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Urothelial Cancer

## Discrepancy Between European Association of Urology Guidelines and Daily Practice in the Management of Non-muscle-invasive Bladder Cancer: Results of a European Survey

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### Abstract

**Background:** The European Association of Urology (EAU) non-muscle-invasive bladder cancer (NMIBC) guidelines are meant to help minimise morbidity and improve the care of patients with NMIBC. However, there may be underuse of guideline-recommended care in this potentially curable cohort.

**Objective:** To assess European physicians' current practice in the management of NMIBC and evaluate its concordance with the EAU 2013 guidelines.

**Design, setting, and participants:** Initial 45-min telephone interviews were conducted with 20 urologists to develop a 26-item questionnaire for a 30-min online quantitative interview. A total of 498 physicians with predefined experience in treatment of NMIBC patients, from nine European countries, completed the online interviews.

**Outcome measurements and statistical analysis:** Descriptive statistics of absolute numbers and percentages of the use of diagnostic tools, risk group stratification, treatment options chosen, and follow-up regimens were used.

**Results and limitations:** Guidelines are used by  $\geq 87\%$  of physicians, with the EAU guidelines being the most used ones (71–100%). Cystoscopy (60–97%) and ultrasonography (42–95%) are the most used diagnostic techniques. Using EAU risk classification, 40–69% and 88–100% of physicians correctly identify all the prognostic factors for low- and high-risk tumours, respectively. Re-transurethral resection of the bladder tumour

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(re-TURB) is performed in 25–75% of low-risk and 55–98% of high-risk patients. Between 21% and 88% of patients received a single instillation of chemotherapy within 24 h after TURB. Adjuvant intravesical treatment is not given to 6–62%, 2–33%, and 1–20% of the patients with low-, intermediate-, and high-risk NMIBC, respectively. Patients with low-risk NMIBC are likely to be overmonitored and those with high-risk NMIBC undermonitored. Our study is limited by the possible recall bias of the selected physicians.

**Conclusions:** Although most European physicians claim to apply the EAU guidelines, adherence to them is low in daily practice.

**Patient summary:** Our survey among European physicians investigated discrepancies between guidelines and daily practice in the management of non-muscle-invasive bladder cancer (NMIBC). We conclude that the use of the recommended diagnostic tools, risk-stratification of NMIBC, and performance of re-TURB have been adopted, but adjuvant intravesical treatment and follow-up are not uniformly applied.

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## 1. Introduction

Bladder cancer (BC) is the most common malignancy of the urinary tract and the seventh most common cancer in men [1]. Approximately 75% of patients with BC present with non-muscle-invasive bladder cancer (NMIBC), confined to either the mucosa (stage Ta, carcinoma in situ [CIS]) or the submucosa (stage T1) of the bladder [2]. Multiplicity of tumours, tumour size, and the previous recurrence are independent factors that influence the risk of recurrence, and tumour stage, grade, and CIS are factors that influence the risk of progression [3]. A systematic review by van den Bosch and Alfred Witjes [4] showed progression from NMIBC to MIBC in 21% of patients after a mean follow-up of 48–123 mo, with long-term survival of 35%.

Prevention of recurrence and progression in NMIBC is of key importance for improving prognosis. In 2006, the European Organization for Research and Treatment of Cancer (EORTC) proposed a set of prognostic factors to develop a scoring system and risk tables for predicting the individual risk of disease recurrence and progression in patients with NMIBC [5]. These prognostic factors and the scoring system can be used to stratify patients into recurrence and progression risk groups, but they may overestimate these risks after Bacillus Calmette–Guérin (BCG) therapy [6]. The European Association of Urology (EAU) NMIBC guidelines use risk group stratification to facilitate treatment and follow-up recommendations according to grading and tumour stage [7].

The EAU NMIBC guidelines are meant to help minimise morbidity and improve the care of patients with NMIBC. However, there are studies that suggest underuse of guideline-recommended care in this potentially curable cohort [8,9]. In addition, there is another study where a significant survival advantage was found among those who received at least half of the guideline-recommended care [10]. The present survey was conducted among European physicians, to assess current daily practice in NMIBC management with regard to diagnosis, treatment, and follow-up. In addition, we aimed to evaluate concordance between current clinical practice and EAU guidelines.

## 2. Patients and methods

Between 1 July 2013 and 31 October 2013, physicians from nine European countries were interviewed by a company specialising in healthcare

research (Ipsos Healthcare). The study was initiated and sponsored by Ipsen Biopharm Ltd.

Urologists who treated patients with NMIBC and performed transurethral resection of the bladder tumour (TURB) were recruited by online invitation. Urologists needed to see a minimum number of patients with NMIBC per month to be included, depending on the region (20 patients/mo [Italy], 14 patients/mo [France, UK, and Germany], five patients/mo [Czech Republic], and 10 patients/mo for the remaining countries). Both members and nonmembers of the EAU were targeted, with a maximum of two respondents from the same centre being permitted in order to maximise the diversity of the sample. Target quotas for enrolment were set according to an equitable geographical distribution by country and experience (>15 or <15 yr of experience, with a threshold of at least 3 yr of experience). The sample included private and hospital-based providers, academic and nonacademic, with and without direct access to blue light technology and/or narrow band imaging.

Initially, in-depth 45-min telephone interviews were conducted with four randomly selected urologists from France, the UK, Germany, Italy, and the Czech Republic ( $n = 20$ ). These interviews assessed urologists' knowledge of the 2013 EAU NMIBC guidelines [11], explored the reasons for following or not following these guidelines, and explored general treatment flow within NMIBC. The output of these qualitative interviews was used to develop a questionnaire for a 30-min online interview in the urologist's native language. Participants received reimbursement for completion of the survey. The interview included questions about the use of diagnostic tools, risk group stratification, treatment options chosen, and the follow-up regimens, in order to quantify clinical practice patterns in the management of NMIBC and assess adherence to the EAU guidelines (questionnaire in the Supplementary material). Recommendations and the strengths of the 2013 EAU NMIBC guidelines, along with the items selected to test for adherence, are summarised in the Supplementary material (guideline recommendations). Descriptive statistical data are expressed in absolute numbers and percentages. All analyses were performed using SPSS Statistics software (version 22; IBM).

## 3. Results

### 3.1. Participants

A panel of 7896 physicians, known to be willing to participate in online research, received the invitation. A total of 1751 physicians started with the initial screening questions (22%). Of these, 708 did not meet the screening criteria and 545 exceeded target quota. A total of 498 physicians completed the questionnaire: urologists (uro-oncologists) in Germany—69 (seven), France—75 (zero), the UK—66 (nine), Italy 59 (16), Poland—69 (six), the Netherlands—28 (four), the Czech Republic—30 (zero), Austria—27 (three), and

Belgium—27 (three). Physicians had a median of 15 yr of clinical experience (interquartile range 3–41 yr). In Germany, 61 (80.2%) physicians were hospital based and 15 (19.8%) were attending.

3.2. Guidelines

At least 87% of all physicians reported that they follow guidelines for the treatment of NMIBC (Table 1). The EAU NMIBC guidelines are the most followed guidelines, except in France and the Netherlands where the national guidelines are most followed [12,13]. In France, this preference seems to stem from the national guidelines being in the native language (Table 1).

The participants were asked to offer reasons for following or not following the guidelines, by indicating agreement or disagreement with eight statements on a sliding scale (totally agree—agree—neutral—do not agree—do not agree at all). In response to these statements, 65–80% of urologists totally agreed that the guidelines help standardise procedures and 60–81% totally agreed that the guidelines were really helpful for risk stratification (Table 1).

3.3. Diagnosis

The diagnostic tools used for initial diagnosis of NMIBC among the urologists surveyed are described in Table 2. Urine molecular markers (most frequently

Table 1 – Guideline adherence.

	France		Germany		UK		Italy		Poland	
	n	%	n	%	n	%	n	%	n	%
Physicians following guidelines	72	96	67	88	71	95	65	87	73	97
EAU guideline		38		88		83		91		93
AUA guideline		11		8		7		8		4
National guideline		96		52		49		22		NA
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
SOP in place for treatment of NMIBC (%)	42	58	87	13	68	32	38	62	80	20
% of physicians	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)
Following EAU guidelines helps standardise procedures	65	4	70	7	77	7	76	7	80	8
EAU guidelines represent the best evidence available	60	7	51	11	76	4	79	1	79	8
EAU guidelines are really helpful for risk stratification	60	7	66	8	79	1	72	8	81	7
The main reason for not complying is related to specific situations	60	16	55	18	45	25	35	43	41	35
I prefer national guidelines because of the native language	48	19	17	71	4	77	9	75	9	83
EAU guidelines are an advice and not strict rules which I should follow	44	21	37	28	37	27	28	44	35	39
I try to strictly follow the EAU guidelines as they provide me security	40	16	51	13	52	9	68	5	60	9
EAU guidelines are theory	40	21	28	46	11	53	13	47	20	63

  

	Czech Republic		Austria		Belgium		Netherlands		Europe	
	n	%	n	%	n	%	n	%	n	%
Physicians following guidelines	28	93	27	90	27	90	31	97	463	93
EAU guideline		96		96		100		71		82
AUA guideline		0		0		15		0		7
National guideline		NA		22		15		74		50
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
SOP in place for treatment of NMIBC (%)	57	43	83	17	57	43	50	50	62	38
% of physicians	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)	I (totally) agree	I don't agree (at all)
Following EAU guidelines helps standardise procedures	73	0	73	0	77	0	50	6	71	4
EAU guidelines represent the best evidence available	60	3	53	3	63	0	50	6	63	5
EAU guidelines are really helpful for risk stratification	73	7	73	7	83	0	75	0	74	5
The main reason for not complying is related to specific situations	30	33	70	10	57	20	41	22	48	25
I prefer national guidelines because of the native language	10	53	7	87	13	60	9	72	14	66
EAU guidelines are an advice and not strict rules which I should follow	7	70	40	47	40	33	34	34	34	38
I try to strictly follow the EAU guidelines as they provide me security	53	7	60	3	70	10	25	16	53	10
EAU guidelines are theory	10	60	13	40	27	27	13	47	19	45

AUA = American Urology Association; EAU = European Association of Urology; NMIBC = non-muscle-invasive bladder cancer; SOP = standard operating procedure; NA = not applicable.  
 "Europe" is the mean of the nine countries.

**Table 2 – Diagnostic tools used for initial diagnosis of NMIBC (usage share for each diagnostic tool, per 100 patients, per country).**

	France	Germany	UK	Italy	Poland	Czech Republic	Austria	Belgium	Netherlands	Europe
<b>Endoscopy</b>										
Cystoscopy	76	76	90	60	70	92	92	78	97	81
Cystoscopy and biopsy	26	34	21	23	30	46	17	20	14	26
<b>Urinary tests</b>										
Cytology	57	37	38	57	20	32	61	56	54	46
Molecular markers	6	18	7	10	24	10	7	15	0	11
<b>Imaging</b>										
Ultrasound	56	87	67	79	95	93	91	62	42	75
CT urography	55	12	45	33	19	37	24	59	60	38
Intravenous urography	3	38	3	4	17	26	39	11	5	16
X-ray	4	22	11	2	16	6	20	5	11	11

CT = computed tomography; NMIBC = non-muscle-invasive bladder cancer.  
 "Europe" is the mean of the nine countries.

NMP22 and fluorescence in situ hybridisation) were used in up to 24% of the patients (Table 2).

**3.4. Risk group stratification**

In eight of the countries surveyed, 60–80% of physicians employ the risk group stratification from the EAU guidelines [11], with 27–47% using the EORTC risk classification [5]. In France, 32% and 11% of physicians, respectively, use these risk group stratifications, while 59% use the French Urological Association (AFU) guideline risk classification. The International Bladder Cancer Group and Club Urológico Español de Tratamiento Oncológico risk group stratifications are used by up to 5% of physicians [14,15].

Physicians were asked to select all applicable prognostic factors that they consider in classifying an NMIBC patient as a low- or high-risk patient (Table 3). All the correct factors for a low-risk tumour were selected by 67% and 48% of physicians with <15 or >15 yr of experience, respectively. The correct prognostic factors for high-risk tumours were selected by 96% and 94% of physicians with <15 or >15 yr of experience, respectively.

**3.5. Treatment**

Urologists were asked about surgical techniques used, whether white light only or white light plus photodynamic diagnosis (PDD) were used, and about the frequency of re-TURB in low- and high-risk disease (Table 4). High-risk disease was generally associated with more PDD use and more re-TURB. Re-TURB was performed within 4 wk after initial resection in 1–13% of patients, after 4–6 wk in 57–87%, after 7–9 w in 3–25%, and after >9 wk in 0–13%. The use of a single adjuvant intravesical instillation of chemotherapy within 24 h of TURB and other adjuvant instillation treatment was recorded for all NMIBC risk categories (Table 4). Adjuvant instillations of BCG were generally used more frequently in higher-risk patients.

**3.6. Follow-up**

Urologists could choose from five fixed schedules for follow-up with cystoscopy (Table 5). A flexible cystoscope was used most frequently for male patients except in Germany and Poland where a rigid cystoscope was used more often.

**Table 3 – Applicable prognostic factors according to urologists, to stratify patients into low- or high-risk NMIBC.**

Risk stratification	France		Germany		UK		Italy		Poland		Czech Republic		Austria		Belgium		Netherlands		Europe	
	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	High
% selecting all correct answers	69	97	65	91	65	96	52	97	40	95	53	97	67	100	53	90	63	88	59	95
<b>Prognostic factor</b>																				
Solitary tumour	100	0	96	4	96	3	99	1	99	1	97	3	100	0	93	3	88	13	96	3
G1 (low grade)	100	0	95	5	100	0	100	0	99	1	100	0	100	0	97	3	100	0	99	1
Ta	97	3	95	5	97	1	96	1	95	4	100	0	100	0	97	3	100	0	97	2
T1	16	81	17	82	19	77	36	64	51	44	40	53	23	77	17	83	9	91	25	72
Multiple and recurrent TaG1-2	12	84	11	88	9	83	9	89	7	92	3	97	10	87	23	70	16	84	11	86
Recurrent tumour	8	88	12	87	9	81	3	96	11	87	13	87	3	97	0	97	13	88	8	90
CIS	4	95	4	95	0	100	8	92	11	89	10	90	0	100	10	90	0	100	5	95
Tumour diameter ≥3 cm	1	97	1	97	1	93	0	100	4	93	0	100	3	97	3	93	3	97	2	96
G3 (high grade)	0	100	3	96	0	100	1	99	0	100	0	100	0	100	0	100	0	100	0	99

CIS = carcinoma in situ; NMIBC = non-muscle-invasive bladder cancer.  
 "Europe" is the mean of the nine countries.

**Table 4 – Treatment of patients with low-, intermediate-, and high-risk NMIBC (usage share for each treatment option, per 100 patients, per country).**

	France			Germany			UK					
	Low	Int	High	Low	Int	High	Low	Int	High			
<b>Surgical treatment</b>												
White light TURB	87	NA	65	57	NA	42	85	NA	76			
White light and PDD TURB	14	NA	38	40	NA	55	12	NA	20			
Re-TURB	42	NA	76	74	NA	91	46	NA	77			
Other <sup>a</sup>	0	NA	0	2	NA	4	0	NA	1			
<b>Instillation treatment</b>												
Single instillation of chemotherapy <24 h	38	35	21	59	63	61	88	84	68			
Adjuvant instillations of chemotherapy for 1 yr	23	44	9	22	47	30	9	23	12			
Adjuvant instillations of BCG for 1 yr	11	25	47	10	20	36	5	11	34			
Adjuvant instillations of BCG for 3 yr	5	15	57	10	13	28	8	9	49			
No adjuvant instillations	33	11	4	23	10	5	6	5	2			
Other <sup>b</sup>	35	38	1	5	9	19	5	29	9			
	Italy			Poland			Czech Republic					
	Low	Int	High	Low	Int	High	Low	Int	High			
<b>Surgical treatment</b>												
White light TURB	83	NA	57	94	NA	91	91	NA	71			
White light and PDD TURB	10	NA	25	3	NA	4	1	NA	6			
Re-TURB	25	NA	54	60	NA	83	53	NA	80			
Other <sup>a</sup>	11	NA	14	1	NA	16	10	NA	17			
<b>Instillation treatment</b>												
Single instillation of chemotherapy <24 h	36	35	24	45	54	57	28	35	33			
Adjuvant instillations of chemotherapy for 1 yr	37	49	29	8	15	12	10	31	23			
Adjuvant instillations of BCG for 1 yr	15	23	43	13	29	33	5	14	32			
Adjuvant instillations of BCG for 3 yr	6	11	35	9	16	37	3	1	22			
No adjuvant instillations	24	4	1	33	14	6	62	33	20			
Other <sup>b</sup>	12	12	15	18	13	30	0	8	13			
	Austria			Belgium			Netherlands			Europe		
	Low	Int	High	Low	Int	High	Low	Int	High	Low	Int	High
<b>Surgical treatment</b>												
White light TURB	61	NA	50	82	NA	61	95	NA	77	82	NA	66
White light and PDD TURB	35	NA	50	15	NA	37	8	NA	19	15	NA	28
Re-TURB	75	NA	98	40	NA	79	49	NA	82	48	NA	80
Other <sup>a</sup>	0	NA	20	0	NA	8	0	NA	2	3	NA	9
<b>Instillation treatment</b>												
Single instillation of chemotherapy <24 h	73	75	73	75	76	66	87	81	74	59	60	53
Adjuvant instillations of chemotherapy for 1 yr	15	27	13	10	39	16	13	61	20	16	37	18
Adjuvant instillations of BCG for 1 yr	10	23	40	7	23	33	1	10	43	9	20	38
Adjuvant instillations of BCG for 3 yr	4	14	38	5	11	55	2	9	50	6	11	41
No adjuvant instillations	23	10	2	14	2	2	16	11	2	27	11	5
Other <sup>b</sup>	15	34	24	20	48	14	10	16	0	13	23	14

BCG = Bacillus Calmette-Guérin; Int = Intermediate; NA = not available/applicable; PDD = photodynamic diagnosis; NMIBC = non-muscle-invasive bladder cancer; TURB = transurethral resection of the bladder.

“Europe” is the mean of the nine countries.

<sup>a</sup> The most given answer for “other” in the low-risk patients was narrow-band imaging and that in the high-risk patients was radical cystectomy.

<sup>b</sup> The most given answer for “other” in the low- and intermediate-risk patients was chemotherapy for 6 mo and that in the high-risk patients was radical cystectomy.

Urinary cytology is used in 60% of patients with low-risk NMIBC in France, Italy, and Austria, and in 10–40% in other countries. The use of ultrasound imaging varies widely between countries: in 10% of patients in the Netherlands, 20% in the UK, 30% in France, 50% in Belgium, 60% in Italy, 70% in the Czech Republic, 80% in Austria and Poland, and 90% in Germany. Computed tomography (CT) urography is used in 40% of patients in France, but in 10–20% in other countries. Intravenous urography is used in 30% of patients in Germany and Austria. Patients with low-risk NMIBC appear to be overmonitored in all countries (Table 5).

In intermediate-risk NMIBC patients, urinary cytology is used in 30–70%. Ultrasound imaging is used in 20–30% of intermediate-risk patients in France, the UK, and the Netherlands, and in 60–90% of patients in other countries. CT urography is used in 50% of intermediate-risk patients in France, and in 20–40% patients in other countries. Follow-up schedules for intermediate-risk patients are generally more intense than those in low-risk patients but less intense than those in high-risk patients (Table 5).

In high-risk NMIBC, urinary cytology is used in 50–80% of patients. In most countries, CT urography is performed in

**Table 5 – Follow-up schedule (frequency of cystoscopy performance and duration of follow-up) in patients with low-, intermediate-, and high-risk NMIBC.**

Follow-up frequency (per year)	Duration of follow-up (yr)	Risk group (%)		
		Low	Intermediate	High
3–4	1	0–17	1–9	0–6
2	1	7–43	0–5	0–1
4	1	32–60	10–37	3–20
2	2			
1	3–5			
4	1	16–37	32–63	33–53
2	2			
1	3–10			
4	1–2	3–12	10–33	28–46
1	3–10			

NMIBC = non-muscle-invasive bladder cancer.

60–70% of high-risk patients; in Germany, it is performed in 40%. In Germany, intravenous urography is utilised more frequently (50%) than in Poland, the Czech Republic, and Austria, where it is used in 30% of high-risk patients. Ultrasound imaging is used in 60–90% of high-risk patients in six countries, and in 10–30% of high-risk patients in the Netherlands, the UK, and France. Patients with high-risk NMIBC appear to be undermonitored in all countries (Table 5).

#### 4. Discussion

At least 87% of surveyed physicians stated that they use guidelines, with the EAU guidelines being most widely used, except in France and the Netherlands. However, our study suggests that physicians do not necessarily adhere to these EAU guidelines, despite stating that they do.

The most commonly used diagnostic tools for NMIBC are cystoscopy (up to 97% of cases) and ultrasound (up to 95% of cases). In countries where ultrasound use is less frequent, CT urography is more commonly used. Urinary cytology is used by 20–61% of urologists. The use of these tools is in line with the EAU guidelines [11]. However, the guidelines do not advocate the use of molecular marker urinary tests, and despite this, these are used in up to 24% of patients in our survey [16–18]. We do not know if these molecular markers are used for screening of the population at risk for BC, investigation of patients with symptoms suggestive of BC, primary detection, or facilitation of follow-up of NMIBC, which are all practical applications discussed in the guidelines. Other explanations for the use of urinary tests may be influence of suppliers/industries and a lack of knowledge about the evidence to justify the use of currently available urinary tests.

We found that most physicians (60–80%) follow risk group stratification according to the guidelines, except in France (32%). However, in France, 69% and 97% of physicians correctly classified all prognostic factors for low- and high-risk NMIBC, respectively (Table 3). Across all countries, however, misclassification is quite common for low-risk disease, with only 40–69% of physicians correctly

identifying all the prognostic factors. High-risk prognostic factors were correctly identified by 88–100% of physicians. Physicians from Italy, Poland, and the Czech Republic score particularly poorly on the identification of low-risk (36–51%) and high-risk (44–64%) factors. This suggests that there could be significant undertreatment of high-risk patients, incorrectly classified as low risk patients, resulting in a higher than expected recurrence rate, a slightly higher progression rate, and undersurveillance. There could be corresponding overtreatment of low-risk patients, incorrectly classified as high-risk patients, leading to a higher treatment burden and costs for the patient, and oversurveillance.

In eight countries, 76–98% of high-risk patients receive a re-TURB (Table 4). The proportion of high-risk patients in Italy receiving re-TURB was lower (55%). This is in line with a report that 49% of high-risk NMIBC patients at eight Italian referral centres underwent a re-TURB [19]. A more surprising finding is that re-TURB is performed in a relatively high percentage of patients with low-risk NMIBC (25–75%). This could mean that the initial TURB was inadequately performed (eg, incomplete resection), there may be doubts about the available evidence (Table 1), or other factors are driving treatment decisions. Misclassification is unlikely to explain this as the criteria for re-TURB are well defined without the use of risk group classification.

Since 2013, the EAU guideline has not recommended a single adjuvant instillation of chemotherapy within 24 h following TURB for high-risk patients [11,20–22]. According to our survey, 21–74% of high-risk NMIBC patients receive a single instillation of chemotherapy; such continued use in high-risk patients may be explained by the updating of the guidelines in the same year that the survey was completed. This continued use is probably unrelated to misclassification of risk group. The results from an individual patient data meta-analysis [7,23] have led to an update of the 2016 EAU guidelines, which now recommend one immediate chemotherapy instillation for patients with low-risk tumours and those with intermediate-risk tumours with a previous low recurrence rate ( $\leq 1$  recurrence per year) and an expected EORTC recurrence score of  $< 5$ .

Underuse of guideline-recommended adjuvant intravesical therapies has been reported previously [19,24]. In a North-American/European online chart review by Witjes et al [24], 24% of intermediate-risk and 9% of high-risk patients did not receive adjuvant treatment, in line with our study showing that 6–62% of the low-risk, 2–14% (excluding the Czech Republic [33%]) of the intermediate-risk, and 1–6% (excluding the Czech Republic [20%]) of the high-risk patients did not receive adjuvant treatment. While instillations of BCG are recommended, adjuvant intravesical instillations with chemotherapy are not recommended for the high-risk group, but are given to 9–30% of patients in our study, compared with 12.5% in previous studies [19,24].

Conversely, overuse of intravesical therapy appears to be commonplace among patients with low-risk disease. In our study, 5–37% of low-risk patients receive adjuvant intravesical chemotherapy (6 mo–1 yr) or 1–15% received

BCG (1–3 yr) instillations in addition to the recommended single instillation. Only 1–16% of intermediate-risk patients are overtreated with BCG for 3 yr.

A more positive finding is that the group of intermediate-risk NMIBC patients (generally the largest group of patients encountered in clinical practice) receive adjuvant instillations according to guideline recommendations, and 54–100% of high-risk patients receive the recommended BCG instillations (1–3 yr).

In general, our follow-up results confirm the suspicion that there is overmonitoring of low-risk and undermonitoring of high-risk NMIBC patients, despite the fact that the follow-up schedules to choose from were fixed and did not entirely correlate with guidelines' recommendations (Table 5).

There are limitations to the present study that should be addressed. The study aimed to compare daily practice with knowledge of guidelines, which means that actual treatments given to patients may differ from the physicians' recall of these treatments. As patients' medical records were not checked prospectively in a randomised fashion, we do not know whether treatment outcomes (recurrence, progression, and survival) differ according to adherence or nonadherence by physicians to the guidelines. A selection bias may be present, as physicians who decided to participate in the interview may have conflicts of interest with the company sponsoring the interviews, or they may have a special interest in the management of NMIBC and could therefore be more knowledgeable.

It would be interesting to know the main reasons why physicians do not adhere to the guidelines. We did not, however, conduct follow-up interviews with nonadherent physicians. Therefore, some questions arise: Do some physicians apply individual experience instead of evidence-based medicine? Do financial motives or scarce resources drive decisions? Does a lack of awareness of guidelines changes play a role? In addition, there will be differences in healthcare systems of the participating countries that we are not aware of, which could influence physicians' decisions, and there may be differences because of shared patient management by the urologist and oncologist in some countries, instead of only the urologist.

One finding of our study is that more physicians claim to adhere to EAU guidelines than actually follow them. Perhaps better training and maintenance of knowledge are needed. Understanding the factors that drive decision making in each country may also be helpful.

## 5. Conclusions

More than 87% of the European physicians claim to apply guidelines, and 82% use the EAU NMIBC guidelines, implicitly underlining the importance of these guidelines, but many may not fully adhere to them in daily practice. To improve the care of patients with NMIBC, it is imperative to further understand the factors that lead to discrepancies between the use of guidelines and routine management. There are national differences in daily treatment practice of NMIBC; we need to understand the background to these

national differences and try to bridge them on an international level.

**Author contributions:** Kees Hendricksen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Acquisition of data:** Ipsos.

**Analysis and interpretation of data:** Hendricksen, Aziz, Xylinas, Seiler, Roghmann.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.euf.2017.09.002>.

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