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Original Article

Nasty or Nice? Findings from a UK Survey to Evaluate the Impact of the National Institute for Health and Clinical Excellence (NICE) Clinical Guidelines on the Management of Prostate Cancer

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Abstract

Aims: Although the National Institute for Health and Clinical Excellence clinical guideline 58 (CG58) for prostate cancer management was expected to have a positive effect, several recommendations raised concern among UK physicians. We conducted a survey of UK oncologists in 2008 and a second, similar survey in 2010 to assess views on these recommendations and to evaluate the change in opinion over time.
Materials and methods: Two semi-structured questionnaires were issued by the British Uro-oncology Group to society members in September 2008 and October 2010.
Results: In 2008, 61 UK oncologists completed the survey; 60% agreed that CG58 would make a positive contribution towards improving patient care. There was strong opposition towards active surveillance as the first-line treatment for men with low-risk localised prostate cancer (49% disagreement); implementing 5 yearly flexible sigmoidoscopy post-prostate radiotherapy (51% disagreement); offering follow-up outside of the hospital (e.g. by general practitioners in primary care) for men with a stable prostate-specific antigen for ≥2 years (44% disagreement); and recommendations against docetaxel retreatment (47% disagreement) or bisphosphonate use (58% disagreement). In 2010, 77 UK oncologists completed the survey. The results were largely consistent with 2008, although several recommendations, particularly for localised disease, seem to have promoted a change in clinical practice, suggesting that they are facilitating a standardised approach. Compared with 2008, the 2010 results indicate a shift in favour of active surveillance (80% agreement) and primary care follow-up (59% agreement), but increasing opposition for docetaxel retreatment (57% disagreement). Opinions remained divided for flexible sigmoidoscopy and bisphosphonates.
Conclusions: Despite initial concerns, the CG58 seems to have had a positive impact on prostate cancer management in the UK, with adherence likely facilitating a standardised approach. However, with new data emerging, these findings underscore the need to regularly update guidelines. A revision of the CG58 is anticipated by 2014.
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Key words: Active surveillance; bisphosphonates; NICE; practice guidelines; prostate cancer; UK

Introduction

In February 2008, the National Institute for Health and Clinical Excellence (NICE) issued its first clinical guideline for the management of prostate cancer in the UK [1]. This guideline, known as CG58, was developed by a group of experts (health professionals, lay representatives and technical experts) who worked as part of a Guideline Development Group to identify clinical questions, systematically search and critically appraise all available evidence, and agree appropriate recommendations. Although it covers the broad spectrum of prostate cancer management, the principle aim was to provide recommendations in areas

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that were known to be controversial, those where there was known variation in clinical practice, and areas where high-quality evidence was lacking.

Although the NICE CG58 was generally expected to make a positive contribution towards improving the care of UK patients, after its release, a number of recommendations were identified as contentious, raising concern among UK physicians. In September 2008, the British Uro-oncology Group (BUG) conducted a survey of 61 UK oncologists to assess views on NICE CG58 recommendations. Overall, 60% of responders agreed that it would make a positive contribution towards improving the care of UK patients. However, there was strong opposition to several recommendations with uncertainty as to what extent they would be followed in clinical practice.

Since that time, data have emerged that directly affect various recommendations. Although some data may serve to reinforce recommendations, other data support a change in clinical practice, suggesting that the NICE CG58 requires updating. As such, 2 years on, BUG conducted an additional survey among a similar group of UK oncologists to assess how the guideline is being adhered to in clinical practice and to evaluate if opinions had changed since its initial introduction.

Materials and Methods

In 2008, a semi-structured questionnaire was compiled comprising 72 survey questions designed to evaluate all recommendations provided in the NICE guideline. The survey was issued by BUG to society members, and was completed and returned during a closed meeting. All data collected from survey responders were entered into a database and summarised using descriptive statistics.

Based on the high level of agreement for the vast majority of recommendations by responders of the 2008 survey, a second survey was compiled in 2010 that was refined to only include 22 questions (Figure 1) regarding recommendations that were identified as contentious in 2008 and those where new data have emerged since the original guideline was introduced. This second survey was designed to assess how these specific recommendations within the guideline are being adhered to in clinical practice, and to evaluate if opinions regarding these recommendations have changed over time by comparing responses from the 2010 survey with those obtained in 2008. The survey was issued by BUG to society members at a similar closed meeting held in September 2010, with data collection and analysis carried out using the same methods as those used for the 2008 survey.

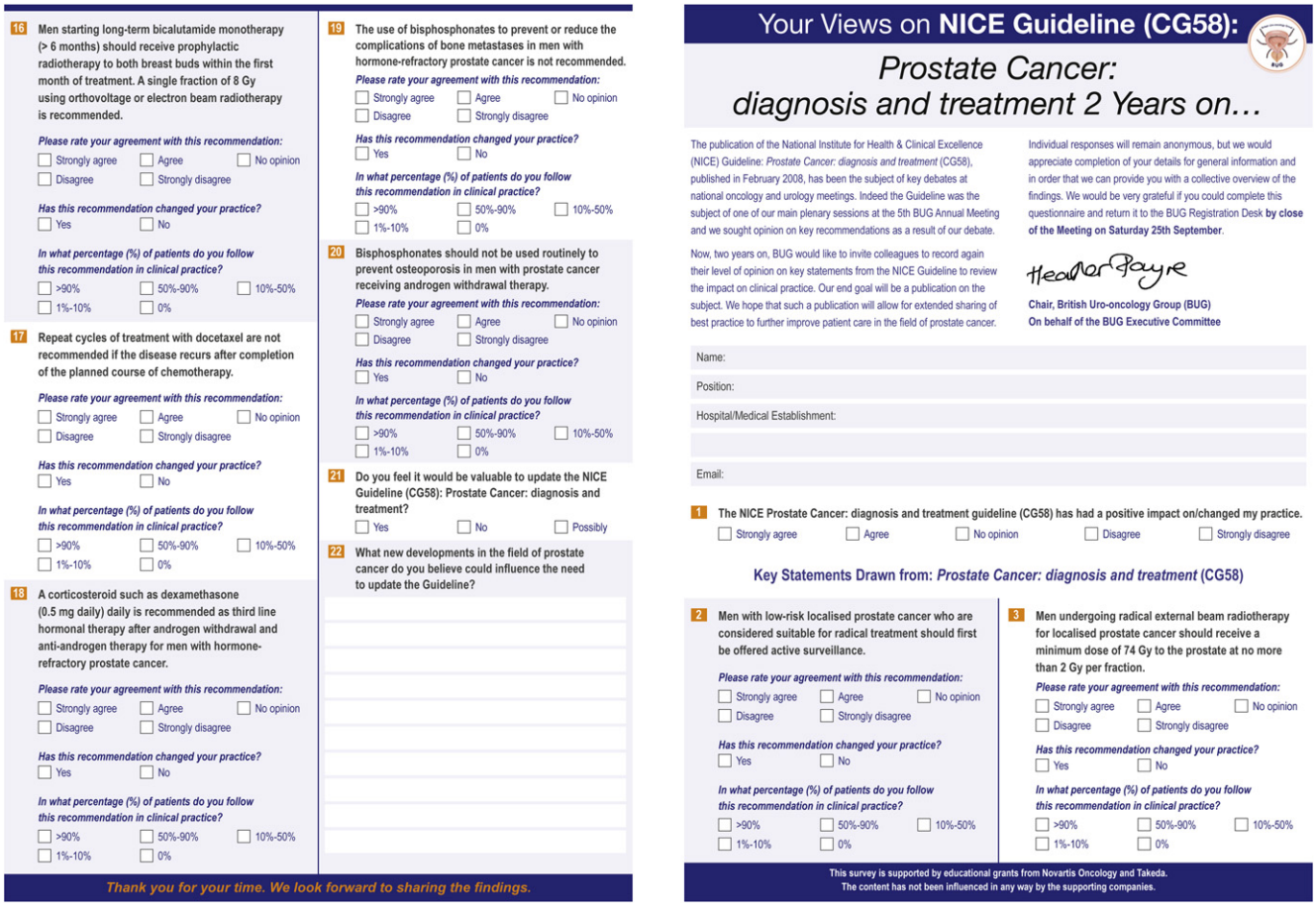

Fig 1. Questionnaire compiled in 2010 to assess how NICE recommendations identified as contentious in 2008 were being adhered to two years on by UK oncologists in their clinical practice.

Fig 1. (*continued*).

Results

Impact of NICE CG58 on Clinical Practice

Overall, 119 UK-based oncologists were members of BUG in 2010 (105 consultant clinical oncologists, nine medical oncologists, five other) and 103 were members in 2008 (93 consultant clinical oncologists, six consultant medical oncologists, four other). Of these, 98/119 (82%) and 88/103 (85%) attended the closed meetings in which the surveys were conducted in 2010 and 2008, respectively. In 2010, 77/98 (79%) questionnaires were completed and returned to BUG for evaluation. More than half (52%) of responders agreed that these guidelines have had a positive effect on or have changed clinical practice since their introduction in 2008, versus 23% who disagreed (17% had no opinion and 8% did not respond). These findings are largely consistent with those from the 2008 survey (61/88 [69%] questionnaires completed and evaluated), where 60% of responders felt that the NICE CG58 would make a positive contribution towards improving the care of UK patients with prostate cancer and 30% felt that they would have a negative impact.

Interestingly, 61% of 2010 survey responders felt that it would be valuable to update the NICE CG58, whereas 2% felt that this would not be of value (possibly valuable 29%; no response 8%). When asked what new developments could influence the need to update the guideline, many responses related to the recently reported efficacy of new therapies for advanced prostate cancer, such as cabazitaxel [2] and abiraterone [3]. Studies that have attempted to identify patient subgroups that require more aggressive therapy, such as SPCG-7 [4] and EORTC 22911 studies [5], were also deemed as important, as were the technological advances leading to improvements in radiotherapy techniques, such as intensity-modulated radiotherapy (IMRT), high dose rate brachytherapy boost (HDRBT), image-guided radiotherapy (IGRT) and hypofractionated radiotherapy [6–10]. In addition, diagnostic techniques addressing accuracy in the initial and repeat biopsy setting, such as transperineal template-guided mapping biopsy (TTMB) [11–13], were listed as developments that could influence the need to update the guideline.

Impact of NICE CG58 on the Management of Localised Prostate Cancer

Questions 2–6 of the 2010 survey comprised key statements/recommendations from the NICE CG58 regarding the management of UK patients with localised prostate cancer.

For most recommendations, the level of agreement remained largely unchanged between 2008 and 2010 (Table 1). However, a change was noted for the recommendation that men with low-risk localised prostate

Table 1
Level of agreement with National Institute for Health and Clinical Excellence (NICE) CG58 recommendations for the management of prostate cancer: comparison of results from a survey of 61 UK oncologists conducted in 2008, shortly after the guidelines were introduced, with those from a similar survey of 77 UK oncologists conducted in 2010

NICE CG58 recommendation	Year of survey	Response (%)					
		Strongly agree	Agree	No opinion	Disagree	Strongly disagree	No response
Localised prostate cancer							
Men with low-risk localised prostate cancer who are considered suitable for radical treatment should first be offered active surveillance	2008	18	33	0	26	23	0
	2010	27	53	7	13	0	0
Men undergoing external beam radiotherapy for localised prostate cancer should receive a minimum dose of 74 Gy to the prostate at no more than 2 Gy per fraction	2008	30	33	21	13	3	0
	2010	34	44	12	6	3	1
HIFU and cryotherapy are not recommended for men with localised prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions	2008	49	33	10	5	3	0
	2010	66	30	3	0	0	1
Men treated with radical radiotherapy for prostate cancer should be offered flexible sigmoidoscopy every 5 years	2008	3	23	23	44	7	0
	2010	6	32	29	27	3	3
After at least 2 years, men with a stable PSA who have had no significant treatment complications should be offered follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications, unless they are taking part in a clinical trial that requires more formal clinic-based follow-up. Direct access to the urological cancer multidisciplinary team should be offered and explained	2008	11	33	11	36	8	0
	2010	16	43	14	20	6	1
Relapse after radical treatment							
Biopsy of the prostatic bed should not be carried out in men with prostate cancer who have had a radical prostatectomy	2008	20	36	26	18	0	0
	2010	40	40	11	7	1	1
For men with evidence of biochemical relapse after radical treatment and who are considering radical salvage therapy, routine MRI scanning should not be carried out before salvage radiotherapy	2008	5	51	5	30	10	0
	2010	16	30	18	23	12	1
For men with evidence of biochemical relapse after radical treatment and who are considering radical salvage therapy, carry out an isotope bone scan if symptoms of PSA trends are suggestive of metastases	2008	5	51	5	30	10	0
	2010	53	43	1	1	1	1
Hormonal therapy is not routinely recommended for men with prostate cancer who have a biochemical relapse unless they have symptomatic local disease progression, any proven metastases or a PSA doubling time <3 months	2008	16	44	13	25	2	0
	2010	20	53	5	20	1	1
Locally advanced prostate cancer							
Adjuvant hormonal therapy is recommended for a minimum of 2 years in men receiving radical radiotherapy for locally advanced prostate cancer who have a Gleason score of ≥ 8	2008	49	43	3	3	2	0
	2010	62	35	1	1	0	1
Clinical oncologists should consider pelvic radiotherapy in men with locally advanced prostate cancer who have a $>15\%$ risk of pelvic lymph node involvement who are to receive neoadjuvant hormonal therapy and radical radiotherapy	2008	13	34	20	31	2	0
	2010	14	46	18	18	1	3
The role of radical surgery and extended lymphadenectomy as primary therapy for locally advanced prostate cancer should be studied in clinical trials	2008	21	61	15	3	0	0
	2010	26	48	14	4	5	3
Metastatic prostate cancer							
Healthcare professionals should offer bilateral orchidectomy to all men with metastatic prostate cancer as an alternative to continuous LHRHa therapy	2008	18	51	10	13	8	0
	2010	13	45	13	21	7	1
Combined androgen blockade is not recommended as a first-line treatment for men with metastatic prostate cancer	2008	21	66	3	7	3	0
	2010	31	64	0	4	0	1

(*continued on next page*)

Table 1 (*continued*)

NICE CG58 recommendation	Year of survey	Response (%)					
		Strongly agree	Agree	No opinion	Disagree	Strongly disagree	No response
Intermittent androgen withdrawal may be offered to men with metastatic prostate cancer providing they are informed that there is no long-term evidence of its effectiveness	2008	11	79	3	7	0	0
	2010	17	54	9	16	1	3
Men starting long-term bicalutamide monotherapy (>6 months) should receive prophylactic radiotherapy to both breast buds within the first month of treatment. A single fraction of 8 Gy using orthovoltage or electron beam radiotherapy is recommended	2008	8	51	11	25	5	0
	2010	12	41	12	28	4	3
Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy	2008	2	33	18	39	8	0
	2010	8	19	12	42	15	4
A corticosteroid such as dexamethasone (0.5 mg daily) is recommended as third-line hormonal therapy after androgen withdrawal and anti-androgen therapy for men with hormone refractory prostate cancer	2008	15	49	18	16	2	0
	2010	29	49	10	6	3	3
The use of bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone-refractory prostate cancer is not recommended	2008	10	28	5	38	20	0
	2010	17	32	8	31	9	3
Bisphosphonates should not be used routinely to prevent osteoporosis in men with prostate cancer receiving androgen withdrawal therapy	2008	15	52	16	11	5	0
	2010	19	41	16	18	3	3

HIFU, high intensity focussed ultrasound; LHRHa, luteinising hormone releasing hormone agonist; MRI, magnetic resonance imaging; PSA, prostate-specific antigen.

cancer, who are suitable for radical treatment, should first be offered active surveillance. This recommendation has led to a change in clinical practice for a quarter of the 2010 survey responders (Table 2), with more than half following this recommendation for most of their patients (Table 3).

Most other recommendations for localised prostate cancer included in the 2010 survey have also led to a change in clinical practice for ≥20% of responders (Table 2). Only the recommendation against the use of high intensity focussed ultrasound (HIFU) and cryotherapy for men with localised disease resulted in minimal change, with this recommendation already followed by the vast majority of UK oncologists.

Findings from our two surveys indicate that opinions remain divided regarding the recommendation that men treated with radical radiotherapy should be offered flexible sigmoidoscopy every 5 years, although there seems to be a slight shift in favour of this recommendation over time (Table 3).

Impact of NICE CG58 on Managing Relapse after Radical Treatment

Questions 7–9 of the 2010 survey comprised key statements/recommendations regarding the management of relapse after radical treatment. Opinions remained largely unchanged between 2008 and 2010 (Table 1), with a continued high level of agreement with and adherence to most of these recommendations (Tables 1 and 3). However, opinions regarding the recommendation against routine magnetic resonance imaging before salvage radiotherapy remain divided. The recommendation against the routine use of hormone therapy for men with biochemical relapse unless they have symptomatic disease progression, proven metastases or a prostate-specific antigen (PSA) doubling time of <3 months, was the only recommendation in this setting that has led to a >20% change in clinical practice among 2010 survey responders (Table 2).

Impact of NICE CG58 on the Management of Locally Advanced Prostate Cancer

Questions 10–12 of the 2010 survey comprised key statements/recommendations regarding the management of locally advanced prostate cancer. These responses remained largely unchanged between 2008 and 2010 (Table 1), with a continued high level of agreement, a lack of change in clinical practice (Table 2) and a high level of adherence to these recommendations noted for most responders (Table 3).

Effect of NICE CG58 on the Management of Metastatic Prostate Cancer

Questions 13–20 of the 2010 survey comprised key statements/recommendations regarding the management of metastatic prostate cancer. More responders agreed with these recommendations, with a few notable exceptions. Firstly, there seems to be a shift in opinion over time

Table 2
National Institute for Health and Clinical Excellence (NICE) CG58 recommendations for the management of prostate cancer: effect of the recommendations on changing clinical practice according to the 77 UK oncologists surveyed in 2010

NICE CG58 recommendation	Change in clinical practice (%)		
	Yes	No	No response
Localised prostate cancer			
Men with low-risk localised prostate cancer who are considered suitable for radical treatment should first be offered active surveillance	24	75	1
Men undergoing external beam radiotherapy for localised prostate cancer should receive a minimum dose of 74 Gy to the prostate at no more than 2 Gy per fraction	26	69	5
HIFU and cryotherapy are not recommended for men with localised prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions	4	92	4
Men treated with radical radiotherapy for prostate cancer should be offered flexible sigmoidoscopy every 5 years	20	74	6
After at least 2 years, men with a stable PSA who have had no significant treatment complications should be offered follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications, unless they are taking part in a clinical trial that requires more formal clinic-based follow-up. Direct access to the urological cancer multidisciplinary team should be offered and explained	30	66	4
Relapse after radical treatment			
Biopsy of the prostatic bed should not be carried out in men with prostate cancer who have had a radical prostatectomy	4	88	8
For men with evidence of biochemical relapse after radical treatment and who are considering radical salvage therapy, routine MRI scanning should not be carried out before salvage radiotherapy	1	92	7
For men with evidence of biochemical relapse after radical treatment and who are considering radical salvage therapy, carry out an isotope bone scan if symptoms of PSA trends are suggestive of metastases	10	87	3
Hormonal therapy is not routinely recommended for men with prostate cancer who have a biochemical relapse unless they have symptomatic local disease progression, any proven metastases or a PSA doubling time <3 months	21	74	5
Locally advanced prostate cancer			
Adjuvant hormonal therapy is recommended for a minimum of 2 years in men receiving radical radiotherapy for locally advanced prostate cancer who have a Gleason score of ≥ 8	12	83	5
Clinical oncologists should consider pelvic radiotherapy in men with locally advanced prostate cancer who have a $>15\%$ risk of pelvic lymph node involvement who are to receive neoadjuvant hormonal therapy and radical radiotherapy	12	80	8
The role of radical surgery and extended lymphadenectomy as primary therapy for locally advanced prostate cancer should be studied in clinical trials	5	84	11
Metastatic prostate cancer			
Healthcare professionals should offer bilateral orchidectomy to all men with metastatic prostate cancer as an alternative to continuous LHRHa therapy	4	90	6
Combined androgen blockade is not recommended as a first-line treatment for men with metastatic prostate cancer	6	91	3
Intermittent androgen withdrawal may be offered to men with metastatic prostate cancer providing they are informed that there is no long-term evidence of its effectiveness	18	78	4
Men starting long-term bicalutamide monotherapy (>6 months) should receive prophylactic radiotherapy to both breast buds within the first month of treatment. A single fraction of 8 Gy using orthovoltage or electron beam radiotherapy is recommended	10	84	6
Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy	8	81	11
A corticosteroid such as dexamethasone (0.5 mg daily) is recommended as third-line hormonal therapy after androgen withdrawal and anti-androgen therapy for men with hormone refractory prostate cancer	18	77	5
The use of bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone-refractory prostate cancer is not recommended	12	80	8
Bisphosphonates should not be used routinely to prevent osteoporosis in men with prostate cancer receiving androgen withdrawal therapy	6	86	8

HIFU, high intensity focussed ultrasound; LHRHa, luteinising hormone releasing hormone agonist; MRI, magnetic resonance imaging; PSA, prostate-specific antigen.

Table 3
National Institute for Health and Clinical Excellence (NICE) CG58 recommendations for the management of prostate cancer: percentage of patients in whom the recommendations are followed in clinical practice according to the 77 UK oncologists surveyed in 2010

NICE CG58 recommendation	Percentage of patients in whom the recommendation is followed (%)					
	>90%	50–90%	10–50%	1–10%	0%	No response
Localised prostate cancer						
Men with low-risk localised prostate cancer who are considered suitable for radical treatment should first be offered active surveillance	18	39	31	4	3	5
Men undergoing external beam radiotherapy for localised prostate cancer should receive a minimum dose of 74 Gy to the prostate at no more than 2 Gy per fraction	58	20	4	3	5	10
HIFU and cryotherapy are not recommended for men with localised prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions	75	6	0	3	8	8
Men treated with radical radiotherapy for prostate cancer should be offered flexible sigmoidoscopy every 5 years	10	10	12	17	35	16
After at least 2 years, men with a stable PSA who have had no significant treatment complications should be offered follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications, unless they are taking part in a clinical trial that requires more formal clinic-based follow-up. Direct access to the urological cancer multidisciplinary team should be offered and explained	9	20	23	22	17	9
Relapse after radical treatment						
Biopsy of the prostatic bed should not be carried out in men with prostate cancer who have had a radical prostatectomy	76	4	1	4	5	10
For men with evidence of biochemical relapse after radical treatment and who are considering radical salvage therapy, routine MRI scanning should not be carried out before salvage radiotherapy	35	22	9	5	17	12
For men with evidence of biochemical relapse after radical treatment and who are considering radical salvage therapy, carry out an isotope bone scan if symptoms of PSA trends are suggestive of metastases	69	21	1	1	3	5
Hormonal therapy is not routinely recommended for men with prostate cancer who have a biochemical relapse unless they have symptomatic local disease progression, any proven metastases or a PSA doubling time <3 months	40	35	9	4	7	5
Locally advanced prostate cancer						
Adjuvant hormonal therapy is recommended for a minimum of 2 years in men receiving radical radiotherapy for locally advanced prostate cancer who have a Gleason score of ≥8	79	10	1	0	3	7
Clinical oncologists should consider pelvic radiotherapy in men with locally advanced prostate cancer who have a >15% risk of pelvic lymph node involvement who are to receive neoadjuvant hormonal therapy and radical radiotherapy	14	23	11	9	22	21
The role of radical surgery and extended lymphadenectomy as primary therapy for locally advanced prostate cancer should be studied in clinical trials	16	7	9	12	35	21
Metastatic prostate cancer						
Healthcare professionals should offer bilateral orchidectomy to all men with metastatic prostate cancer as an alternative to continuous LHRHa therapy	7	9	13	35	27	9
Combined androgen blockade is not recommended as a first-line treatment for men with metastatic prostate cancer	83	8	1	0	4	4
	20	22	19	17	13	9

Intermittent androgen withdrawal may be offered to men with metastatic prostate cancer providing they are informed that there is no long-term evidence of its effectiveness	23	19	13	17	19	9		
Men starting long-term bicalutamide monotherapy (>6 months) should receive prophylactic radiotherapy to both breast buds within the first month of treatment. A single fraction of 8 Gy using orthovoltage or electron beam radiotherapy is recommended	25	22	18	7	10	18		
Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy	38	31	10	4	9	8		
A corticosteroid such as dexamethasone (0.5 mg daily) is recommended as third-line hormonal therapy after androgen withdrawal and anti-androgen therapy for men with hormone refractory prostate cancer	37	14	19	10	10	10		
The use of bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone-refractory prostate cancer is not recommended	59	5	6	9	9	12		
Bisphosphonates should not be used routinely to prevent osteoporosis in men with prostate cancer receiving androgen withdrawal therapy								

HIFU, high intensity focussed ultrasound; LHRHa, luteinising hormone releasing hormone agonist; MRI, magnetic resonance imaging; PSA, prostate-specific antigen.

against the recommendation that repeat cycles of docetaxel should not be used if disease recurs after completion of the planned chemotherapy (Table 1). Conversely, there seems to be a shift in opinion over time in favour of the recommendation against the use of bisphosphonates to prevent or reduce complications associated with bone metastases (Table 1). Finally, although there was a high level of agreement with the recommendation that intermittent androgen withdrawal may be offered to men with metastatic prostate cancer providing they are informed that there is no long-term evidence of its effectiveness, the level of agreement seems to have decreased over time (Table 1).

Discussion

Findings from the surveys conducted in 2008 and 2010 were based on the opinions of 61 and 77 UK-based oncologists, respectively. As BUG comprised a total membership of 103 and 119 UK-based oncologists in 2008 and 2010, respectively, 88 (85%) and 98 (82%) of whom attended the closed meetings, the high proportion of questionnaires completed and returned during these closed meetings (61/88 [69%] in 2008 and 77/98 [79%] in 2010) means that the findings reported here are broadly representative of the overall target sample. However, as not all physicians treating men with prostate cancer in the UK are members of BUG, our findings may not be representative of all UK clinical practice patterns and opinion and so should be interpreted with caution.

The findings from the 2010 survey showed that about half of responders felt that the NICE CG58 has had a positive impact on, or has resulted in a change in clinical practice, since its introduction in 2008. These findings are largely consistent with those obtained from the 2008 survey, where 60% of responders felt that the NICE guideline would have a positive influence over the care of prostate cancer patients. This ongoing support for the guideline is somewhat surprising, given the initial concerns raised when it was introduced. However, this may be explained by the fact that our survey responders seemed to agree with the vast majority of recommendations, with strong opposition restricted to a minority.

Despite the high level of support for the NICE CG58, 61% of 2010 survey responders felt it would be useful to update the guideline, with recent data for new therapies in advanced prostate cancer, improvements in radiotherapy techniques and improvements in diagnostic accuracy in the initial and repeat biopsy setting identified as the main developments driving this need. Findings from phase III studies have recently shown that both cabazitaxel [2] and abiraterone acetate [3] improve overall survival in patients with advanced castration-resistant prostate cancer who have progressed after first-line chemotherapy with docetaxel, suggesting that they should be recognised as second-line treatment options in this setting. Both of these agents are licensed in the USA and have received European Union licence approval. However, they are the subject of ongoing

technology appraisals by NICE and so will not be included in any revisions to their guidelines.

In terms of radiotherapy, there have been a number of significant advances in recent years, which have led to the introduction and/or further evaluation of various new techniques, including three-dimensional conformal radiotherapy (3D-CRT), IMRT, IGRT and HDRBT [6–10]. Although the use of 3D-CRT is recommended by NICE, findings from recent studies suggest that IMRT and HDRBT [14–16] may improve the precision of radiation delivery, allowing greater dose escalation, and so may warrant inclusion in future NICE guidelines.

Developments in biopsy technique were also identified as a key area driving the need to update the NICE CG58. Currently, transrectal ultrasound-guided biopsy is the standard approach for men with suspected prostate cancer, and NICE recommends that prostate biopsies are carried out after the procedure described by the Prostate Cancer Risk Management Programme [17]. However, recent reports have documented the diagnostic superiority of TTMB, particularly in the anterior and apical regions of the prostate [11,13], suggesting that these newer approaches should be considered.

A comparison of findings from the 2008 and 2010 survey results revealed a number of areas with no change in opinion (Table 1), and little or no effect on clinical practice (Table 2). Interestingly, in the localised prostate cancer setting, there was continued support for the recommendation against the use of HIFU and cryotherapy other than in the context of controlled clinical trials. These findings are in contrast to current opinion among some UK urologists, where there is growing support for the use of these minimally invasive technologies [18–20].

In the metastatic setting, the recommendation to offer intermittent androgen therapy to men with metastatic prostate cancer providing they are informed that there is no long-term evidence of its effectiveness, may soon need to be revisited as there is now long-term data to support this approach for patients with non-metastatic prostate cancer [21], with results from a phase III study evaluating intermittent androgen therapy in patients with metastatic disease showing equivalence with continuous treatment but substantial time off treatment with the intermittent approach [22]. However, as most of the UK oncologists participating in both the 2008 and 2010 surveys agreed with and adhere to this recommendation, new data are unlikely to have a significant effect on clinical practice.

The 2010 survey results indicate that several recommendations have resulted in a change in clinical practice, suggesting that they may be facilitating a standardised approach to prostate cancer management in the UK. For example, the recommendation that men with low-risk localised prostate cancer, who are suitable candidates for radical treatment, should first be offered active surveillance, has changed clinical practice among 24% of responders, with 57% adhering to this recommendation for >50% of their patients. Although it is widely acknowledged that many prostate cancers are indolent and unlikely to progress into clinically significant cancers, making surveillance an attractive approach to prevent over-treatment and avoid unnecessary risk of toxicity/comorbidity, traditionally there has been concern regarding our ability to identify which prostate cancers are truly indolent [23]. However, it is possible that advances in technology, such as TTMB, are allowing us to better identify patients with 'insignificant cancers', and hence those who are most suitable for active surveillance [11].

Another area that has led to a large (26%) change in clinical practice is the recommendation that men undergoing radical external beam radiotherapy for localised prostate cancer should receive a minimum dose of 74 Gy to the prostate at no more than 2 Gy per fraction. This was based on findings from the Medical Research Council RT01 study, which showed that an escalated dose of 74 Gy using 3D-CRT was associated with 5 year biochemical progression-free survival rates of 71% versus 60% for a standard dose of 64 Gy [24], and was included in the NICE CG58 because of the large variation in total dose and fractionation schedules used in clinical practice. Indeed, findings from another survey of 62 UK oncologists indicated that only 26% of responders used a total dose of 74 Gy in 37 fractions [25]. Inclusion of this recommendation has probably contributed to a more consistent approach to radiotherapy in the UK, as reflected by our survey findings, which showed that this schedule is now followed by 58% of UK oncologists for >90% of their patients. Despite recent advances, the optimum radiotherapy dose and fractionation schedule is yet to be defined. Findings from some studies suggest that HDBRT may allow the administration of higher doses of radiation that tightly conform to the target volume while minimising radiation exposure to adjacent tissue [14–16,26]. Further studies to optimise the use of radiotherapy in prostate cancer are ongoing, including the Conventional or Hypofractionated High Dose IMRT for Prostate Cancer (CHHiP) study [8]. CHHiP is comparing standard fractionation IMRT (74 Gy in 37 fractions) with two hypofractionated regimens (60 Gy in 20 fractions or 57 Gy in 19 fractions) in combination with neoadjuvant hormone therapy [8], and findings from a preliminary safety analysis of data from the first 457 patients enrolled suggest that high-dose hypofractionation schedules are as well tolerated as standard fractionation schedules [27].

The NICE recommendation that men with a stable PSA for at least 2 years who have had no significant treatment complications during this time should be offered follow-up outside of the hospital, for example, in primary care, has led to a change in clinical practice for 30% of survey responders and has also spawned much debate. Traditionally, follow-up has been led by secondary care in outpatient clinics, and the recommendation to move away from this model has raised concern regarding the appropriateness/ability of primary care to provide a similar level of high-quality follow-up. Indeed, concern regarding the lack of specific guidance to general practitioners who would potentially take on monitoring of these patients was recently highlighted [28], and emphasised the need to agree local policies and procedures to ensure general practitioners are better informed and have a clear understanding of the

follow-up required, thus avoiding any confusion, duplicate testing and/or the potential for some men to be lost to follow-up. However, despite these concerns, findings from another survey of healthcare professionals, conducted after the introduction of the NICE CG58, showed that most felt there was scope for primary care to play a greater role, particularly for men with stable disease, with the caveat that for this to be successful, relevant education (including guidance on the interpretation of PSA values), introduction of robust follow-up systems, easy access back into secondary care, and appropriate resourcing would be needed [29]. Taken together with findings from our survey, these findings suggest that primary care may be a viable solution that could also alleviate workload pressure in secondary care.

Another area that has led to a change in clinical practice among 20% of responders is the recommendation that men treated with radical radiotherapy for prostate cancer should be offered flexible sigmoidoscopy every 5 years. This shift is surprising, given that its inclusion was unexpected and opinions regarding its use have remained divided ever since (38% agreed and 30% disagreed in 2010, compared with 26% who agreed and 51% who disagreed in 2008). Although there is evidence to suggest that the risk of rectal cancer is increased after prostate radiotherapy, with a hazard ratio of 1.7 reported for rectal cancer among men surviving more than 5 years after prostate radiotherapy [30], there is currently no level 1 evidence to support 5 yearly screening using flexible sigmoidoscopy in this setting. The implementation of regular screening for these patients would also have a significant effect on costs and clinical caseload, and could be further complicated if patients are receiving long-term follow-up in primary care (based on the recommendation discussed above). Moreover, the optimum method of screening for colorectal cancers is yet to be established, with current methods, such as total endoscopy, flexible sigmoidoscopy and faecal immunochemical testing, criticised for their low cost-effectiveness, limited diagnostic accuracy and/or side-effects [31,32]. Further studies are therefore required to identify the optimum screening and/or follow-up for these patients.

Findings from our survey indicate that the NICE recommendation against the use of hormonal therapy for men with biochemical relapse in the absence of symptomatic local disease progression, metastases or a PSA doubling time of <3 months, has led to a change in clinical practice among 21% of responders. Although the use of early versus delayed androgen deprivation therapy has been an area of debate for many years, various trials have now shown that the clinical benefits of hormonal therapy, either alone or following radical prostatectomy or radiotherapy, seem to be restricted to higher risk patients and those with a more advanced stage of disease [33–36]. Hormone therapy is associated with significant side-effects, including cardiovascular risk and osteoporosis [37,38], and its early use in patients with localised disease has been linked with poorer survival [39]. Given this, it is not surprising that our survey results indicate growing support for this recommendation over time, with 73% agreeing in 2010 versus 60% in 2008. Moreover, the change in clinical practice and high level of adherence to this recommendation suggest that it has helped to establish a standardised approach to the use of hormonal therapy in clinical practice.

Finally, the recommendations against the use of bisphosphonates, either to prevent or reduce the complications of bone metastases in men with castration-resistant prostate cancer, or to prevent osteoporosis in men with prostate cancer receiving androgen deprivation therapy, has led to a change in clinical practice among 12% and 6% of responders, respectively. These recommendations were deemed as contentious among some survey responders, given the existence of data to support the benefits of bisphosphonates [40–45], and may explain the high level of disagreement with these recommendations, low change in clinical practice, and low adherence to these recommendations indicated in our 2010 survey. However, although findings from the randomised placebo-controlled study showed that zoledronic acid was associated with a significant reduction in skeletal-related events and bone pain compared with placebo, these benefits were not accompanied by an improvement in overall survival or quality of life [42,45]. Further studies, such as TRAPEZE and STAMPEDE, which are evaluating the utility of bisphosphonates in high-risk and/or metastatic disease, will help clarify the benefits of bisphosphonates in these patient groups [46–48].

Conclusions

The findings from these surveys suggest that the NICE CG58 has made a positive contribution towards improving the care of UK patients with prostate cancer. There seems to be a high level of adherence to most of the recommendations, suggesting that they may have helped to establish a standardised approach to patient management. Although a number of recommendations were considered as contentious in 2008, in most cases, support for these recommendations has grown over time. However, with a plethora of data emerging since the introduction of the NICE CG58, our findings also underscore the need to ensure that guidelines are updated regularly to incorporate clinically relevant advances so that an optimum and standardised approach to patient care is maintained throughout the UK. Indeed, NICE is currently undertaking a revision of the CG58, and it is projected that the updated guideline will be published in 2014.

Conflict of Interest

H. Payne has attended and received honoraria for advisory boards and served as a consultant for AstraZeneca, Janssen, Johnson and Johnson, Sanofi Aventis, Takeda, Ferring and Novartis.

N. Clarke has served as a consultant for Janssen, Takeda, AstraZeneca, Astellas and Amgen; has received research grants from AstraZeneca; and has provided guest lectures

on behalf of AstraZeneca, Astellas, Amgen, Janssen and Takeda.

R. Huddart has received sponsorship for meeting attendance from Ferring, Johnnson and Johnson and Sanofi Aventis.

C. Parker has received honoraria from Bayer, Dendreon, Astellas, Ferring and Takeda; and was a member of the NICE CG58 Guideline Development Group.

J. Graham was the NICE CG58 Guideline Development Group Lead Clinician and received payment from NICE for his contribution towards the development of the guideline. Since February 2009, he has also received payment from NICE for his role as Director of the Cancer Guideline Programme.

J. Troup has no conflict of interest to disclose.

The British Uro-Oncology Group was invited to comment on the scope and the draft version of the NICE CG58 during its development.

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