document lacks a section on methodology. General methodological considerations are described on the NCCN's website that apply to any of its GLs. It is not specified which databases are consulted. There are no search terms provided and no criteria for selecting the evidence. The methods for formulating the recommendations are clearly described on the website and minutes of meetings with votes (yes/no/abstain) are publicly accessible. The document assigns levels of evidence. Description of side effects is not discussed.

On the NCCN's website it is asserted that "All active NCCN Guidelines are reviewed and updated at least annually".

**4: Clarity of presentation.** Key recommendations are clearly summarised in a comprehensive algorithm. In the first pages of the document, it is clearly indicated which items were changed as compared to the previous version (2014). In the full text of the report, recommendations are not clearly visible.

**5: Applicability.** A clear and comprehensive algorithm for the treatment of bladder cancer is included. Facilitators and barriers to the application of the GL, potential resource implications or monitoring or auditing criteria are not considered.

**6: Editorial independence.** On its website, NCCN asserts that "All NCCN content is produced completely independently. Support from industry is accepted only for distribution of independently developed content." Conflicts of interests of the GDG members are provided and are updated on the website.

**We attributed this GL an overall score of 4.0 in the AGREE-II instrument. Its strength is its user-friendliness thanks to the inclusion of a comprehensive management algorithm. Its major weakness is that a description of the evidence search strategy is lacking.**

**Up-to-dateness: this is a 2015 GL in progress. Search dates are not provided.**

### 3.10 National Institute for Health and Care Excellence (NICE) – 2015

This GL is accessible from the NICE website (<https://www.nice.org.uk/guidance/ng2>). It considers the diagnosis and management of bladder cancer (all stages).

**1: Scope and purpose.** The overall objective and the target population of this GL are adequately described. One small demerit could be that the health questions are not separately summarised but they can be retrieved in the extensive table of content and in each section.

**2: Stakeholder involvement.** In the full version of the guideline and on the NICE website a list can be found of all participants. The GDG and the development team consisted of a multidisciplinary group of clinicians, researchers and patient representatives. The names, affiliations and role within the development process are clearly mentioned. Patient representatives contributed as full GDG members to writing the clinical questions, addressing their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-users research to the attention of the GDG. The target users, in this guideline defined as the involved healthcare professionals, as well as the persons involved in clinical governance in care, are clearly described.



**3: Rigour of development.** Every step in the development process is clearly described from formulation of the clinical question to the wording of the recommendation. This domain scored the maximum score on almost all items. Only the review procedure is less described: it is uncertain if external experts (beyond the GDG and the public consultation) have reviewed the guideline. The update procedure is only vaguely described: no formal date is foreseen to start with the update procedure.

**4: Clarity of presentation.** Different algorithms give a nice overview of the recommendations per treatment strategy. Also the structure of the chapters is very clear starting with the clinical question, the results on the clinical evidence, the GRADE profiles, the results on the cost-effectiveness evidence and ending with the recommendation (and the underlying considerations on the value of the outcomes, the quality of the evidence, the trade-off between benefits and harms and the trade-off between net health benefits and resource use).

**5: Applicability.** An additional excel-sheet is provided with a clinical audit tool and a baseline assessment tool.

**6: Editorial independence.** On the NICE website and in the full version of the guideline the conflicts of interests of all authors are clearly mentioned. Also a disclaimer mentions the financing of the guideline.

**We attributed this GL an overall score of 7.0 in the AGREE-II instrument. Its major strengths are the comprehensiveness of the guideline development process and its clear presentation. No major weaknesses could be found.**

**Up-to-dateness: the most recent search date is June 2014.**



Summary scores per AGREE domain for each of the guidelines are shown in Table 1 **Error! Reference source not found.** NICE's guideline clearly came out as being the currently best available.

**Table 1 – Summary scores of selected guidelines according to the AGREE-II instrument, in descending order of “Overall Score”**

Guideline producer	Domain 1 Scope and purpose	Domain 2 Stakeholder involvement	Domain 3 Rigour of development	Domain 4 Clarity of presentation	Domain 5 Applicability	Domain 6 Editorial independence	Overall Score (1–7)
<b>NICE</b>	<b>91.7</b>	<b>97.2</b>	<b>93.8</b>	<b>88.9</b>	<b>91.7</b>	<b>95.8</b>	<b>7.0</b>
<b>EAU (Invasive)</b>	41.7	44.4	32.3	58.3	10.4	91.7	<b>5.0</b>
<b>Alberta (Invasive)</b>	75.0	22.2	93.6	63.9	6.3	41.7	<b>4.5</b>
<b>Italian Urological Association</b>	36.1	38.9	46.9	55.6	2.1	33.3	<b>4.5</b>
<b>EAU (Non-invasive)</b>	38.9	13.9	32.3	61.1	10.4	95.8	<b>4.0</b>
<b>NCCN</b>	38.9	25.0	25.0	50.0	18.8	50.0	<b>4.0</b>
<b>Alberta (Non-invasive)</b>	77.8	19.4	30.2	63.9	6.3	41.7	<b>3.5</b>
<b>French Urological Association Cancer Committee</b>	41.7	5.6	16.7	58.3	12.5	62.5	<b>3.5</b>
<b>International Bladder Cancer Group</b>	44.4	5.6	21.9	55.6	10.4	25.0	<b>3.0</b>
<b>HAS</b>	47.2	55.6	18.8	75.0	0	0	<b>2.0</b>

Domain scores were calculated by summing up the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. Further details on this are provided in Appendix 2. “Overall score” is the average of the overall scores (ranging from 1 to 7) attributed by the two appraisers. Invasive: Muscle-invasive bladder cancer. Non-invasive: Non-muscle-invasive bladder cancer.

### 3.11 Discussion

The KCE researchers found that the recently published NICE guideline represents the most up-to-date and methodologically sound practice guideline on the diagnosis and management of bladder cancer. The evaluation of existing guidelines by KCE researchers was circulated to Belgian Professional Associations and patient representatives (cf. names in the colophon) and discussed in a guideline development group (GDG) meeting on March 30, 2015.

The GDG agreed on the methodology used by the KCE authors and supported the decision to refer to the NICE guideline as being the best guideline currently available. The development of a new Belgian guideline on bladder cancer seemed redundant to them and a waste of research time and money.



## 4 THE NICE 2015 GUIDELINE ON DIAGNOSIS AND MANAGEMENT OF BLADDER CANCER

On 25 February 2015, NICE put its guideline on diagnosis and management of bladder cancer on line: <http://www.nice.org.uk/guidance/ng2>.

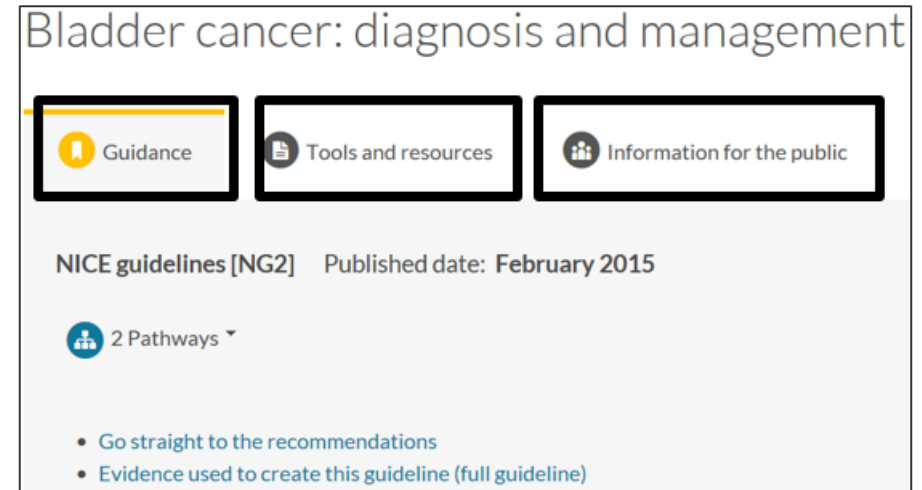
NICE commissioned the National Collaborating Centre for Cancer to develop this guideline. The Centre established a Guideline Development Group (GDG), which reviewed the evidence and developed the recommendations. The GDG was composed of a uro-oncology nurse specialist, urological surgeons, a uro-pathologist, a uro-oncology clinical nurse specialist, clinical oncologists, a medical oncologist, three patients and carer members, a general practitioner, and a radiologist.

The general methods and processes for developing NICE clinical guidelines are described in the guidelines manual that is available on-line (<http://www.nice.org.uk/article/PMG6/chapter/1%20Introduction>).

On the front page of NICE's GL (Figure 2), three separate sections can be accessed:

1. Guidance
2. Tools and resources
3. Information for the public

Figure 2 – Screenshot of NICE's web-based bladder cancer guideline



Source: <http://www.nice.org.uk/guidance/ng2>

### 4.1 The “Guidance” section of NICE’s guideline

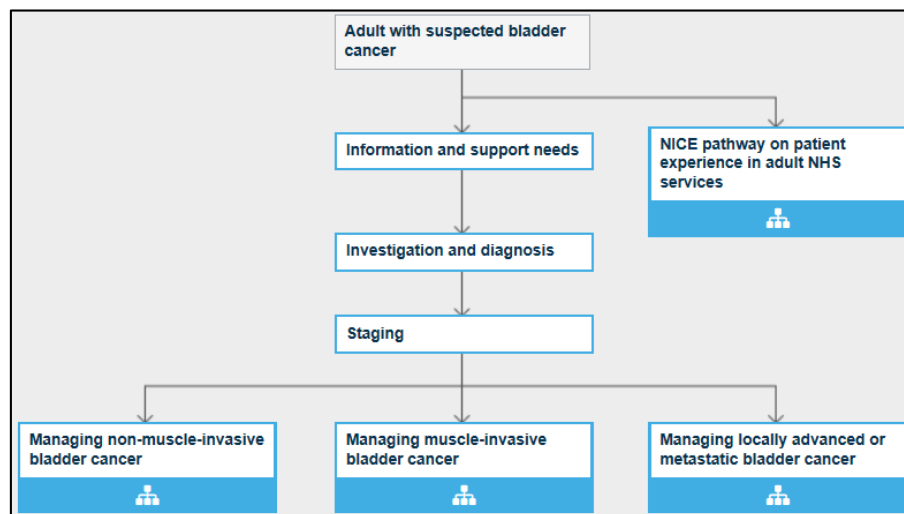
In the “Guidance” section, the actual recommendations can be accessed, either through a series of algorithms (Figure 3), a list of recommendations, or a text version of the GL where a choice can be made between a 929 pages “evidence review” and a 500 pages “full guideline”.

The “Bladder cancer overview” algorithm (Figure 3) incorporates hyperlinks leading to separate additional algorithms on the management of muscle-invasive, non-muscle-invasive and locally advanced or metastatic bladder cancer. One hyperlink leads to the “Patient experience in adult NHS services overview” where recommendations related to patient information, communication and shared decision making are presented.





Figure 3 – NICE’s “Bladder cancer overview” algorithm



#### 4.2 The “Tools and resources” section of NICE’s guideline

The “Tools and resources” section provides a bladder cancer risk classification table, a baseline assessment tool and a clinical audit tool.

The baseline assessment tool is intended to be used by organisations to evaluate whether their practice is in line with the recommendations in bladder cancer. Data can be entered about current activity relevant to the recommendation, actions needed to meet the recommendation, deadlines, and the names of the responsible leads.

The clinical audit tool includes standards and quality indicators based on the NICE guideline, data collection sheets in which audit data can be entered, a clinical audit report that provides basic information about the audit and automatically displays the audit results, and an action plan template.

The “Tools and resources” section also includes a costing template, a spreadsheet that can be used to estimate the local cost of the guideline implementation.

#### 4.3 The “Information for the public” section of NICE’s guideline

In the “Information for the public” section, a plain language translation of the GL intended for the general public, is provided. It clearly advises patients what care they should be offered.

An example extract from the text reads as follows: *“If you have high risk non-muscle-invasive bladder cancer, you should be offered another TURBT operation as soon as possible and no later than 6 weeks after your last TURBT (for more information about the TURBT operation see taking tissue samples for testing). You may also be offered more CT scans or MRI scans. The TURBT operation and the scans are to double-check how far your cancer has grown before you and your care team talk about possible treatments”.*

The “Information for the public” section also stimulates patients to ask their care team for additional information such as:

- Can you tell me more about the difference between low-risk, intermediate-risk and high-risk non-muscle-invasive bladder cancer?
- How will I know if the cancer has come back after my treatment? What should I look out for?
- Is there anything I can do to reduce the chance of the cancer coming back?
- What will happen if the cancer does come back?
- Who should I call if I have problems urinating or there's blood in my urine?



## 5 CONCLUSION

Although at the outset the KCE intended to produce a *de novo* guideline (GL) on the management of bladder cancer, it was found that 10 recently updated bladder cancer guidelines produced by international agencies were available, two of them published in 2015, and two others in 2014. Upon critical appraisal of those GLs, the one produced by the UK's National Collaborating Centre for Cancer and commissioned by NICE came out as the most comprehensive and methodologically most solid guideline. It was also the most up-to-date document, including published research until June 2014. Our Guideline Development Group (GDG) concluded that the development of a new Belgian guideline on bladder cancer would be redundant and a waste of time and resources.

Some GDG members commented that the NICE guideline is less well known among Belgian clinicians as compared to the EAU (European Association of Urology) guidelines, but the GDG saw this KCE report as an opportunity to inform their colleagues on the high quality of the NICE guideline. They emphasised also the important role of the Belgian urological and oncological societies to disseminate this guideline to their members.

The full version of the NICE guideline is a comprehensive document, including a 929 pages "evidence review" and a 500 pages "clinical guideline". It is too large for hands-on use in daily practice. However, the algorithms that are produced by NICE and displayed on its website clearly guide clinicians through the clinical pathway per cancer stage. The GDG members emphasised the importance of such tools which could be re-used on the College of Oncology's website.

The GDG stressed the importance of the "Information for the public" section on NICE's website and mentioned the need to raise awareness to the general Belgian public for early signs of bladder cancer (haematuria) and its relation to smoking. The lack of a French and Dutch version of the guideline could hamper patients to retrieve this information. During the GDG meeting the scientific organisations and the organisation of patient representatives discussed opportunities to collaborate to translate NICE's patient information to French and Dutch. The European Urology Week in September 2015 was mentioned as an excellent opportunity to inform patients about bladder cancer.

This concise report will be published on the KCE website including links to relevant NICE documents for which permission was obtained by NICE. A press release will be published in collaboration with the BMUC (Belgian Multidisciplinary Meeting on Urological Cancers), a cooperation between the Belgian Society of Medical Oncology ([www.bsmo.be](http://www.bsmo.be)), the Belgian Association of Urologists ([www.bvu.be](http://www.bvu.be) and [www.societebelgeurologie.be](http://www.societebelgeurologie.be)), the Belgian Association of Radiation-Oncology ([www.abro-bvro.be](http://www.abro-bvro.be)), representing medical oncologists, urologists and radiation oncologists.



## ■ APPENDIX

### APPENDIX 1. SEARCH STRATEGY FOR INTERNATIONAL GUIDELINES

This search was executed on Sept 11, 2014 and updated Jan 8, 2015

Source	Search terms	Total number of hits	Relevant titles
<b>National guideline clearinghouse</b>	Bladder cancer	111, update: 1	<p>Alberta Provincial Genitourinary Tumour Team. Nonmuscle invasive bladder cancer. Edmonton (Alberta): CancerControl Alberta; 2013 Oct. 29 p. (Clinical practice guideline; no. GU-009). <a href="http://www.albertahealthservices.ca/hp/if-hp-cancer-guide-gu009-noninvasive-bladder.pdf">http://www.albertahealthservices.ca/hp/if-hp-cancer-guide-gu009-noninvasive-bladder.pdf</a></p> <p>Alberta Provincial Genitourinary Tumour Team. Muscle invasive and locally advanced/metastatic bladder cancer. Edmonton (Alberta): CancerControl Alberta; 2013 Oct. 17 p. (Clinical practice guideline; no. GU-002). <a href="http://www.albertahealthservices.ca/hp/if-hp-cancer-guide-gu002-bladder.pdf">http://www.albertahealthservices.ca/hp/if-hp-cancer-guide-gu002-bladder.pdf</a></p>
<b>GIN</b>	Bladder cancer	16, update: 0	Cancer de la vessie: guide-affection longue durée (HAS, 2010)
<b>EAU</b>	Bladder cancer	2, update: 0	<p>Witjes JA, Compérat E, Cowan NC, De Santis M, Gakis G, Lebre T, Ribal MJ, Sherif A. Guidelines on muscle-invasive and metastatic bladder cancer. Arnhem (The Netherlands): European Association of Urology (EAU); 2014 Mar. 82 p.</p> <p>Babjuk M, Burger M, Zigeuner R, Shariat S, Van Rhijn B, Compérat E, Sylvester R, Kaasinen E, Böhle A, Palou J, Rouprêt M. Guidelines on non-muscle-invasive bladder cancer (TaT1 and CIS). Arnhem (The Netherlands): European Association of Urology (EAU); 2014 Mar. 42 p.</p>
<b>EBMPracticeNet</b>	Blaaskanker Bladder cancer	6, update: 0 0, update: 0	/
<b>SIGN</b>	Full list of guidelines	139, update: 0	/
<b>Medical Journal of Australia</b>	Full list of guidelines	94, update: 0	/
<b>Canadian Medical Association</b>	Bladder cancer	3, update: 1	Moretto P, Wood, L, Emmenegger U et al, Management of small cell carcinoma of the Bladder: Consensus guidelines from the Canadian Association of Genitourinary Medical Oncologists (CAGMO),



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Can Urol Assoc J, 2013;7:E44-E56 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3650822/pdf/cuaj-1-2-e44.pdf>  
→ Excluded for population

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<b>Diliguide (CHO, the Netherlands)</b>	Blaaskanker	Full list of guidelines, update: 0	/
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<b>National Health and Medical Research Council (NHMRC)</b>	Bladder cancer	Full list of guidelines, update: 0	/
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<b>The New Zealand Guidelines Group (NZGG)</b>	Full list of guidelines	55, update: 0	/
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<b>NICE</b>	Bladder cancer	1, update: 0	Bladder cancer: diagnosis and management (NICE, expected Feb 2015)
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<b>Nederlands Huisartsen genootschap (NHG)</b>	Blaaskanker	19, update: 0	/
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<b>HAS</b>	Cancer vesicule	du 171, update: 0	/
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<b>Google custom search</b>	Bladder cancer		British Uro-oncology group (BUG), British Association of Urological surgeons (BAUS) Section of Oncology, Action on Bladder Cancer (ABC): Multi-disciplinary team (MDT) guidance for managing bladder cancer, 2 <sup>nd</sup> edition (January 2013) <a href="http://www.actiononbladdercancer.org/downloads/36904mdtguidanceformanagingbladdercancer2013.pdf">http://www.actiononbladdercancer.org/downloads/36904mdtguidanceformanagingbladdercancer2013.pdf</a> → Excluded for design (no methods mentioned)
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## APPENDIX 2. CALCULATION OF SUMMARY AGREE SCORES

Domain scores were calculated by summing up the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. An example is given in the table below where the detailed scores of both appraisers (HVB and ADS) are provided on the items in Domain 3 “Rigour of Development” for the 2014 GL produced by the European Association of Urology on non-muscle-invasive cancer.

In this example, the following calculations were made:

- Maximum possible score = 7 (strongly agree) x 8 (items) x 2 (appraisers) = 112.
- Minimum possible score = 1 (strongly disagree) x 8 (items) x 2 (appraisers) = 16.
- Obtained score = 25 + 22 = 47.
- Scaled domain score = (Obtained score - Minimum possible score) / (Maximum possible score - Minimum possible score):  $(47-16)/(112-16)=32.3\%$ .

	Appraiser 1	Appraiser 2	Scaled score
<b>Domain 3. Rigour of Development</b>			
7. systematic search	2	3	
8. selection criteria	2	1	
9. strengths and limitations of evidence	4	4	
10. formulation of recommendations	2	1	
11. benefits, side effects and risks	4	4	
12. explicit link	6	6	
13. external review	2	1	
14. update procedure	3	2	
<b>SUM</b>	<b>25</b>	<b>22</b>	<b>32,30%</b>



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