National Institute for Health and Care Excellence

Prostate Cancer (update)
Guideline Consultation Table
16th July 2013 - 10th September 2013

Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	1	Full	414	11	Spelling error 'chryotherapy'	We have made this change.
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	2	Full	346	36-7	Typo error 'was found' is duplicated	We have made this change.
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	3	Full	237	7	The algorithm (page 27) states 'Offer biopsy of the prostate only to men being considered for local salvage therapy in the context of a clinical trial' . The comment also relates to page 237, on which we are not supposed to comment, where it states 'Clinical trials should be set up to examine the effect of local salvage therapies on survival and quality of life in men with biochemical relapse after radiotherapy. [2008]'. Our comment - following the initial NICE guidance on cryotherapy a meeting was held between representatives of BAUS, NICE & the National Institute for Health Research Health Technology assessors technology group. It was agreed that registration of patients on a national or international database would satisfy the recommendation on use of cryotherapy, enabling PCT funding. Professors Kirby and Fitzpatrick published this in the BJUI 2008, but it was never clarified on the NICE website. We were the largest recruitment centre to CROP before the trial was closed due to poor recruitment at	The recommendations on salvage therapy were not updated during development of the guideline and so we are unable to make any changes.

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					other proposed centres. The NICE focal prostate cryotherapy guidance states 'Clinicians should enter details about all patients undergoing focal therapy using cryoablation for localised prostate cancer onto the European Registry for Cryosurgical Ablation of the Prostate (EuCAP) register and review clinical outcomes locally.' We continue to receive referrals by oncologists, from both within and outside our Network, of patients who have received radical radiotherapy at a relatively young age and have developed biochemical relapse. When we apply for individual funding, different panels apply varying interpretations on whether EuCAP registration should be seen as entry into a clinical trial or not. This causes considerable patient distress, patients often appeal if the decision is against funding and also creates a considerable workload for ourselves. NICE needs to take the opportunity of clarifying the situation in this current guidance. It also difficult to explain to patients when discussing ongoing observation vs salvage prostatectomy vs salvage cryotherapy, that there is usually no difficulty in funding salvage surgery whereas funding for cryotherapy is somewhat of a lottery, despite no evidence base for superiority.	
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	4	Full	139	2	Isotope bone scan is mentioned repeatedly. However, there is evidence suggesting that MRI skeletal survey is more sensitive at detecting small vertebral metastases. It also avoids national shortages of Technetium which arise from time to time. We now use this routinely. The research question is whether whole skeleton scanning is necessary or whether this can be limited to pelvis/lumbar spine, and this has been debated at scientific meetings. We believe this option should be mentioned in the new guidance	MRI skeletal survey was not within the scope of this guideline. We are therefore unable make any recommendations on this issue.

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Arrowe Park Hospital (Wiirral NHS Foundation Trust)	5	Full	Various pages		ADT is mentioned throughout the guidance including the glossary of definitions. However, in some sections it suggests that ADT encompasses testosterone reduction by orchidectomy or LHRH antagonists/agonists only, whereas in other sections ADT appears to include the use of anti-androgens. There is a need for a consistent definition throughout the document.	We have reviewed the content of the guideline and made amendments to improve consistency of terminology.
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	6	Full	306-317		SEE BELOW	Thank you.
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	7	Full	333 (29)	19 (0)	The algorithm states ' Offer anti-androgen monotherapy with bicalutamide (150mg) if willing to accept the adverse impact on overall survival and gynaecomastia • Stop bicalutamide treatment and begin androgen withdrawal if biacalutamide (NOTE SPELLING ERROR ALSO) monotherapy does not maintain satisfactory sexual function'.This suggests that the only advantage to bicalutamide monotherapy in metastatic disease is to maintain sexual function. In 1999 we established at Wirral what was the first clinic in Europe for routine measurement of BMD in patients about to commence hormone manipulation for PCa. A group of 253 osteoporotic men in an inception cohort of 618 patients with either locally advanced or metastatic disease, were treated by bicalutamide monotherapy and showed no significant change in BMD up to six years, whereas those with osteopenia or normal BMD and whom were treated with LHRHa showed ongoing bone loss over this period [1]. Findings from the Swedish PCBaSe are in keeping with our results, although reporting on any antiandrogen monotherapy regime, rather than specifically bicalutamide monotherapy. The Swedish Prostate Cancer Database (PCBaSe) identified 76,000 men diagnosed	Thank you for this information. The typo in the algorithm has been corrected. The section on anti-androgen monotherapy was not updated during development of the guidelines. We are therefore unable to make any changes to the recommendations. However, this area could be considered when the guidelines are next updated.

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					with prostate cancer between 1997 and 2006 and compared the occurrence of fractures requiring hospitalisation with the Swedish male population [2]. In total 4427 men with prostate cancer suffered fractures requiring hospitalisation during the observation period. Men treated with medical or surgical castration had an increased incidence of 25/1000 person-years when compared to an incidence of 16/1000 person-years from a standardised group in the general male population. Standardised incidence ratios for all, vertebral and hip fractures were 1.6, 1.6 and 1.7 respectively. Men treated with either antiandrogen monotherapy, or with curative intent (radical prostatectomy/radical radiotherapy), or managed by surveillance had no increased fracture risk. The authors also place the increase in fracture risk requiring hospitalisation into perspective by providing comparative incidences of 33/1000, 4/1000 and 97/1000 for ischaemic heart disease, deep venous thrombosis and death from prostate cancer within the same patient cohort. Furthermore, the costs of antiandrogen monotherapy for bicalutamide 150mg are not stated in page 395 of the current draft. A annual cost of £903 is given for LHRHa. Bicalutamide is off patent and costs £220/annum. We have presented this data previously to BAUS and more recently to the AUA, as there are considerable health economic benefits. In summary, bicalutamide monotherapy has the advantage of also preserving BMD without recourse to bisphosphonates, which are not without side effects, in men who are willing to trade off a small reduction in survival benefit. In addition, this survival benefit may only apply to those with bulky metastases and PSA >400[3]. This has potential for very large costs savings across the	

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					NHS and should be highlighted.[the reason for cost reduction in bicalutamide prescriptions needs to be clarified in page 91 of the draft, because one might assume that cost has reduced because of a fall in prescriptions rather than generic competition]. I appreciate that reference [1] relates to level 1b evidence, rather than from a RCT. Furthermore, [2] is also not from a RCT, but is a very large and pivotal population study, which should not be ignored when developing guidance, particularly as the Swedish hospital admission data is believed to be particularly robust. Others have also argued that data from large population studies should be considered when constructing guidelines. Finally, I am part of a UK expert group developing guidelines for maintenance of bone health in PCa. I believe that the Chairperson, Janet Brown, may be responding on behalf of the group with regard to the osteoporosis section. However, I have also responded as the current draft guidelines in their present format would lead to a significant reversal of cost savings for our Trust. References:- [1] Wadhwa VK, Mistry R, Weston R, Parr NJ. Long-term changes in bone mineral density and predicted fracture risk in patients receiving androgen-deprivation therapy for prostate cancer, with stratification of treatment based on presenting values. BJUI 2009;104:800-5 [2] Thorstenson, A., Bratt, O., Akre, O., Hellborg, H., Holmberg, L., Lambe, M., Bill-Axelson, A. Incidence of fractures causing hospitalisation in prostate cancer patients: Results from the population-based PCBaSe Sweden. European Journal of Cancer 2012;48:1672-1681 [3] Kaisary AV, Iversen P, Tyrrell CJ, Carroll K, Morris T.	

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					Is there a role for antiandrogen monotherapy in patients with metastatic prostate cancer? Prostate Cancer Prostatic Dis 2001;4:196-203.	
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	8	Full	317	Gynaecomastia section	We believe the recommendation is unbalanced and should have been updated. ' Although tamoxifen was shown to be an effective treatment 5 of bicalutamide induced gynaecomastia, there is a theoretical concern that, as an anti-oestrogen, it could have an adverse effect on prostate cancer control' In a double-blind, parallel-group, multicentre trial in which 282 patients with prostate cancer were randomised to receive bicalutamide 150 mg/d plus either daily tamoxifen (1, 2.5, 5, 10, or 20 mg) or placebo there were no differences in PSA response at any dose of tamoxifen [1]. Since the theoretical concern is thought to be hormone mediated, then any impact would be likely to impact upon PSA. This ought to be mentioned. The IOG suggested that patients with cancer should be offered as many treatment options as possible and clearly a choice of both breast bud radiation and tamoxifen should be offered, particularly as tamoxifen can be discontinued if bicalutamide is not tolerated due to GIT upset, whereas chest wall radiation is irreversible. Furthermore, there are economic benefits to support tamoxifen - cost around £6/month at highest dose used for gynaecomastia prophlaxis Reference - [1] Fradet Y, Egerdie B, Andersen M, Tammela TLJ, Nachabe M, Armstrong J, Morris T, Navani S. Tamoxifen as Prophylaxis for Prevention of Gynaecomastia and Breast Pain Associated with Bicalutamide 150 mg Monotherapy in Patients with Prostate Cancer: A	The recommendations on gynaecomastia were not updated during development of the guideline and so we are unable to make any changes. The proposal not to update these sections was subject to consultation with stakeholders during development of the guideline scope.

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					Randomised, Placebo-Controlled, Dose–Response Study. Eur Urol 2007;52:106–115	
Arrowe Park Hospital (Wiirral NHS Foundation Trust)	9	Full	179	1	Recommendation - 'Commissioners should ensure that robotic systems for the surgical treatment of localised prostate cancer are based on centres that perform at least 150 radical prostatectomies per year' We are a robotic centre, but the equipment is also used for other procedures as well as radical prostatectomy and in other specialties. The Ramsey comparative cost-effectiveness study is quoted in the evidence and appears to be used a key evidence at arriving at the 150 number. However, cost analysis in the full 2013 paper in European Urology demonstrates that the authors calculated equipment costs of the robot only being acquired and used for prostatectomy. This should be highlighted. Furthermore, both the Ramsey and Hohwu cost-effectiveness reports are mentioned in the previous section with the statement ' Potentially serious limitations were identified in the study by Hohwu *et al*.' However, in the Ramsey paper the authors themselves volunteer that ' considerable uncertainty persists in the absence of directly comparative randomised data'. In addition, estimates had to be made of key variables, rather than having firm data available in the model. Why is this not mentioned in a key document which is likely to influence commissioning? Unfortunately this failure to acknowledge the serious limitations of both studies suggests a possibility of bias within the expert panel compiling the updated guidance, with selective reporting of the strengths and limitations of evidence	The recommendation for basing robots in centres performing at least 150 radical prostatectomies per year was based on cost-effectiveness evidence which only considered use of the robot to perform radical prostatectomies. The recommendation has been amended and text added to the LETR section to clarify this. The appraisal of the Ramsey and Hohwu papers was conducted by an independent health economist and the limitations of both papers have been acknowledged on p194-6 and in the Evidence Review which accompanies this guideline. The Ramsay paper was considered to be of higher overall quality than the Hohwu paper for several reasons: the longer time horizon it considered (10 years compared to one year in the Hohwu study); and the more complete sensitivity analyses that were conducted. In addition, the Ramsay paper was more applicable to our decision problem than the Hohwu paper because it considered a UK setting (Hohwu considered the healthcare setting in Denmark). The recommendation was made on the basis of the evidence presented to the whole Guideline Development Group.
Association of	1	Full	306		Osteoporosis management - needs to add about	The Winters-Stone et al (2010) systematic review includes

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Chartered Physiotherapists in Oncology and Palliative Care					providing advice regarding weight bearing exercise and where appropriate onward referral. Winters-Stone et al A review of exercise interventions to improve bone health in adult cancer survivors J. Cancer Survivosrhip 2010 43 187-201 (results encouraging but inconsistent)	mostly non-prostate cancer studies and does not include any randomised trials in prostate cancer. It was not included in the review of the evidence because there is now a relevant randomised trial in this area '*Galvao, DA et al. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial. Journal of Clinical Oncology 2010; 28(2): 340-347.'*
Association of Chartered Physiotherapists in Oncology and Palliative Care	2	Full	323	5	More information on benefits of exercise would be good. There is increasing evidence about exercise in prostate cancer in relation to: • Lowering risk of mortality by as much as 30% • Lowering rate to disease progression by 57% http://www.macmillan.org.uk/Documents/AboutUs/Commissioners/Physicalactivityevidencereview.pdf It would also be useful to promote exercise not only for fatigue but also in the management of weight reduction and osteoporosis when on hormone therapy.	Unfortunately we are not able to cross reference to external information resources. The role of exercise in weight reduction in men on long-term ADT was not investigated by this guideline. We are therefore unable make any recommendations on this issue. Although the evidence showed exercise can improve quality of life in men with prostate cancer on long term ADT, it was not possible to determine if this improvement in quality of life was due to the effect on osteoporosis. As this was the topic under investigation, it was not possible to make any recommendations on the role of exercise in the management of osteoporosis. Information on the QoL measures used is included in the evidence review for this clinical question.
Association of Chartered Physiotherapists in Oncology and	3	Full	220	32	The wording of "ensuring access to incontinence services" could be interpreted as just having a service available to access. It would be more useful to have wording that promotes	The recommendations on managing urinary dysfunction resulting from radical treatment were not updated during development of the guideline and so we are unable to make any changes.

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Palliative Care					referral to physiotherapy for the management of faecal and urinary incontinence through pelvic floor re-education. Ideally this would occur pre- operatively to encourage the patient to self-manage. These services are often but not always aligned with continence services. We are aware however that evidence is scanty and of poor quality to support this. Would also like to see that for those procedures where we know urinary incontinence is a predictable outcome of intervention i.e. radical prostatectomy, that patients are referred to continence services before intervention to ensure that patients have access to pads and support before the symptoms appear.	
Astellas Pharma Ltd	2	Full	General		CG58 is due to be published in January 2014, and the NICE technology appraisal for enzalutamide for the treatment of metastatic hormone relapsed prostate cancer previously treated with a docetaxel-containing regimen is due to be published in February 2014. This will make the guideline almost immediately out of date. Considering the timescale for updating the previous version of this guideline it would seem unfortunate for the guideline not to be re-scheduled to include this imminent technology appraisal.	Unfortunately we are unable to change the publication date of the prostate guideline. The technology appraisal for enzalutamide has already been listed in section 3.2 of the NICE version of the guideline.
Astellas Pharma Ltd	4	Full	29		In the treatment pathway abiraterone is incorrectly listed under chemotherapy. We suggest that there should be a further box, below chemotherapy, for treatments licensed in the post-docetaxel setting ie. enzalutamide and abiraterone.	We have made the suggested change to the algorithm.
Astellas Pharma Ltd	5	Full	85	27	This section 1.3.4 lists all the available treatments for prostate cancer, but does not include enzalutamide, which has been available in the UK since June 2013.	This data on systemic therapy for prostate cancer covers practice until 2011, as this was the latest data available. Therefore does not include new drugs such as enzalutamide and abiraterone.
Astellas Pharma	6	Full	93	1-10	The following statement is made 'Second line treatment	We have deleted this sentence.

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Ltd					after docetaxel-containing chemotherapy failure is limited to abiraterone acetate...' Post docetaxel treatment is no longer limited to abiraterone. Enzalutamide received a marketing authorisation for the treatment of metastatic hormone relapsed prostate cancer previously treated with a docetaxel-containing regimen in June 2013, and the outcome of the NICE technology appraisal of enzalutamide is scheduled for February 2014. The following statement is made 'Drug development for HRPC is a fast growing field with many phase III trials due for completion in the next few years for novel agents such as enzalutamide and Radium 223 chloride..' This section needs updating; A phase III trial for enzalutamide has already been completed and published (NEJM 2012; 367:1187-97).	We have amended the text to clarify that there are several agents currently being investigated by NICE.
Astellas Pharma Ltd	7	Full	420		The section on published NICE guidance should include: • Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (TA101).	Docetaxel is included on p446 line 30 (under guidance that will be incorporated/updated).
Astellas Pharma Ltd	8	Full	421		The section on NICE guidance under development needs updating: • Cabazitaxel TA255 was published in May 2012 • Abiraterone (post-docetaxel) TA259 was published in June 2012 • Abiraterone (pre-docetaxel) TA is currently suspended • Enzalutamide for the treatment of metastatic hormone relapsed prostate cancer previously treated with a docetaxel-containing regimen will be published in February 2014	The text on p445 is the scope of the guideline which was produced in March 2012. We are not able to change the content of this.
Astellas Pharma	3	NICE	**419**	5	**Inconsistency between 'Full' and 'NICE' versions of**	The full version of the guideline differs to the NICE version

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Ltd					**the guideline.** The NICE guideline does not cover treatment of mCRPC post-docetaxel, but it does not state that this is the case. It is not apparent from this version that there is any treatment available post–docetaxel. At the end of section 1.5 it would be useful to refer to the treatment options available post-docetaxel and the relevant TAs, including enzaluatamide. Information regarding post-docetaxel treatment is referred to in the 'full' guideline. On Page 419 'cabazitaxel and abiraterone for castrate resistant metastatic prostate cancer' is listed under 'Key Issues that will not be covered'. But then abiraterone is discussed in various parts of the guideline and is included in the treatment pathway pg.29.	in that it is able to include background information, which is where the various published technology appraisals have been referenced. The NICE version of the guideline includes a list of published and ongoing technology appraisals in section 3.2. In addition, the NICE pathway developed for this guideline will link to the various published technology appraisals guidance on prostate cancer. The text on p445 is the scope of the guideline. Cabazitaxel and abiraterone for castrate resistant metastatic prostate cancer are listed under 'Key issues that will not be covered' because technology appraisals on these interventions were in development when the prostate guideline scope was produced. Both of these technology appraisals have been published since this time. In line with NICE process the technology appraisal on abiraterone has been cross referenced in the guideline and the algorithm. We have now also cross-referenced the technology appraisal on cabazitaxel.
Astrazeneca UK Ltd	3		88	4	Why is the economic cost only included for ADT? The use of radiotherapy and surgery has a cost to commissioners through Payment by Results. We feel this should also be communicated through the guideline in line with the 3.5 in the final scope.	The equivalent data for the cost of surgery and radiotherapy was not available. We have added text under both these sections (on pages 95 and 99) to clarify this.
Astrazeneca UK Ltd	1	Full	85	17	Please highlight that two strengths of bicalutamide are available with different licensed indications – 150mg - monotherapy or adjuvant to radical prostatectomy or radiotherapy in locally advanced prostate cancer at high risk of progression 50mg - Treatment of advanced prostate cancer in combination with luteinising hormone-releasing hormone	This text is part of the needs assessment, conducted as part of the development of the guideline, to illustrate the variation in current practice. It does not make any recommendations. Where bicalutamide is included in a recommendation (e.g. page 354) the dosage is given.

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					(LHRH) analogue therapy or surgical castration. If this is not clarified it could put patient safety at risk with confusing arising from the correct dosing of bicalutamide at the correct stage of the disease.	
Astrazeneca UK Ltd	2	Full	86	11	Novgos hasn't been available in the UK since February 2011 when a Class 3 Drug Alert was enacted..	Thank you for this information.
Astrazeneca UK Ltd	4	Full	241	19	A comparative trial has shown that 3 years of adjuvant goserelin gives significant survival improvement compared with radiotherapy alone	Thank you for this information
Astrazeneca UK Ltd	5	Full	241	19	Neo-adjuvant goserelin prior to radiotherapy has been shown to improve disease-free survival in patients with high risk localised or locally advanced prostate cancer	Thank you for this information.
Astrazeneca UK Ltd	6	Full	241	3	On p88, the licenses were clarified for all available UK LHRHas and there were significant differences between the licensed indication. There has been no evidence of a comparative effectiveness between ADT discussed in the Guideline. We therefore recommend that the studies are clarified which drug they studied. Particularly when Degarelix is undergoing appraisal by NICE and therefore its evidence base should not be included in any GDG recommendations (section 8.1.4.3 '*Publication of recommendations*' in the Guidelines Manual 2012).	Although there are differences in licensing indications the GDG agreed that the physiological effects of all LHRH analogues was the same and was equivalent to orchidectomy. Therefore we do not think it is necessary to specify which drugs were used in which studies. None of the included studies use Degarelix.
Astrazeneca UK Ltd	7	Full	241	3	Highlight that not all ADT are licenses for adjuvant or neoadjuvant treatment and state that 'The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.'. This makes it in line with other mention of unlicensed or off-label medicines throughout the draft guidelines and specifically the recommendations in 9.3.6.3 '*Off-label use*' in the Guidelines Manual 2012	We are unclear how this comment relates to the text on p263 line 3. The guideline does not make recommendations for the use of any specific LHRHa's (it only recommends the use of this class of drug). Therefore it is not appropriate to use the footnote you have suggested as the wording of this needs to contain the name of a specific drug.

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Astrazeneca UK Ltd	8	Full (Appendix)	241 (37)	3 (34)	We also note that in Appendices it is stated that for Kumar et al, 2006 'most of the evidence relates to goserelin given for three years, but a single randomised trail (Tyrell et al, 2005) suggests that the survival benefit of adjuvant bicalutamide monotherapy is comparable. If the majority of evidence relates to goserelin, what evidence does the GDG have access to that suggests goserelin is comparable to other ADT?	The text you are quoting comes from evidence reviewed as part of the 2008 guideline. This topic has been updated in the 2014 guideline and this evidence has been superseded. In line with NICE processes for updating guidelines the 2008 text has been deleted from the guideline and moved to an Appendix. Therefore no changes will be made to this.
Astrazeneca UK Ltd	9	Full	317	3	Please clarify dose of bicalutamide.in the statement 'Gynaecomastia is common, troublesome complication of long-term bicalutamide monotherapy' and this should be reflected throughout the section 7.4.5	This is background text which describes the issue under consideration. It is not appropriate to include drug dosages here. The recommendations on gynaecomastia were not updated during development of the guideline and so we are unable to make any changes.
Bayer HealthCare	1	Full	93	9	Please replace 'Radium 223 chloride' with 'radium-223 dichloride'.	This sentence has been removed.
Bayer HealthCare	2	Full	93	10	Please include that radium-223 dichloride is also currently undergoing NICE review: 'Radium-223 dichloride for treating metastatic hormone relapsed prostate cancer with bone metastases' [ID576]. Expected date of issue: February 2014.	We have amended the text to clarify that there are several interventions currently being investigated by NICE.
Bayer HealthCare	3	Full	336	18	Please replace 'Radium-223' with 'radium-223 dichloride'.	We have made this change.
Bayer HealthCare	4	Full	336	18	We suggest it is made clear at this point that radium-223 dichloride is currently undergoing NICE technology appraisal review.	The ongoing NICE technology appraisal on radium 223 dichloride has been listed in section 3.2 of the NICE version of the guideline.
Bayer HealthCare	5	Full	337	23	Please replace 'Radium-223' with 'radium-223 dichloride'.	We have made this change.
Bayer HealthCare	6	Full	337	23	We suggest it is made clear at this point that radium-223 dichloride is currently undergoing NICE technology appraisal review.	The ongoing NICE technology appraisal on radium 223 dichloride has been listed in section 3.2 of the NICE version of the guideline.
British Association of Urological Surgeons	1	Full	general		Although the term prostatectomy does get used in parts of these guidelines so does the term radical prostatectomy. Some generally agreed consistency of terms might be helpful eg. TURP, radical prostatectomy, total prostatectomy, etc.	We have reviewed the content of the guideline and made amendments to improve consistency of terminology.

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British Association of Urological Surgeons	2	Full	84		Androgen deprivation therapy. Men presenting to A&E with acute or chronic urinary retention may be found to have prostate cancer. For those patients who are not suitable for radical treatment it is not uncommon for a TURP to be delayed until the cancer is hormone controlled. In men presenting with acute/chronic retention found to have prostate cancer is there evidence to support whether proceeding to TURP prior to, or at the time of, introduction of hormone therapy would be deleterious to the outcome?	This text is part of the needs assessment, conducted as part of the development of the guideline, to illustrate the variation in current practice. It does not make any recommendations. The topic of TURP at the time of prostate cancer diagnosis was within the scope of this guideline. We are therefore unable make any recommendations on this issue.
British Association of Urological Surgeons	3	Full	121	1	NHS doesn't fund PCA3; should men have repeat biopsies in any PIN or just multifocal PIN?	This recommendation was based on evidence that an elevated PCA3 score was associated with a statistically significant increased risk of prostate cancer in subsequent biopsies. However, the GDG acknowledge that no formal cost-effectiveness analysis has been conducted on the use of PCA3 tests. They have therefore deleted PCA3 from the recommendation and instead have made a recommendation for further research into the clinical and cost-effectiveness of this test in determining the need for prostate rebiopsy in men who have had a negative first biopsy and whose multiparametric MRI is normal. In addition, PCA3 has been referred to the NICE Diagnostics Assessment Programme for consideration for additional assessment. In the evidence reviewed, both PIN and multifocal PIN were identified as risk factors, the GDG therefore made a recommendation for PIN.
British Association of Urological Surgeons	4	Full	121	1	Negative biopsy, is it worth adding that risk is increased if DRE is abnormal?	Having reviewed the evidence again, we have added DRE to the list of risk factors.
British Association of Urological Surgeons	5	Full	129	1	As written this implies that there should be mpMRI on everyone with a negative biopsy?	The term 'consider' is used by NICE where the benefit of an intervention is less certain and where a discussion about risks and benefits is required. Since the recommendation is to "Consider multiparametric MRI..." we would anticipate

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					Or should mpMRI be done only if PSA is rising?	that not all men with a negative biopsy will have an MRI. The recommendation is not dependant on PSA kinetics.
British Association of Urological Surgeons	6	Full	156	8	Active surveillance protocol: how should prostate be re-biopsied after 1 year? Any comment on role of, or place for, template biopsies?	Since that the components of the active surveillance protocol were based on consensus, the GDG did not feel it was possible to be more specific about the type of biopsy to use.
British Association of Urological Surgeons	7	Full	179	1	Under trade off between net health benefits and resource used the GDG recommended robotic systems should be based in centres where the caseload is greater than 150 cases per year. However the recommendation refers to centres that perform at least 150 radical prostatectomies per year. The GDG need to clarify whether the comment on cost effectiveness applies only to radical prostatectomy or to any robotic procedure. We suggest that commissioners should be advised to only consider commissioning robotic prostatectomy in centres where there are sufficient cases over all to make the procedure cost effective ie a minimum of 150 robotic pelvic procedures per system.	The recommendation for basing robots in centres performing at least 150 radical prostatectomies per year was based on cost-effectiveness evidence which only considered use of the robot to perform radical prostatectomies. The recommendation has been amended and text added to the LETR section to clarify this. It is not possible to say, based on the available evidence, that performing procedures other than radical prostatectomies would accrue the same cost-effectiveness because we do not know about the robots effectiveness in other settings.
British Association of Urological Surgeons	8	Full	305	5	Psychosexual counselling is not available/funded on the NHS. Similarly penile implants are not funded on the NHS.	We believe that both psychosexual counselling and penile implants are available on the NHS. Access to these interventions is an issue for implementation and will be highlighted to the Implementation Team at NICE.
British Association of Urological Surgeons	9	Full	323	5	Supervised exercise for 12 weeks in not NHS funded.	This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
British Lymphology Society	1	Full	General	General	There appears to be no mention of the risks of developing lymphoedema (of the legs or genitals). This disabling and distressing side effect should be highlighted	The risks of developing lymphoedema were not within the scope of this guideline. We are therefore unable make any recommendations on this issue.

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British Uro-Oncology Group	1	Full	129 / 138	1 / 12	The addition to the guidelines of the use of imaging for men with a histological diagnosis of prostate cancer is welcomed by BUG members. The recommendation to consider MRI imaging in men after a negative biopsy is also welcomed as a way of detecting men with significant disease missed at first transrectal biopsy. However, BUG considers that the use of MRI for the detection of prostate cancer should be carried out and reported to agreed standards and would support the use of the recently published UK recommendations for the conduct and reporting of prostate MRI (Kirkham, et al). BUG suggests that reference to these recommendations would be a useful addition to the guidelines. We also suggest including reference to the ESUR guidelines, which contain details of the recommended PIRADS reporting scheme, of which a modified version is detailed in the UK recommendations; overall score rather than score per MR sequence (Barentsz, et al). BUG would support the inclusion of the option of carrying out MRI prior to biopsy in selected men in those units where this pathway is feasible. As this is an area of growing evidence where new papers are published on a monthly basis, BUG would like to see a commitment to an early review of the guidance for the use of MR imaging in prostate cancer, to accommodate new data as it becomes available. Furthermore, two large series (n = 1448, Watanabe 2012, and n = 583, Siddiqui 2013) assessing the use of MRI for prostate cancer detection have been published recently and NICE may wish to include these in their current analysis. In particular the analysis by Siddiqui demonstrates that targeting of biopsies to MR lesions results in greater detection of high grade disease than standard biopsy alone. The series by	Thank you. Unfortunately these issues were not included as part of the evidence review for this topic therefore we unable to make any recommendations. Thank you. NICE are currently piloting a process for the rapid update of guidelines. If implemented this process could be used where publication of further data is prioritised in an area covered by the guideline requires early review.

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					Watanabe shows that the negative predictive value of MRI for the presence of clinically significant disease is high (87%). Kirkham AP, et al, Prostate MRI: Who, when, and how? Report from a UK consensus meeting. Clin Radiol. 2013; Jul 1. pii: S0009-9260(13)00184-0. doi: 10.1016/j.crad.2013.03.030 Barentsz JO, et al. ESUR prostate MR guidelines 2012. Eur Radiol. 2012;22:746–757. Watanabe Y, et al. Detection and Localization of Prostate Cancer With the Targeted Biopsy Strategy Based on ADC Map: A Prospective Large-Scale Cohort Study. Journal of Magnetic Resonance Imaging. 2012;35:1414–1421. Siddiqui MM, et al. Magnetic Resonance Imaging/Ultrasound-Fusion Biopsy Significantly Upgrades Prostate Cancer Versus Systematic 12-core Transrectal Ultrasound Biopsy. Eur Urol. 2013 Jun 12. pii: S0302-2838(13)00598-8. doi: 10.1016/j.eururo.2013.05.059. [Epub ahead of print]	
British Uro-Oncology Group	2	Full	150	14	BUG suggests that this statement is changed to 'Consider active surveillance for men with favourable (Gleason 3+4) intermediate-risk localised prostate cancer...' as BUG does not consider that all men with intermediate risk are suitable candidates for active surveillance.	The GDG explored dividing risk groups into sub-groups but could find no evidence to support making any alterations to the existing D'Amico classification.
British Uro-Oncology Group	3	Full	156	1	BUG agrees that a baseline MRI should be carried out at entry into active surveillance. MRI should also be considered at 1 year. Although either MRI or biopsy is appropriate in this situation, BUG considers that recent data supports the use of MRI because it is safer and more effective. If biopsy is being recommended then the	As stated on p 168 lines 11-12, no evidence comparing the effectiveness of active surveillance protocols in use against one another was found. The GDG believed that developing an active surveillance protocol would help to standardise clinical practice and used a Delphi consensus method to do this (see p168, lines 24-36). Given that the components of

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					guidelines should also state the type of biopsy to be used in this setting. Further MRI ± re-biopsies should be carried out every 2.5–3 years. In this table outlining a protocol for active surveillance, we note that the conclusion on the frequency of timing of re-biopsy is based on consensus (see note 21 referring to page 114 below) and we would question the validity of basing guidance on consensus of opinion rather than evidence from peer reviewed studies. This protocol should take in to consideration more of the available data.	the active surveillance protocol were based on consensus, the GDG did not feel it was possible to be more specific about the type of biopsy to use or the frequency of MRI.
British Uro-Oncology Group	4	Full	267	7	BUG believes there is ongoing debate over the evidence for the use of intermittent therapy for men with advanced disease and asks that a caveat to this effect is added to this statement.	Since the recommendation is to "consider" intermittent therapy" not to "offer it" and notes the need for discussion about the issues, we think this is an adequate caveat.
British Uro-Oncology Group	5	Full	192 / 237	1 / 7	BUG is aware that data currently exist on the research recommendations covered in bullets 2 and 3. Instead we would recommend that studies on therapy sequencing in CRPC and prostate cancer biomarkers are key areas where data are currently lacking and recommend these as key research recommendations in place of the currently proposed topics.	The GDG did not feel that sufficient data existed in these areas and hence voted for them to be in the 5 key priorities for research. Therapy sequencing in hormone-refractory prostate cancer was not within the scope of this guideline. We are therefore unable make any recommendations on this issue.
British Uro-Oncology Group	6	Full	26		BUG suggests a slight modification to this algorithm, as follows: add a line stating 'Consider' from the **High-risk localised prostate cancer** box to a new box **Radical prostatectomy** and change the box **Radical prostatectomy or radical radiotherapy** to **Radical radiotherapy** (and move the subsequent boxes as appropriate).	The wording used in the algorithm reflects that used in the recommendations. The recommendations on high-risk localised prostate cancer were not updated during development of the guideline and so we are unable to make any changes.
British Uro-Oncology Group	7	Full	256	29	Second bullet – change 'Offer men with intermediate high-risk localised prostate cancer 6 months...' to 'Consider...'	'Offer' is appropriate wording for a recommendation where the GDG is confident that, for the vast majority of people, the recommendation will do more good than harm.

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						'Consider' is the appropriate wording for a recommendation where the benefit is less certain and where a discussion about risks and benefits is required.
British Uro-Oncology Group	8	Full	28		This algorithm needs to clarify the protocol for men considered suitable for local salvage and those considered unsuitable. It should also include statements to the effect that: • Patients considered suitable for salvage treatment should be referred to a team with adequate experience of salvage treatment • Re-staging should be conducted by this specialist team and not carried out locally.	The recommendations on salvage therapy were not updated during development of the guideline and so we are unable to make any changes. These recommendations are covered by the algorithm on 'Biochemical relapse' on p42.
British Uro-Oncology Group	9	Full	259	3	BUG considers this advice to be incorrect Immediate post-operative radiotherapy should be considered as an option for the treatment of men with locally advanced prostate cancer. BUG asks NICE to consider changing this guidance from 'Do not offer' to 'Consider offering'. Data from randomised clinical trials exist to support the use of radiotherapy in this situation (Swanson GP, Thompson IM, Tangen C, et al. Update of SWOG 8794: adjuvant radiotherapy for pT3 prostate cancer improves metastasis free survival. Int J Rad Oncol Biol Phys 2008;72:S31).	These recommendations were not updated during development of the guideline and so we are unable to make any changes.
British Uro-Oncology Group	10	Full	29 (107)	0 (11)	Prostate biopsy is often needed if patients are to be recruited on a clinical trial, or if histological confirmation may influence treatment. Therefore a caveat to this effect needs to be added to the statement in the top box. Such a statement currently exists in the relevant section of the text.	We have made this change.
British Uro-Oncology Group	11	Full	334	6	The recommendation for all treatment options to be discussed by the urological cancer multidisciplinary team is not considered (MDT) feasible as these local teams (in	These recommendations were not updated during development of the guideline and so we are unable to make any changes.

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					terms of physical meetings) are unlikely to have the capacity to discuss every case of relapse. BUG suggests re-wording this to say 'Treatment options to be discussed with the uro-oncology multidisciplinary team'.	
British Uro-Oncology Group	12	Full	29	Box – Chemotherapy	BUG considers it would be useful for NICE to refer to the NICE guidance in relation to abiraterone following chemotherapy (TA259).	NICE technology appraisal 259 is already included in the algorithm on p44. However we have amended this algorithm to make it clearer that use of abiraterone is recommended following chemotherapy.
British Uro-Oncology Group	13	Full	29	Last row of boxes	BUG considers that a 5th box needs to be added for antagonists – and the recommendation to 'Consider offering' antagonists should be included.	LHRH antagonists were not investigated by this guideline. We are therefore unable make any recommendations on this issue or include them in the algorithm. Degarelix is currently the subject of an ongoing technology appraisal.
British Uro-Oncology Group	14	Full	336	23	BUG recommends changing from 'Do not offer' to 'Consider offering' bisphosphonates to prevent/reduce the complications of bone metastases in men with hormone relapsed prostate cancer, considering the TRAPEZE data recently presented at ASCO 2013. This trial involved 757 patients treated with strontium-89 after six cycles of docetaxel. It reported that the use of zoledronic acid significantly improved the median skeletal related events-free interval in these patients, (mostly post progression), suggesting a role for bisphosphonates as a post chemotherapy maintenance therapy. James ND, et al. Clinical outcomes in patients with castrate-refractory prostate cancer (CRPC) metastatic to bone randomized in the factorial TRAPEZE trial to docetaxel (D) with strontium-89 (Sr89), zoledronic acid (ZA), neither, or both (ISRCTN 12808747). J Clin Oncol.	These recommendations were not updated during development of the guideline and so we are unable to make any changes. This issue could be considered when the guidelines are next updated.

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					31;2013 (Suppl; abstr LBA5000)	
British Uro-Oncology Group	15	Full	30	Urinary obstruction – box	BUG suggests that 'Discuss the risk of bladder cancer' should be added to this part of the algorithm.	The risk of second malignancy was not within the scope of this guideline. We are therefore unable make any recommendations on this issue or include it in the algorithm.
British Uro-Oncology Group	16	Full	317 / 293 / 323	8 / 5 / 5	**Gynaecomastia** – BUG considers that weekly tamoxifen rather than radiotherapy should be offered in this situation **Hot flushes** – BUG does not recommend the long-term use of medroxyprogesterone, due to the risk of side effects **Fatigue** – BUG is supportive of the recommendation to 'Offer men who are having androgen deprivation therapy supervised resistance and aerobic exercise at least twice a week for 12 weeks to reduce fatigue'. However, we would question how 'supervised exercise' can be implemented and delivered within the current NHS infrastructure.	The recommendations on gynaecomastia were not updated during development of the guideline and so we are unable to make any changes. The clinical evidence supports the use of medroxyprogesterone, because it demonstrates reduced frequency and severity of hot flushes and has less side effects that the other drugs. This information documented in the linking evidence to recommendations table on p317-318. Consequently this is what the guideline has recommended. This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
British Uro-Oncology Group	17	Full	107	11	The guidelines state 'If the clinical suspicion of prostate cancer is high, because of a high PSA value..' – BUG recommends that the definition of a high PSA value in this	Only the new and updated recommendations in this guideline formed part of the consultation process. As these refer to sections that were not updated we are unable to comment.

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					statement should be clarified.	
British Uro-Oncology Group	18	Full	108	16–34	BUG suggests inclusion of the following papers, in addition to the four currently discussed. These papers have been recently published and include a large number of men, thus their inclusion will strengthen the evidence supporting this guideline update. • Watanabe, et al: 1448 consecutive patients referred with a raised PSA: 890 had a positive MRI of whom 70.9% had cancer on biopsy. All had standard positive targeted biopsy. 558 had a negative MRI (no ADC lesions) of whom 13% had cancer on biopsy. All had standard biopsy (8 cores) • Siddiqui, et al (Pinto group): 583 men at the NIH had standard biopsy + MRI-targeted biopsy, 320 of these had a prior negative biopsy (262 at 1st biopsy). This paper demonstrates that targeted biopsy misses more Gleason 6 and less higher grade disease than standard 12 core biopsy. The following studies could also be considered for inclusion: • Robertson, 2013: Prostate cancer risk inflation as a result of targeted biopsy. A computer modelling study which models the different histological outputs of standard biopsy and MRI-targeted biopsy, using lesions from a radical prostatectomy database. It shows that higher Gleason grade and greater cancer core length tend to occur with targeted biopsy • Puech, 2013: This study evaluated MpMRI with cognitive and fusion guidance versus systematic biopsy. It was a prospective multi-centre study French study of 95 men. It reported no statistically significant difference between cognitive and fusion targeted	Watanabe et al (2012) does not compare MRI targeted and systematic cores in the same patients – but separates patients into 2 groups (depending on whether they had prostate lesions on MRI). Consequently it was not included in our evidence review. Siddiqui et al (2013), Robertson (2013) and Puech (2013) were all published after our literature search cut-off date of May 2013 and therefore are not included in the evidence review.

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					biopsies. Watanabe Y, et al. Detection and Localization of Prostate Cancer With the Targeted Biopsy Strategy Based on ADC Map: A Prospective Large-Scale Cohort Study. Journal of Magnetic Resonance Imaging. 2012;35:1414–1421. Siddiqui MM, et al. Magnetic Resonance Imaging/Ultrasound-Fusion Biopsy Significantly Upgrades Prostate Cancer Versus Systematic 12-core Transrectal Ultrasound Biopsy. Eur Urol. 2013;pii: S0302-2838(13)00598-8. doi: 10.1016/j.eururo.2013.05.059. [Epub ahead of print] Robertson NL, et al. Prostate Cancer Risk Inflation as a Consequence of Image-targeted Biopsy of the Prostate: A Computer Simulation Study. Eur Urol. 2013;S0302-2838:1587–1584. Puech P, et al. Prostate Cancer Diagnosis: Multiparametric MR-targeted Biopsy with Cognitive and Transrectal US-MR Fusion Guidance versus Systematic Biopsy--Prospective Multicenter Study. Radiology. 2013;268:461-469.	
British Uro-Oncology Group	19	Full	109	1–22	Please see comment 18 above, which is also relevant to this section.	Please see response to comment 18.
British Uro-Oncology Group	20	Full	113	32	BUG read with interest the proposed economic model, however, we believe there are more data (that was not available at the time that this analysis was undertaken) that support the use of MRI and which have not been included in this model (see comment 18 above). It is also noted that this cost effectiveness model for the use of imaging prior to biopsy did not include the option of MRI for those men with a negative biopsy, as recommended. It is felt that inclusion would be likely to alter the cost	With regard to the comment on the use of MRI in men with a previous negative biopsy, this issue is covered by a separate question in the guideline and was covered by a published economic analysis undertaken by Mowatt et al. (2013) In addition, the model that considers the use of MRI before an initial biopsy *does* include the use of MRI before a re-biopsy. It was assumed that 50% of men being investigated

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					effectiveness calculation in favour of imaging prior to biopsy in men fit for radical treatment, who would be likely to get an MRI if the initial biopsy was negative. It should also be noted that the use of MRI prior to biopsy is likely to speed up treatment initiation in men for whom it is appropriate, thus further impacting on likely patient outcomes and costs.	following an initial negative biopsy would receive a MRI prior to a potential biopsy. Speeding up treatment initiation in men positive for prostate cancer by using an MRI was not something that was captured in the model. It is not always possible to capture every aspect of clinical practice in an economic model and a pragmatic approach must be adopted. However, the GDG believe that this particular issue is unlikely to have a sufficiently large cost and QALY impact to change the conclusion of the analysis.
British Uro-Oncology Group	21	Full	114	42	BUG questions the finding that cognitive targeting approach was found to be less effective than systematic TRUS biopsy, considering the former detects more clinically significant cancers (Haffner et al). Haffner J, Lemaitre L, Puech P, et al. Role of magnetic resonance imaging before initial biopsy: comparison of magnetic resonance imaging targeted and systematic biopsy for significant prostate cancer detection. BJU Int 2011;108:E171e8.	You are correct that the cognitive targeting approach detects more significant cancers. However, the result that you have observed is down to the assumptions regarding patients that are negative after the first biopsy. The GDG felt that it was likely that 50% of patients that underwent a systematic biopsy would receive a scheduled re-biopsy, whereas this would not be necessary in patients that had a MRI and a biopsy. Thus, patients in the systematic biopsy arms would get re-biopsies more quickly and this ultimately leads to the systematic biopsy arm being more effective. This is already explained in the results section of Appendix B with an accompanying graph showing the number of cancers detected at the initial biopsy and at subsequent biopsies. We have added this information to the cost-effectiveness text for clarity.
British Uro-Oncology Group	22	Full	181	15	In relation to brachytherapy, whilst BUG was pleased to see it as a recognised treatment for early prostate cancer we think the long-term results from combined LDR Brachytherapy and EBRT should be included. It should also be a treatment option in intermediate/high-risk patients. The use of prostate brachytherapy, both LDR and HDR, in Europe is increasing. The document only mentions HDR in respect to combination treatment but	The GDG made recommendations on HDR-BT and EBRT combinations because evidence from randomised trials was available for this combination. Evidence for LDR-BT and EBRT was limited to observational studies and so no recommendations were made on this combination. This is mentioned in the LETR statement on p212.

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					most of the available long-term data is LDR combinations.
					
					Please see the main studies relating to this below, particularly note Grimm, et al, that summarises all the recent studies:
					• **Critz FA, et al**: A series of 3546 hormone-naive men were treated with combination therapy from 1984-2000. Until 1995, the older retropubic technique was used to implant the Iodine-125 seeds. The median follow-up was 11 years (range 0.25–26 years). They defined biochemical recurrence according to the PSA used by the AUA for radical prostatectomy of a PSA nadir greater than 0.20 ng/mL
					  ○ The disease-free survival (DFS) rates for all men (n=3546) were as follows: Table 1: 10-yr DFS = 75%, 15-yr DFS = 73%, 20-yr DFS = 73%, 25-yr DFS = 73%
					  ○ Among men implanted with the modern transperineal method from 1995, 15-yr DFS was 79%. This study confirmed durable disease-free survival with combination therapy
					• **Grimm, et al:** This comprehensive review of the 2000–2010 literature of studies of the treatment of localised prostate cancer suggests that combination therapies involving EBRT and brachytherapy plus or minus ADT for high-risk prostate cancer appear superior to more localised treatments such as LDR brachytherapy alone, EBRT or radical prostatectomy alone, in terms of progression-free survival
					• **Guedea, et al**: This study shows that combination therapy (LDR brachytherapy combined with EBRT) produces durable biochemical control of localised prostate cancer. The use of prostate brachytherapy, both LDR and HDR, in Europe is increasing.
						Our reasons for not including the studies you have cited are given below.
						
						Critz et al was not identified in our literature search – its entry date onto the Medline database was after our literature search cut-off date of May 2013.
						
						Grimm et al (2012) was not included because it summarises non comparative case series and there was a good quality systematic review of comparative studies of radiotherapy for localised prostate cancer (Bannuru et al 2011).
						
						Guedea et al is a descriptive study which evaluated current clinical practices, staffing and equipment (rather than a patient outcomes study) and was not included for this reason.
						
						Langenhuijsen et al (2013) was published after our

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					Other studies to consider including in this section are: • Langenhuijsen JF, et al. Continuous vs. intermittent androgen deprivation therapy for metastatic prostate cancer. Urol Oncol. 2013 31(5):549–556. • Kotecha R, et al. Clinical outcomes of high-dose-rate brachytherapy and external beam radiotherapy in the management of clinically localized prostate cancer. Brachytherapy 2013 12(1):44–49. Critz FA, et al. 25-year disease-free survival rate after irradiation for prostate cancer calculated with the prostate specific antigen definition of recurrence used for radical prostatectomy. J Urol. 2013 189:878–883. Grimm P, et al. Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high-risk prostate cancer treatment by radical therapy. Results from the prostate cancer results study group. BJU Int. 2012;109 Suppl 1:22–29. Guedea F, et al. Patterns of care for brachytherapy in Europe: updated results. Radiother Oncol. 2010;97:514–520.	literature search cut-off date of May 2013. Kotecha et al (2013) was published after our literature search cut-off date of May 2013.
British Uro-Oncology Group	23	Full	129	1	BUG suggests changing the recommendation statement from 'Consider' to 'Offer a multiparametric MRI (using T2- and diffusion-weighted imaging) for all men with a negative transrectal ultrasound 10=12 core biopsy who are considered still at risk of having a cancer, to determine whether another biopsy is needed.	'Offer' is appropriate wording for a recommendation where the GDG is confident that, for the vast majority of people, the recommendation will do more good than harm. 'Consider' is the appropriate wording for a recommendation where the benefit is less certain and where a discussion about risks and benefits is required. Based on the available evidence for this topic, 'consider' is the appropriate term to use.

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					We also suggest adding contrast enhanced imaging to T2 and diffusion weighted imaging, in line with the UK consensus statement ((Kirkham, et al), as discussed and referenced in comment #1. In addition, BUG suggests that this recommendation should include a statement that MRI should not be conducted within 3 months of obtaining a negative biopsy. This recommendation statement also needs to include guidance on when it is appropriate to repeat a negative biopsy; BUG suggests that a repeat biopsy should be considered at least 3 months after the initial negative biopsy.	Kirkham et al was published after our literature search cut-off, and as a consensus statement would not have been included in the evidence appraised for this topic. The GDG reached their own consensus on the basis of evidence from primary studies and their own experience. The GDG were aware of this issue but there was no evidence to support making a specific recommendation on the timing of the MRI and/or re-biopsy. We have added text to the LETR section to clarify this.
British Uro-Oncology Group	24	Full	155	1	BUG questions the role of these consensus survey results in the development of these guidelines and do not think the results are valid evidence on which to base clinical guidance. Guidance should be based on the available evidence from peer reviewed studies.	As stated on p 168 lines 11-12, no evidence comparing the effectiveness of active surveillance protocols in use against one another was found. The GDG believed that developing an active surveillance protocol would help to standardise clinical practice and used a Delphi consensus method to do this (see p168, lines 24-36).
British Uro-Oncology Group	25	Full	218	12	Informing partners about the effect of treatments on sexual function should be done in agreement and with the consent of the patient.	We agree and this is why we have amended the terminology of the 2008 recommendation to clarify that partners should be involved if the man wishes.

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British Uro-Oncology Group	26	Full	258	28	We found the following guidance unhelpful - *Clinical oncologists should consider pelvic radiotherapy in men with locally advanced prostate cancer who have a > 15% risk of pelvic lymph node involvement and who are to receive neoadjuvant hormonal therapy and radical radiotherapy.* [2008] *Qualifying statement: This recommendation is based on evidence from one large, randomised trial.* There is no clear evidence either way for the use of pelvic radiotherapy in this situation and the NICE guidance to 'consider' does not help guide our practice or guide the commissioners in setting up and paying for such a service.	The recommendations on pelvic radiotherapy were not updated during development of the guideline and so we are unable to make any changes.
British Uro-Oncology Group	27	Full	General		BUG recommends that the guidance in relation to CRPC should be considered for early review, as further data in this area is due to be published imminently.	Thank you. NICE are currently piloting a process for the rapid update of guidelines. If implemented this process could be used where publication of further data is prioritised in an area covered by the guideline requires early review.
C. R. Bard, Inc.	1	Full	181-192		Concerning the validation of HDR- and LDR-Brachytherapy in their role in combination with EBRT in intermediate- and high-risk patients the literature concerning LDR Brachytherapy appears to be underrepresented. The number of observational reports about LDR-Brachytherapy in combination with EBRT or of LDR-Brachytherapy alone in intermediate risk prostate cancer are numerous, demonstrating a high effectiveness of the combination of LDR-Brachytherapy with EBRT in both risk groups. Therefore a recommendation on the combination of HDR-Brachytherapy with EBRT only does not appear justified. Also the evidence concerning both Brachytherapy approaches is rather equal, so that a recommendation for the combination of LDR-Brachytherapy and EBRT should	The GDG made recommendations on HDR-BT and EBRT combinations because evidence from randomised trials was available for this combination. Evidence for LDR-BT and EBRT was limited to observational studies and so no recommendations were made on this combination. This is mentioned in the LETR statement on p212.

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					also be given. Concerning tables 29, 30 and 31 the wording in the row "number of patients" has to be corrected to LDR-Brachytherapy as the stated investigations dealt with LDR- and not with HDR-Brachytherapy.	
Cheshire and Merseyside SCN	1	Full	179	3	In response to the following recommendation; *Commissioners should ensure that robotic systems for the surgical treatment of localised prostate cancer are based in centres that perform at least 150 radical prostatectomies per year.* This recommendation is based upon Ramsey et al's 2012 economic modelling paper. However this paper considers the costs of robotic systems that are used for prostate surgery alone and the recommendation can therefore only be valid in this setting. In a centre where a robot is used in a multi-disciplinary manner, the economic modelling is completely different and the recommendation therefore has no evidence base in such a setting.	The recommendation for basing robots in centres performing at least 150 radical prostatectomies per year was based on cost-effectiveness evidence which only considered use of the robot to perform radical prostatectomies. Text has been added to the LETR section to clarify this.
Coloplast Limited	1	Full	219	32	With regards to the algorithm on managing complications of treatment (urinary symptoms) – while we welcome the recognition that men with urinary symptoms should be referred to specialist continence advice, we are concerned that this section does not mention that conservative management options should be made available. This should include the use of collecting devices such as urinary sheaths. There is evidence to show that men using collecting devices prefer to use a sheath and bag system instead of pads.	The recommendations on managing urinary dysfunction resulting from radical treatment were not updated during development of the guideline and so we are unable to make any changes.

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					For example, see *Chartier-Kastler et al. Randomised, crossover, prospective, multicentre study comparing quality of life related to use of urinary sheaths versus diapers in incontinence men. British Journal of Urology. Published online October 2010.* Southampton University have also produced research which shows that most men benefit from using male-specific devices either instead of or combined with their usual pads. Sheaths and clamps were found to be particularly popular. This work is currently awaiting publication and was presented at the International Conference Society in August 2013 – see abstract at http://www.ics.org/Abstracts/Publish/180/000264.pdf	
Coloplast Limited	2	Full	219-220	32	With regards to the management options for incontinence following prostate intervention there is currently only mention of pelvic floor exercise and surgery. We would argue that there needs to be inclusion of conservative management options, particularly the use of collecting devices such as urinary sheaths, as an alternative to pelvic floor exercises and surgery. We appreciate that this is not one of the areas highlighted for review, but access to continence services and products is essential during the initial post-operative period and then on an ongoing basis if incontinence persists. As noted above, there is evidence to show that men using collecting devices prefer to use a sheath and bag system instead of pads. (See *Chartier-Kastler et al. Randomised,*	The recommendations on managing urinary dysfunction resulting from radical treatment were not updated during development of the guideline and so we are unable to make any changes.

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					crossover, prospective, multicentre study comparing quality of life related to use of urinary sheaths versus diapers in incontinence men. British Journal of Urology. Published online October 2010 as well as the University of Southampton research).	
CPPC & ACPWH	1	Full	219	31	Men who are scheduled to have radical prostatectomy should start immediately on a course of pre-operative pelvic floor exercises to help to avaid urinary incontinence: Sueppel C, Kreder K, See W (2001); Centemero et al (2009); Patel et al (20130; Tientforti et al (2012)	The recommendations on managing erectile dysfunction resulting from radical treatment were not updated during development of the guideline and so we are unable to make any changes.
CPPC & ACPWH	2	Full	218	14	Men who have had radical prostatectomy may benefit from early pelvic floor exercises to treat erectile dysfunction: Prota et al (2002)	The recommendations on managing erectile dysfunction resulting from radical treatment were not updated during development of the guideline and so we are unable to make any changes.
Department of Health	1				Thank you for the opportunity to comment on the draft for the above clinical guideline. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you.
Ferring Pharmaceuticals	1	Full	General		NICE are currently undertaking a technology appraisal for degarelix (and also for enzalutamide and abiraterone). Therefore we thought it might be worth considering waiting for the outcomes of these TAs before updating these guidelines in order to avoid the risk of the guidelines being out of date shortly after publication. There are a couple of sections on which we have not been invited to comment that could perhaps be updated should degarelix receive a positive TA recommendation (in particular section 8).	Unfortunately we are unable to change the publication date of the prostate guideline. The technology appraisals for enzalutamide, degarelix and abiraterone have already been listed in section 3.2 of the NICE version of the guideline. This could be considered when the prostate guideline is next updated.
Ferring Pharmaceuticals	2	Full	29 (84)	0 (43)	Men with hormone naïve prostate cancer box - Consider including 'GnRH antagonist' where ADT is mentioned	LHRH antagonists were not investigated by this guideline. We are therefore unable make any recommendations on

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					throughout the guideline to ensure consistency with the phrase on page 84 (lines 43/44) 'Androgen blockade can be administered in one of three ways….(ii) injection of a LHRH agonist or antagonist…'	this issue or include them in the algorithm. Degarelix is currently the subject of an ongoing technology appraisal.
Ferring Pharmaceuticals	3	Full	263	6	Consider including 'GnRH antagonist' where ADT is mentioned throughout the guideline to ensure consistency with the phrase on page 84 (lines 43/44) 'Androgen blockade can be administered in one of three ways….(ii) injection of a LHRH agonist or antagonist…'	LHRH antagonists were not investigated by this guideline. We are therefore unable make any recommendations on this issue or include them in the algorithm. Degarelix is currently the subject of an ongoing technology appraisal.
Ferring Pharmaceuticals	4	Full	28		Locally advance prostate cancer algorithm – 'Hormone therapy alone not covered by this guideline'. Hormone therapy is referred to in a later algorithm on page 32 but refers back to the locally advanced prostate cancer algorithm.	We have amended the algorithms on p43 and p47 to clarify that the guideline makes no specific recommendations on hormone therapy alone for locally advanced prostate cancer, but there are recommendation on radiotherapy plus hormones.
Ferring Pharmaceuticals	5	Full	333 (29)	19 (0)	Men with hormone naïve prostate cancer box – bicalutamide monotherapy recommended but not licenced in this indication. This is also mentioned on page 333, line 19 however we are not invited to comment on this section.	These recommendations were not updated during development of the guideline and so we are unable to make any changes. A footnote has already been included about the off license indication for bicalutamide.
Ferring Pharmaceuticals	6	Full	268		Consider a section on managing CV risk. Recent data presented at EAU, AUA and ASCO GU suggests a reduction in CV risk with degarelix compared with LHRH agonists (Albertsen et al, Poster 781. AUA 2013). The full paper has been submitted with a view to publication early in 2014.	The management of cardiovascular risk was not investigated by this guideline. We are therefore unable make any recommendations on this issue.
Ferring Pharmaceuticals	7	Full	268	13	The evidence that long term decrease in testosterone levels comes mainly from trials looking at testosterone decrease with LHRH agonists. Some controversy surrounds whether the increase in risk is simply down to testosterone reduction. For example, some studies have shown that orchidectomy does not increase CV risk (Keating et al. J Clin Onc 2006) and recent data presented at EAU, AUA and ASCO GU suggests a reduction in CV risk with degarelix compared with LHRH agonists (Albertsen et al, Poster 781. AUA 2013). The	Keating (2006) has already been included in the evidence review for this topic (see page 957 of the full Evidence Review). It is not cited in the text on page 290 as the evidence statements here are only supposed to cover the highlights of the appraised evidence. We look forward to the publication of the Albertsen et al data.

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					full paper has been submitted with a view to publication early in 2014.	
Ferring Pharmaceuticals	8	Full	279	5	The evidence for adverse CV effects seen with ADT has largely been in trials with LHRH agonists. Some controversy exists in this area. For example, some studies have shown that orchidectomy does not increase CV risk (Keating et al. J Clin Onc 2006) and recent data presented at EAU, AUA and ASCO GU suggests a reduction in CV risk with degarelix compared with LHRH agonists (Albertsen et al, Poster 781. AUA 2013). The full paper has been submitted with a view to publication early in 2014.	Keating (2006) has already been included in the evidence review for this topic (see page 957 of the full Evidence Review). It is not cited in the text on page 290 as the evidence statements here are only supposed to cover the highlights of the appraised evidence. We look forward to the publication of the Albertsen et al data.
Ferring Pharmaceuticals	9	Full	421	22	Degarelix technology appraisal is not mentioned in this section.	The text on p445 is the scope of the guideline which was published in March 2012 after consultation with stakeholders. We are therefore not able to change the content of this.
Ferring Pharmaceuticals	10	Full	87	4	Degarelix was introduced in the UK in 2009	We have made this amendment to the text.
Galil Medical	1	Full	93	19	Our comments are as follows: the statement on the method of action of Cryotherapy is inadequate. A longer more detailed description is required. We suggest the following; Minimally invasive cryosurgical ablation treatments can be used as both a primary and salvage (recurrence) line of defence against prostate cancer. Cryotherapy utilises extreme cold temperatures (lower than -40C) delivered through precisely placed needles, to sculpt an iceball to completely engulf the prostate and destroy targeted prostatic tissue killing all cancer cells within the prostate gland. Modern cryoablation systems are driven by the use of argon gas to produce the freeze and thaw effects (Joule-Thomson). Cryotherapy is highly controllable and predictable. Temperatures below -20C will induce cell death and temperatures below -40C destroy all cellular activity. Data has been collected into the EuCAP registry with over 1,000 patients with	This text is part of the needs assessment, conducted as part of the development of the guideline, to illustrate the variation in current practice. It does not make any recommendations. However we have expanded the description of cryotherapy to make it a similar length to that of HIFU in the previous paragraph.

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					prospective or retrospective outcome data now registered, including multiple sites within the UK. The US COLD registry has also provided substantial data that has been reported in the literature. Current EAU guidelines support the use of Cryotherapy, especially in its salvage role.	
Galil Medical	2	Full	147	29	Our comments are as follows: The list provided at this point is in no logical order and is difficult to follow. The list places Cryotherapy at the bottom, with no reason as to why it should be so. Simple alphabetical order would impart no judgement.	Thank you for raising this issue. We have moved the section on watchful waiting to reflect the order in which treatment options would be considered.
Galil Medical	3	Full	193	3	Our comments are as follows: Please see attached list of papers that we have prepared for your review, which we believe demonstrate the efficacy and safety of all Cryo therapy options.	Thank you for providing this information. The recommendations on cryotherapy were not updated during development of the guideline and so we are unable to make any changes.
Galil Medical	4	Full	237	7 (list following 7)	Our comments are as follows: It should be noted that Cryotherapy offers the ability to collect data for these reasons using the EuCAP registry (within the EU recognised and mentioned by NICE) and the COLD registry (in the US).	Thank you for this information.
Galil Medical	5	Full	408	2	Our comments are as follows: the statement on the method of action of Cryotherapy is inadequate. A longer more detailed description is required. We suggest the following; Minimally invasive cryosurgical ablation treatments can be used as both a primary and salvage (recurrence) line of defence against prostate cancer. Cryotherapy utilises extreme cold temperatures (lower than -40C) delivered through precisely placed needles, to sculpt an iceball to completely engulf the prostate and destroy targeted prostatic tissue killing all cancer cells within the prostate gland. Modern cryoablation systems are driven by the use of argon gas to produce the freeze and thaw effects (Joule-Thomson). Cryotherapy is highly controllable and predictable. Temperatures below -20C will induce cell death and temperatures below -40C	The purpose of the glossary is to give a brief, simple and easy to understand definition of the terms used in the guideline. As such we feel that the current definition is appropriate.

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					destroy all cellular activity. Data has been collected into the EuCAP registry with over 1,000 patients with prospective or retrospective outcome data now registered, including multiple sites within the UK. The US COLD registry has also provided substantial data that has been reported in the literature. Current EAU guidelines support the use of Cryotherapy, especially in its salvage role.	
Ipsen Ltd	1	Full	241	26	We would question the relevance of "not offering adjuvant hormonal therapy, even to men with marginal positive disease, other than in the context of a clinical trial" for patients with locally advanced prostate cancer, whom receive Prostatectomy. The EAU guidelines 2013, page 50 suggests that "when nodal involvement is detected post surgery, adjuvant androgen deprivation therapy may be selected"	These recommendations were not updated during development of the guideline and so we are unable to make any changes.
Ipsen Ltd	2	Full	331	23	We would question the value of offering "bilateral orchidectomy as an alternative to continuous LHRHa therapy" as it is well understood that most patients prefer the depot LHRH agonists because of the psychological implications of the loss of the testicles. *Cassileth BR, Soloway MS, Vogelzang NJ. et al. Patients' choice of treatment in stage D prostate cancer. Urology. 1989;33 Suppl:57–62.*	These recommendations were not updated during development of the guideline and so we are unable to make any changes
Ipsen Ltd	3	Full	92	22	0.7 nmol/l corresponds to 20 ng/dl. According to the EAU prostate cancer guidelines the cut-off is still < 50 ng/dl (i.e.1.735 nmol/l). Whilst it is usually desirable to be as low as possible, the clinical relevance of a serum testosterone of below 20 ng/dl has not yet been confirmed.	We have deleted this sentence.
Ipsen Ltd	4	Full	263	8	We would like to highlight that there is no reference to GnRH antagonists here, as they also have an immedicate onset of action, rapidly reducing testosterone levels without an initial surge.	LHRH antagonists were not investigated by this guideline. We are therefore unable make any recommendations on this issue or include them in the algorithm. Degarelix is currently the subject of an ongoing technology appraisal.

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Ipsen Ltd	5	Full	393	4	We would like to point out that the annualised cost of leuprorelin acetate given continuously is greater than the figure of £870.86 quoted and should remain the same as for the metastatic treatment strategy costs quoted in the model on page 394 at £902.88	A cost of £902.88 was used in all areas where hormones were given continuously. The cost of £870.86 reflects scenarios where hormones might be given continuously or intermittently in current practice. Thus it is a cost weighted by our estimation that 89% is given continuously and 11% is given intermittently.
Janssen	7	Appendices	418	40	'Hormone-refractory prostate cancer' is listed as 'a key issue covered by NICE clinical guideline 58 for which the evidence will not be reviewed'. We assert that 'hormone-refractory prostate cancer' is an outdated term due to greater understanding of the pathogenesis of advanced prostate cancer. 'Castration-resistant prostate cancer (CRPC)' is now the term most commonly used amongst the clinical and research community. The wording in the guideline should be changed accordingly. We also assert that evidence should have been reviewed for this topic given the significant changes in the management of CRPC which have occurred since CG58 was published in 2008, most notably the licensing or imminent licensing of numerous new drugs (e.g. abiraterone, enzalutamide, sipuleucel-T, radium-223). We suggest that appropriate wording should be added that reflects the changes in clinical practice since 2008.	We agree that hormone-refractory prostate cancer is an outdated term and have replaced this in the guideline with hormone-relapsed prostate cancer. Patient/carer groups appreciate the fact that the guidelines no longer refer to "castrate resistant", but instead refer to "hormone relapsed" prostate cancer. At the time that the scope was produced, "hormone-refractory" was the terminology in use and appendix H1 has to show the scope as published. The Guidelines Manual, 2012 states that "The GDG must not publish its own recommendations in a clinical guideline in areas already covered in the scope of any relevant ongoing technology appraisal. This also applies to areas covered in existing published technology appraisals unless NICE has agreed that the technology appraisal guidance will be updated in the clinical guideline (see section 8.1.3)." Since abiraterone, enzalutamide, sipuleucel-T and radium-223 dichoride are the subject of published and ongoing technology appraisals, we are not able to include any recommendations on these interventions in the guideline. However all of these technology appraisals have been included in section 3.2 of the NICE version of the guideline.
Janssen	8	Appendices	419	5	Abiraterone is listed as a 'key issue that will not be covered' because it is 'the subject of an ongoing NICE technology appraisal'. The relevant appraisal, TA259, was published in June 2012, therefore we feel that this statement is inaccurate. The statement should be	The text on p445 is the scope of the guideline which was produced in March 2012. We are not able to change the content of this.

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					changed to reflect the publication of TA259.	
Janssen	9	Appendices	421	32	Abiraterone's NICE technology appraisal TA259 is again listed as 'under development'. As discussed in comment 8 this is incorrect. The section should be amended to reflect the publication of TA259 in June 2012.	The text on p445 is the scope of the guideline which was published in March 2012 after consultation with stakeholders. We are therefore not able to change the content of this.
Janssen	1	Full	29	n/a	Abiraterone is listed as 'chemotherapy' in the figure on this page; abiraterone is not a chemotherapy agent. Abiraterone's WHO ATC code is L02BX 'other hormone antagonists and related agents', and its post-ADT failure pre-chemotherapy licence wording makes reference to when 'chemotherapy is not yet clinically indicated'. The figure should be amended to place abiraterone in a separately-labelled box.	We have amended this algorithm to make it clearer that use of abiraterone is recommended following chemotherapy.
Janssen	2	Full	89	n/a	Abiraterone is listed as an 'anti-androgen' in table 9; this is incorrect. Abiraterone does not act as an androgen receptor antagonist (the mechanism of action of the other drugs listed in the 'anti-androgen' box), it is a CYP17 enzyme inhibitor. The term 'androgen biosynthesis inhibitor' is in common use to describe abiraterone's mechanism of action. The table should be amended to place abiraterone in a separately-labelled box.	We have amended the drug class to "androgen modifiers" for clarity.
Janssen	3	Full	334	17	Reference to recommendations for the use of abiraterone for mCRPC after docetaxel failure are made in a section entitled 'chemotherapy'. As discussed in comment 1 above, abiraterone is not a chemotherapy agent. A separate section should be written to account for this, to contain recommendations on abiraterone and potentially other new non-chemotherapy agents.	The paragraph on abiraterone has been moved from section 8.6 to section 8.5.2 which has been re-titled "Additional systemic treatments".
Janssen	4	Full	334	21	The recommendations from NICE TA101 on the use of docetaxel are spelled out in full, yet whilst abiraterone is mentioned as an alternative in section 8.6, the recommendations from NICE TA259 on the use of abiraterone after docetaxel failure are not outlined in the same way. We argue that this is imbalanced and suggest that the same level of detail should be given for	When the topic of a newly commissioned clinical guideline covers an area for which there are one or more previously published technology appraisals, the Guidelines Manual (2012) stipulates that there are four possible approaches to dealing with this: • The technology appraisal guidance is incorporated verbatim into the clinical guideline.

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					abiraterone as for docetaxel.	• The clinical guideline cross-refers to the technology appraisal guidance. • The technology appraisal guidance is updated through the relevant technology appraisal process. • The technology appraisal guidance is updated through the clinical guideline development process If technology appraisal guidance is incorporated into a clinical guideline, the technology appraisal will usually be placed on the static list. When the scope of the prostate guideline was created, the technology appraisal on abiraterone was in development. Consequently it was agreed that cross-referencing this technology appraisal would be the most appropriate approach to use.
Janssen	5	Full	General	n/a	Throughout the guideline, a range of new therapies which have received or are about to receive a marketing authorisation are either not mentioned because they are under a current NICE TA process (e.g. abiraterone in its post-ADT failure pre-chemotherapy indication, enzalutamide) or are not referred to at all for no stated reason (sipuleucel-T, radium-223). We are concerned about the justification for this, given that all such agents have strong phase III evidence supporting their licensing. We argue that the guideline cannot truly be considered current and evidence-based in the light of such omissions. The prostate cancer landscape is rapidly changing and the guideline should account for this as far as possible.	The NICE Guidelines Manual, 2012 states that "The GDG must not publish its own recommendations in a clinical guideline in areas already covered in the scope of any relevant ongoing technology appraisal. This also applies to areas covered in existing published technology appraisals unless NICE has agreed that the technology appraisal guidance will be updated in the clinical guideline (see section 8.1.3)." Since abiraterone, enzalutamide, sipuleucel-T and radium-223 dichoride are the subject of published and ongoing technology appraisals, we are not able to include any recommendations on these interventions in the guideline. However, a list of all of these technology appraisals has been included in section 3.2 of the NICE version of the guideline.
Janssen	6	Full	335	12	Corticosteroids are recommended for men with hormone-relapsed prostate cancer after androgen deprivation	The recommendations on corticosteroids were not updated during development of the guideline and so we are unable

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					therapy and anti-androgens on the basis of 'evidence from several case series'. As discussed in comment 5 above, new agents with data from large randomised controlled trials, a much stronger level of evidence than case series, are not recommended in the guidelines. We argue that this discrepancy is unjustifiable and compromises the guideline's evidence-based nature.	to make any changes
Janssen	10	Full	General	n/a	The identification of men with advanced prostate cancer whose disease is progressing is becoming an increasingly important issue given the range of new agents now available in this setting. For example, abiraterone is specifically licensed for patients who are 'asymptomatic or mildly symptomatic' in the post-ADT failure pre-chemotherapy setting. This could potentially be open to different interpretation by different clinicians. We suggest that the guideline could include some consideration of how such men with progressive disease could be identified, such as key symptoms which should be asked about, frequency of imaging, or clinical tools (e.g. the Brief Pain Inventory score) that could be used.	The Guidelines Manual, 2012 states that "The GDG must not publish its own recommendations in a clinical guideline in areas already covered in the scope of any relevant ongoing technology appraisal. This also applies to areas covered in existing published technology appraisals unless NICE has agreed that the technology appraisal guidance will be updated in the clinical guideline (see section 8.1.3)." Since abiraterone is the subject of both published and ongoing technology appraisals, we are not able to include any recommendations on this intervention in the guideline.
National Osteoporosis Society	2	Full	316	1	We are pleased to see the link from this guidance to CG146 'Osteoporosis: assessing the risk of fragility fracture' reinforcing the need for men undergoing ADT to have their fracture risk assessed. As ADT affects bone mineral density (BMD) we would like to stress that fracture risk assessment in these patients includes DXA assessment of BMD.	Thank you. Unfortunately we are not able to make changes to the wording of a recommendation made by another guideline.
National Osteoporosis Society	3	Full	316	1	In line with the language and recommendations in CG146 'Osteoporosis: assessing the risk of fragility fracture' we would like to see this recommendation refer to *men who are having androgen deprivation therapy and are at increased risk of fracture*	We believe that the current wording is already consistent with the wording of the recommendation in 'Osteoporosis: assessing the risk of fragility fracture'.
National Osteoporosis Society	4	Full	316	1	In line with the language and recommendations in CG146 'Osteoporosis: assessing the risk of fragility fracture' we would like to see this recommendation refer to *men who*	We believe that the current wording is already consistent with the wording of the recommendation in 'Osteoporosis: assessing the risk of fragility fracture'.

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					are having androgen deprivation therapy and are at increased risk of fracture if …	
National Osteoporosis Society	5	Full	317	1	We are pleased to see that there is recognition of the importance of further research into the clinical and cost-effectiveness of treating this group of patients with bisphosphonates and denosumab.	Thank you.
National Osteoporosis Society	1	NICE	General		The National Osteoporosis Society welcomes the update to the Prostate Cancer guideline and the inclusion of new recommendations relating to osteoporosis and fractures.	Thank you.
NCRI/RCP/ACP	1	Full	General		Overall, our experts found this to be a tremendous document. We would like to commend the team on a very thorough piece of work.	Thank you.
NCRI/RCP/ACP	2	Full	General		We believe that the guideline should include more on the role of PET, especially for imaging biochemically relapsed patients after radical treatment, potentially as a research priority.	The role of PET was not within the scope of this guideline. We are therefore unable make any new recommendations on this issue.
NCRI/RCP/ACP	3	Full	General		We believe that the guidelines should allude to the issue on fractionation for exterrnal beam radiotherapy, in two specific areas. Firstly, incorporating the potential for CHHiP to show non-inferiority with a 20# treatment schedule into their cost effectiveness modelling; secondly, the additional potential for extreme hypofractionation to show equivalence; this is also a research priority.	The role of radiotherapy fractionation was not within the scope of this guideline. We are therefore unable to make any new recommendations on this issue. In addition, it is not possible for an evidence based guideline to make recommendations based upon data that is not in the public domain.
NCRI/RCP/ACP	4	Full	33		We believe that the risk factors section (page 33) needs to be more comprehensively referenced for the genetic predisposition aspects. We recommend that the authors use Goh et al 2012. *Genetic variants associated with predisposition to prostate cancer and potential clinical implications. Goh CL, Schumacher FR, Easton D, Muir K, Henderson B, Kote-Jarai Z, Eeles RA. J Intern Med. 2012 Apr;271(4):353-65. doi: 10.1111/j.1365-2796.2012.02511.x. Erratum in: J Intern Med. 2013 May;273(5):527.*	We have made this change.
NHS Direct	1	Full			NHS Direct welcome the guideline and have no	Thank you.

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					comments as part of the consultation.	
NHS England	1	Full	121	1	PCA 3 is mentioned. This is not widely available in Trusts, is expensive and should be removed or put in as an option.	This recommendation was based on evidence that an elevated PCA3 score was associated with a statistically significant increased risk of prostate cancer in subsequent biopsies. However, the GDG acknowledge that no formal cost-effectiveness analysis has been conducted on the use of PCA3 tests. They have therefore deleted PCA3 from the recommendation and instead have made a recommendation for further research into the clinical and cost-effectiveness of this test in determining the need for prostate rebiopsy in men who have had a negative first biopsy and whose multiparametric MRI is normal. In addition, PCA3 has been referred to the NICE Diagnostics Assessment Programme for consideration for additional assessment.
NHS England	2	Full	221	16	Suggest early discharge at 12-18 mths into a Community Nurse led clinic within an integrated cancer system, as an option. This is more cost effective without detriment to quality.	The recommendations on follow-up were not updated during development of the guideline and so we are unable to make any changes.
NHS England	3	Full	305	5	There is no mention of penile rehabilitation which is widely practiced. This should read at least PDE5 prn and VCD daily, where nerve sparing is undertaken.	This is covered by the recommendation to ensure men have access to specialist erectile dysfunction services.
NHS England	4	Full	129	1	Not all centres have access to multi-parametric MRI. Despite the cost analysis the imaging is very timely. The paragraphs refer to risks outlined on P121. These risks fail to mention PSA dynamics and should not include PCA3, see comments above re P24.	This is an issue for implementation and will be highlighted to the Implementation Team at NICE. The recommendations were based on a critical appraisal of the available evidence and did not support making a recommendation on PSA dynamics. This recommendation was based on evidence that an elevated PCA3 score was associated with a statistically significant increased risk of prostate cancer in subsequent biopsies. However, the GDG acknowledge that no formal cost-effectiveness analysis has been conducted on the use of PCA3 tests. They have therefore deleted PCA3 from the

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						recommendation and instead have made a recommendation for further research into the clinical and cost-effectiveness of this test in determining the need for prostate rebiopsy in men who have had a negative first biopsy and whose multiparametric MRI is normal. In addition, PCA3 has been referred to the NICE Diagnostics Assessment Programme for consideration for additional assessment.
NHS England	5	Full	152	10	The GDG should consider evidence for multi-parametric MR or DWI MR and Template biopsies in pts being considered for Active Surveillance, it should also consider recommending this as an area for further research.	Multi-parametric MRI is recommended as part of the active surveillance protocol in the guideline. Our evidence review on active surveillance did not support making a specific recommendation on the use of template biopsy. The GDG felt it was not appropriate to recommend research into the most effective active surveillance protocol because there is currently no established control arm for such a trial. The ProtecT study is due to be published in 2016 and should provide some data for comparison.
NHS England	6	Full	221	16	Nurse led (CNS) Community Follow up after 12-18 mths is also reasonable. Especially within an integrated cancer system.	The recommendations on follow-up were not updated during development of the guideline and so we are unable to make any changes.
NHS England	7	Full	237	1-7	There is reasonable evidence – although not RCT, to offer salvage cryotherapy to intermediate and high risk patients, after radiotherapy.	The recommendations on salvage therapy were not updated during development of the guideline and so we are unable to make any changes.
NHS England	8	Full	General		The GDG have not mentioned anything within the guidance about patient and primary care education within the community, especially within high risk populations (African/West Indian/Family History). This falls within the NHS Framework Domains and should be included somewhere within the guidance..	The identification of men with suspected prostate cancer in the community is not within the scope of this guideline. It is covered by 'Referral guidelines for suspected cancer' (NICE clinical guideline 27) which is currently being updated.
NHS England	9	Full	General		It would be useful for the NICE guidance to have some format that aligns itself to the NHS Outcomes Framework Domains. This would allow the Clinicians/Trusts/Patients/Stakeholders to see how the NICE guidance can mirror future Quality Dashboards and	This is something that is not currently part of the NICE process – we will pass on your suggestion. We recognise the importance of clinical teams auditing their practice based on the guideline recommendations and these audits would cover all five domains of the NHS Outcomes

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					produce potential CQUINs. Unless this is felt not be within the remit of the NICE guidance	Framework.
NHS England	10	Full	General		There is little mention regarding the need for patient education after diagnosis, to help provide patients with autonomy and the potential for self care. This would align itself with the Outcomes Framework and NCSI.	Patient education after diagnosis was not within the scope of this guideline. We are therefore unable make any recommendations on this issue. Chapter 2 contains recommendations about communication and support, which apply through all stages of the pathway.
NHS England	11	Full	193	1	The guidance suggests that HIFU and Cryotherapy have limited evidence of effectiveness and should only be done within the context of trials. Does this cover Primary and Salvage Therapy? In addition the GDG need to clarify whether this guidance supersedes current NICE guidance on these interventions.	The recommendation on p214 covers these interventions as primary therapy. Salvage therapy is covered in chapter 5 and makes a recommendation for further research on the effect of local salvage therapies on survival and quality of life (see p259 line 7). We assume that you are referring to the NICE interventional procedure guidance on HIFU and cryotherapy. The NICE website clarifies that the IP guidance should be read in conjunction with the recommendations in this guideline.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	1	Full	129	1	**Key Priorities for Implementation** 1.2.7 Consider multiparametric MRI (using T2- and diffusion-weighted imaging) for men with a negative transrectal ultrasound 10–12 core biopsy to determine whether another biopsy is needed. [new 2014] ***Comments*** ***Agree in principle with this measure however, not current practice in Y&H SCN and it would have significant impact on the workload for MRI/radiology department***	This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network	2	Full	156	8	**Key Priorities for Implementation** 1.3.6 Consider using the protocol (see table 2) for men who have chosen active surveillance. [new 2014] ***Comments*** ***Agree in principle with this measures however, not***	This is an issue for implementation and will be highlighted to the Implementation Team at NICE.

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(joint response)					***current practice in Y&H SCN and it would have significant impact on the workload for MRI/radiology department. The pathway/protocol would need to be commissioned and fully funded*.**	
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	3	Full	211	8	**Key priorities for implementation** 1.3.31 Ensure that men with signs or symptoms of radiation-induced enteropathy are offered care from a team of professionals with expertise in radiation-induced enteropathy (who may include oncologists, gastroenterologists, bowel surgeons, dietitians and specialist nurses). [new 2014] ***Comments*** ***Not current practice across Y&H SCN. Would need a standard policy developing regarding the management of radiation induced complication.***	This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	4	Full	121	1	**Additional new/updated recommendations** 1.2.5 The results of all prostate biopsies should be reviewed by a urological cancer MDT. If a biopsy is negative, rebiopsy should be offered only after an MDT review of the man's risk factors. **[2008, amended 2014]** ***Comments*** ***Not standard policy to review all negative biopsies at MDT across the Y&H SCN*** ***Urology teams strongly disagree that all negative prostate biopsy need to be discussed at MDT. MDT is for discussion of proven cancer cases. If all suspected cancers were discussed then this would make MDT's unworkable. Only negative biopsies with risk factors (PIN/ASAP) should be considered for review.***	We have amended the wording of this recommendation to clarify that the discussion of risk factors with the man by a core member of the MDT is most important. The GDG agreed that the MDT would be responsible for designing protocols to ensure this happened, and supervising that it was done.
North Trent Cancer Network / Humber	5	Full	121	1	**Additional new/updated recommendations** 1.2.6 If the first biopsy is negative, advise the man that:	This recommendation was based on evidence that an elevated PCA3 score was associated with a statistically

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and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*					there is still a risk that prostate cancer is present **and** the risk is slightly higher if any of the following risk factors are present: prostate cancer antigen 3 (PCA3) is above 35 the biopsy showed high-grade prostatic intra-epithelial neoplasia the biopsy showed atypical small acinar proliferation (ASAP). **[new 2014]** ***Comments*** ***PCA3 test is not offered routinely in the Y&H SCN and there is no clear benefit to using this test.***	significant increased risk of prostate cancer in subsequent biopsies. However, the GDG acknowledge that no formal cost-effectiveness analysis has been conducted on the use of PCA3 tests. They have therefore deleted PCA3 from the recommendation and instead have made a recommendation for further research into the clinical and cost-effectiveness of this test in determining the need for prostate rebiopsy in men who have had a negative first biopsy and whose multiparametric MRI is normal. In addition, PCA3 has been referred to the NICE Diagnostics Assessment Programme for consideration for assessment.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	6	Full	129	1	**Additional new/updated recommendations** 1.2.8 Do not offer another biopsy if the multiparametric MRI (using T2- and diffusion-weighted imaging) is negative, unless any of the risk factors listed in recommendation 1.2.6 are present. **[new 2014]** ***Comments*** ***Agree in principle with this measures however, not current practice in Y&H SCN and it would have significant impact on the workload for MRI/radiology department, as well as the number of cases that need to be discussed at SMDT***	This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	7	Full	179	1	**Additional new/updated recommendations** 1.3.14 Commissioners should ensure that robotic systems for the surgical treatment of localised prostate cancer are based in centres that perform at least 150 radical prostatectomies per year. **[new 2014]** ***Comments*** ***Disagree with this recommendation and would rather have robust audit regarding outcome of surgery continually carried out, in order to drive up standards.***	There is already a national prostate cancer audit which should address this concern. Therefore we have not made

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					Not in agreement with a definitive number of prostatectomies mandated. ***Also concerns that inequitable access to radical prostatectomies across the UK would result if this recommendation was implemented***	any recommendations on audit in the guideline. The recommendation for basing robots in centres performing at least 150 radical prostatectomies per year was based on cost-effectiveness evidence which only considered use of the robot to perform radical prostatectomies. The recommendation has been amended and text added to the LETR section to clarify this. The GDG felt that the limitations in the evidence along with the overall uncertainty in this area prohibited them from strongly recommending robotic surgery. However, a 'consider' recommendation was deemed appropriate given the potential benefits that could be accrued from robotic surgery. The GDG consider that there is already inequity in access to robotic radical prostatectomies and believe that the recommendations in the guideline will help to resolve this inequity rather than exacerbate it.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	8	Full	293	5	**Additional new/updated recommendations** 1.5.3 Offer medroxyprogesterone8 (20 mg per day), initially for 10 weeks, to manage troublesome hot flushes caused by long-term androgen suppression and evaluate the effect at the end of the treatment period. **[new 2014]** ***Comments*** ***An anti-androgen (usually Cyproterone Acetate) is currently being used as the primary treatment for hot flushes across the Y&H SCN and we are unconvinced for reason to change.***	The clinical evidence only supported the use of cyproterone acetate if medroxyprogesterone is not effective or not tolerated. Consequently this is what the guideline has recommended.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer	9	Full	293	5	**Additional new/updated recommendations** 1.5.4 Consider cyproterone acetate or megestrol acetate9 (20 mg twice a day for 4 weeks) to treat troublesome hot flushes if medroxyprogesterone is not effective or not	The clinical evidence only supports the use of cyproterone acetate if medroxyprogesterone is not effective or not tolerated. Consequently this is what the guideline has recommended.

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Network / Yorkshire Cancer Network *(joint response)*					tolerated. [new 2014] ***Comments*** ***An anti-androgen (usually Cyproterone Acetate) is currently being used as the primary treatment for hot flushes across the Y&H SCN and we are unconvinced for reason to change.***	
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	10	Full	305	5	**Additional new/updated recommendations** 1.5.10 Offer PDE5 inhibitors to men having long-term androgen deprivation therapy who experience loss of erectile function. **[new 2014]** ***Comments*** ***Do not agree with this measure and should be deleted***	Although there was only one study supporting this recommendation, the GDG felt there was enough evidence to recommend the use of PDE5 inhibitors in men having long-term ADT.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	11	Full	218	12	**Additional new/updated recommendations** 1.5.11 If PDE5 inhibitors fail to restore erectile function or are contraindicated, offer a choice of: intraurethral inserts penile injections penile prostheses vacuum devices. **[new 2014]** ***Comments*** ***Across the Y&H SCN the Urology Teams refer men with erectile function problems to specialist erectile dysfunction clinics.***	The guideline has recommended that men have early and ongoing access to specialist erectile dysfunction clinics.
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	12	Full	316	1	**Additional new/updated recommendations** 1.5.13 Consider assessing fracture risk in men with prostate cancer who are having androgen deprivation therapy, in line with Osteoporosis fragility fracture (NICE clinical guideline 146). **[new 2014]** ***Comments*** ***Current practice is not to assess the risk for fractures.***	The recommendation on assessing fracture risk comes from 'Osteoporosis: assessing the risk of fragility fracture' (NICE clinical guideline 146). This also makes the following research recommendation "What is the utility of FRAX and QFracture in detecting risk of fragility fracture in adults with causes of secondary osteoporosis?"

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					The urology teams request further research and evidence nationally in order to help them identify the appropriate patients with risk factors for osteoporosis	
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	13	Full	316	1	**Additional new/updated recommendations** 1.5.14 Offer bisphosphonates to men who are having androgen deprivation therapy and have osteoporosis. **[new 2014]** ***Comments*** ***The urology teams request further research and evidence nationally in order to help them identify the appropriate patients who are at risk of osteoporosis.***	The recommendation on assessing fracture risk comes from 'Osteoporosis: assessing the risk of fragility fracture' (NICE clinical guideline 146). This also makes the following research recommendation "What is the utility of FRAX and QFracture in detecting risk of fragility fracture in adults with causes of secondary osteoporosis?"
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	14	Full	316	1	**Additional new/updated recommendations** 1.5.15 Consider denosumab for men who are having androgen deprivation therapy and have osteoporosis if bisphosphonates are contraindicated or not tolerated. **[new 2014]** ***Comments*** ***Not currently offered. More research is required in order to identify the appropriate patients who are at risk of osteoporosis.***	The recommendation on assessing fracture risk comes from 'Osteoporosis: assessing the risk of fragility fracture' (NICE clinical guideline 146). This also makes the following research recommendation "What is the utility of FRAX and QFracture in detecting risk of fragility fracture in adults with causes of secondary osteoporosis?"
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	15	Full	323	5	**Additional new/updated recommendations** 1.5.19 Offer men who are starting or having androgen deprivation therapy supervised resistance and aerobic exercise at least twice a week for 12 weeks to reduce fatigue and improve quality of life. **[new 2014]** ***Comments*** ***This is not currently being offered however it was thought to be a good recommendation. The CCG's would need to establish and fund the supervised exercise as a community based initiative***	This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
North Trent Cancer	16	Protocol	156	8	Year 1 of active surveillance.	The principal recommendation states "consider using the

Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*		for active surveillance			Tests: Every 3–4 months: measure PSA[2] Throughout active surveillance: monitor PSA kinetics[3] Every 6–12 months: DRE[4] At 12 months: prostate rebiopsy ***Comments*** ***DRE should be considered rather than stipulated at every 6-12 months***	following protocol". Accordingly, all the components within the active surveillance protocol are to be "considered" rather than "stipulated".
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	17	Protocol for active surveillance	156	8	Years 2–4 of active surveillance Tests: Every 3–6 months: measure PSA[2] Throughout active surveillance: monitor PSA kinetics[3] Every 6–12 months: DRE[4] ***Comments*** ***DRE should be considered rather than stipulated at every 6-12 months***	The principal recommendation states "consider using the following protocol". Accordingly, all the components within the active surveillance protocol are to be "considered" rather than "stipulated".
North Trent Cancer Network / Humber and Yorkshire Coast Cancer Network / Yorkshire Cancer Network *(joint response)*	18	Protocol for active surveillance	156	8	Year 5 and every year thereafter until active surveillance ends Tests: Every 6 months: measure PSA[2] Throughout active surveillance: monitor PSA kinetics[3] Every 12 months: DRE[4] ***Comments*** ***DRE should be considered rather than stipulated at every 12 months. If appropriate patients were referred into primary care after 5 years follow up in secondary care performing DRE would have resource implications, as training would need establishing.***	The principal recommendation states "consider using the following protocol". Accordingly, all the components within the active surveillance protocol are to be "considered" rather than "stipulated". The guideline identifies the need for training and competency in performing DRE. This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
PCaSO Prostate Cancer Network	1	Full	General		We are pleased to see the additions bringing, in general, more detail in greater clarity especially regarding side	Thank you.

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					effects of treatment.	
PCaSO Prostate Cancer Network	2	Full	116	12	As a patient-run patient support organisation with over 1000 members our groups have frequent presentations by senior clinicians in the prostate cancer field and our representatives meet them on various panels and committees. This year, 2013, PCaSO has heard regular and frequent references by these clinicians to the benefits of mpMRI scans before a biopsy to target the prostate. These are matched with caustic comments on the problems of viewing the prostate scans after an invasive biopsy. From the patient's point of view we strongly support moves to use mpMRI to target the prostate before a biopsy.	The combination of uncertainty over clinical protocols, the rapidly evolving clinical practice and the lack of robust cost-effectiveness results led the GDG to make no recommendations for clinical practice in this area. However the GDG noted that the ongoing PROMIS trial is investigating the optimal MRI and biopsy strategy and hopefully should provide additional evidence on this topic in future. Please see p132-133 for detailed information about the GDGs decision.
Prostate Cancer UK	16	Appendix G	409	21	We appreciate the fact that the guidelines no longer refer to 'castrate resistant', instead referring to 'hormone relapsed'. We know from our own research that men find the term castrate resistant distressing so this is a welcome amendment.	Thank you.
Prostate Cancer UK	1	Full	156	1	In our initial consultation response we called for several updates and reviews regarding treatment for prostate cancer. We are pleased the evidence for active surveillance has been reviewed and updated. We are particularly pleased to see a new protocol for men who have chosen active surveillance. It is an area which has previously been neglected, but as more men chose active surveillance over immediate treatment, it is right that they are given as much information as possible.	Thank you.
Prostate Cancer UK	2	Full	129	1	Whilst we are pleased there is a new emphasis on MRI, specifically multiparametric, we are aware that this is not currently widely available.	This is an issue for implementation and will be highlighted to the Implementation Team at NICE.
Prostate Cancer UK	3	Full	31		As survivorship increases it is all the more important to pay attention to the side effects of treatment as men will potentially be living with them for much longer. With this in mind we were hopeful of seeing a review about the side effects of treatment alongside further, more detailed	Thank you. We will consider a review of the side effects of treatment alongside more detailed advice for clinicians on accessing support needs of men with prostate cancer when the guideline is considered by NICE for update.

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					advice for clinicians on assessing support needs of men with prostate cancer. As such we welcome the updated protocol for managing a wide range of complications for treatment.	
Prostate Cancer UK	4	Full	69	9	We have reports that there is a lot of inconsistency in the NHS regarding the provision of template biopsies for men considering active surveillance. We know from our helpline that this is performed in some centres across the UK and not in others. We would welcome some clarification from NICE around whether this is recommended best practice or so we can ensure consistency across the UK.	This text is part of the needs assessment, conducted as part of the development of the guideline, to illustrate the variation in current practice. It does not make any recommendations. Our evidence review on active surveillance did not support making a specific recommendation on the use of template biopsy.
Prostate Cancer UK	5	Full	71	3	We welcome the update on the efficacy of different methods for performing radical prostatectomies.	Thank you.
Prostate Cancer UK	6	Full	99	1	We believe it was an error not to review the section of the guidelines on communication, support and follow up care. We would urge NICE to reconsider. As more men are diagnosed with prostate cancer the issue of follow up care becomes increasingly important. There are a wide range of factors to take into consideration and it is vital that clinicians feel able to given men all of the relevant information. Prostate Cancer UK have produced a Quality Checklist which details the standards of care men can expect to receive from diagnosis through to end of life care. **(http://prostatecanceruk.org/get-involved/campaign/our-campaigns/quality-care-everywhere).** Our checklist aims to ensure that, amongst other things, all men have a written care plan, regular check-ups to monitor side effects and referral into specialist services to help manage adverse side effects.	The recommendations on communication and support and follow up were not updated during development of the guideline and so we are unable to make any changes. The proposal not to update these sections was subject to consultation with stakeholders during development of the guideline scope. We will pass on the information about your Quality Checklist to the NICE implementation team.
Prostate Cancer UK	7	Full	121	1	We would like to note that, as we understand, currently PCA3 testing is only available privately and only a few	This recommendation was based on evidence that an elevated PCA3 score was associated with a statistically

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					labs in the UK are able to offer the test.	significant increased risk of prostate cancer in subsequent biopsies. However, the GDG acknowledge that no formal cost-effectiveness analysis has been conducted on the use of PCA3 tests. They have therefore deleted PCA3 from the recommendation and instead have made a recommendation for further research into the clinical and cost-effectiveness of this test in determining the need for prostate rebiopsy in men who have had a negative first biopsy and whose multiparametric MRI is normal. In addition, PCA3 has been referred to the NICE Diagnostics Assessment Programme for consideration for additional assessment.
Prostate Cancer UK	8	Full	140	9	We note there is a reference to PET in diagnosing localised prostate cancer but not for recurrence. We believe, and evidence from the European Association of Urology supports this, that PET is more useful in spotting recurrence rather than diagnosing. We would welcome clarification of whether NICE has reviewed this evidence in making the recommendation. (**Guidelines on Prostate Cancer, European Association of Urology, A. Heidenreich (chair) et al, P116)**	The role of PET was not within the scope of this guideline. We are therefore unable make any new recommendations on this issue.
Prostate Cancer UK	9	Full	181	29	We are pleased the evidence for the use of brachytherapy in combination with external beam radiotherapy has been reviewed and updated.	Thank you.
Prostate Cancer UK	10	Full	192	2	We would encourage a review of the guidance for high intensity focused ultrasound (HIFU) as new evidence on long term survival becomes available.	This could be considered when the guidelines are next reviewed.
Prostate Cancer UK	11	Full	194	2	Whilst we are pleased to see a review of side effects following hormone therapy and rectal problems after radiotherapy, we are disappointed that the updated guidelines do not offer a review of side effects following other treatments, such as surgery. As a number of different types of surgery are now used, for example, robotic surgery, we feel there has been a missed opportunity to document and review the side effects	Side effects of other forms of radical treatment were not within the scope of this guideline. We are therefore unable make any recommendations on these issues. However as part of the evidence review on radical prostatectomy we have reported details of treatment related morbidity, incontinence, erectile dysfunction and health related quality of life following surgery (see p180-1).

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					related with each of these options.	
Prostate Cancer UK	12	Full	256	29	We would welcome clarity over whether there is sufficient evidence of the efficacy of three years of androgen deprivation therapy (ADT) for men with high risk localised prostate cancer, compared to ADT over two years.	We have amended the recommendation to clarify the uncertainty about the optimal duration of long-term ADT.
Prostate Cancer UK	13	Full	263	28	The draft guidance does not refer to the SWOG-9346 trial, which indicated that survival outcomes may not be as positive for intermittent androgen deprivation therapy as for continuous for patients with metastatic prostate cancer. We would welcome clarification of whether this trial was considered.	The SWOG 9413 trial is already included in the evidence review (Hussain et al, 2013).
Prostate Cancer UK	14	Full	307	22	We are pleased the evidence for bisphonates has been reviewed and updated.	Thank you.
Prostate Cancer UK	15	Full	318	11	We are pleased to see exercise offered to reduce fatigue for men on androgen deprivation therapy. This compliments a programme we are already running '*Get back on track'* run by our specialist nurses aimed at helping men with experience of prostate cancer to improve fatigue symptoms. For more information please visit http://prostatecanceruk.org/we-can-help/help-with-fatigue	Thank you .
Prostate Cancer UK	17	Full	147	31	We are concerned that there is no protocol for watchful waiting in the same way that there is for active surveillance. We appreciate the updated definition but feel this does not go far enough. It would be useful to have a protocol in place which includes recommendations on when men should be taken off of watchful waiting.	A protocol for watchful waiting was not within the scope of this guideline. We are therefore unable make any recommendations on this issue.
Prostate Cancer UK	18	General			We are disappointed that there is no recommendation for clinicians to be kept up to date with technology appraisals or trials on treatments for prostate cancer. With new drugs coming to the market at an increased rate, and the end of the cancer drugs fund, it is essential that clinicians are aware of what is available so they can ensure men with prostate cancer can make an informed choice. We would	We believe that keeping up to date with technology appraisals and recent clinical trials would be a requirement of clinical appraisal and revalidation. NICE also send out regular bulletins and all updated guidance can be accessed on the NICE website. As such we do not think it is necessary for a guideline to recommend this.

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					urge NICE to reconsider.	
Royal College of Nursing	1				This is just to let you know that the feedback I have received from nurses working in this area of health suggest that there is no additional comments to submit to inform on the consultation of the above draft guidelines.	Thank you.
Royal College of Pathologists	1				I am just writing to inform you that the Royal College of Pathologists does not have any comments to make on this guideline at this stage.	Thank you.
Royal College of Radiologists	1	Full	129	1	The RCR welcome the conclusion that there are likely benefits from the wider use of mpMRI. We recognise the current limited clinical evidence and note the strong assumptions made in the analysis. We support the recommendations to consider mpMRI in the range of clinical scenarios as stated and remain committed to continuing to gather robust clinical evidence to guide future updates.	Thank you.
Royal College of Surgeons of Edinburgh	1	Full	156	8	The Royal College of Surgeons of Edinburgh believes that the NICE guideline on prostate cancer is well-written and balanced. The College has some concerns about the role of mpMRI pre-biopsy with TRUS, however, it appears like the authors have assessed the evidence very well and their recommendations seem appropriate. The only significant question mark from the College, relates to the justification for a baseline MRI scan in all patients entering active surveillance. There lacks evidence that this is indeed cost effective or worthwhile.	Thank you. Thank you. The GDG used a Delphi consensus method to develop the recommendations on an active surveillance protocol (see p168, lines 24-36). Most men undergoing staging for localised prostate cancer will now have an MRI and this recommendation ensures that those who have not will have a baseline scan done for future comparison purposes.
Royal College of Surgeons of Edinburgh	2	Full	221	16	Is it really necessary to maintain hospital follow-up for two years?	The recommendations on follow-up were not updated during development of the guideline and so we are unable to make any changes.
Royal College of	3	Full	179	1	Is the basis for >150 RARP economic?	The recommendation for basing robots in centres

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Surgeons of Edinburgh						performing at least 150 radical prostatectomies per year was based on cost-effectiveness evidence which only considered use of the robot to perform radical prostatectomies. Text has been added to the LETR section to clarify this.
Royal College of Surgeons of Edinburgh	4	Full	39	4	The guideline states: "The British Association of Urological Surgeons (BAUS) collects information on the stage at diagnosis through the newly diagnosed registry of urological cancers. However, reporting is voluntary and has decreased substantially in recent years (British Association of Urological Surgeons 2012). The proportion of diagnoses reported through this registry whose stage is unknown has also increased from 19% in 1999 to 48% in 2010." As reporting is voluntary and has decreased substantially in recent years, has the BAUS cancer registry been discontinued?	The BAUS cancer registry has been discontinued. We have amended the text to clarify this.
Royal College of Surgeons of Edinburgh	5	Full	93	39 - 42	The reference from the British Association or Urological Surgeons needs to be revised.	We have made this change.
Royal College of Surgeons of Edinburgh	6	Full	94	24 - 27	The reference from the European Association of Urology needs be revised.	We have made this change.
Royal College of Surgeons of Edinburgh	7	Full	156	8	In relation to the recommendation to consider mp-MRI at enrolment in AS programme, the College does not see any evidence that supports this recommendation in the section on imaging on prostate cancer, nor even in the section describing the Delphi process that looked for consensus on AS protocols. It seems to the College from the evidence on MRI, that its use could be considered during AS (as recommended) to provide additional reassurance/information rather than being a pre-requisite.	The GDG used a Delphi consensus method to develop the recommendations on an active surveillance protocol (see p168, lines 24-36). Most men undergoing staging for localised prostate cancer will now have an MRI and this recommendation ensures that those who have not will have a baseline scan done for future comparison purposes.

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Royal College of Surgeons of Edinburgh	8	Full	263		In relation to hormone deprivation, there appears to be no mention of LHRH antagonists as a means of androgen deprivation, which should be included.	LHRH antagonists were not investigated by this guideline. We are therefore unable make any recommendations on this issue or include them in the algorithm. Degarelix is currently the subject of an ongoing technology appraisal.
Royal College of Surgeons of Edinburgh	9	Full	264	36	The letter 'n' is missing in the word 'intermittent'.	We have made this change.
Royal Surrey County Hospital NHS Trust	1	Full	93	22	There was confusion in the last NICE Guidance on Prostate Cancer regarding the position of HIFU and the nature of the study that patients should be enrolled into, should they be treated by this modality. Such studies should have ethical approval and standard financial and clinical governance as required by GCP. Patients should undergo informed consent that they are participating in a clinical study. It is not acceptable for patients to merely be enrolled in a treatment registry.	Thank you for this information. The recommendations regarding the use of HIFU were not updated during development of the guideline and have not been changed. The guideline does not contain any specific recommendations on clinical trials involving HIFU.
Sanofi	1	Full	92	26	Our comments are as follows, Mitoxantrone is referred as being the "previous gold standard" treatment of hormone relapse prostate cancer (HRPC). However, mitoxantrone was never licenced for this indication by the European Medicines Agency (EMA) in the EU or by the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK.	The GDG recognised that although not licenced for this use, mitoxantrone was the standard treatment for hormone relapsed prostate cancer. However, they did delete the term "gold" in recognition of the stakeholder comments.
Sanofi	2	Full	92	27	Our comments are as follows, Cabazitaxel was also licensed by the EMA.	We have clarified this in the text.
Sanofi	3	Full	92	31	Our comments are as follows, The results of FIRSTANA, comparing docetaxel with cabazitaxel, will be published in 2015.	We have made this change.
Sanofi	4	Full	409	21	Our comments are as follows, The definition of "hormone relapsed" prostate cancer appears to be ambiguous. HRPC is replacing what was	Patient/carer groups appreciate the fact that the guidelines no longer refer to "castrate resistant", but instead refer to "hormone relapsed" prostate cancer.

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					known as castrate resistant, hormone resistant and hormone refractory. However, castrate resistant metastatic prostate cancer may still be the most clinically accurate terminology for this sub-group of patients.	
Society and College of Radiographers	5		317		The GDG considered that the clinical benefits and cost-effectiveness of using bisphosphonates in men with osteoporosis may have been underestimated because the study didn't take into account all types of fractures and limited itself to hip fractures. In addition the calculation of reference costing may have been greater than that applicable in the UK. The GDG therefore agreed to recommend the use of bisphosphonates for treating osteoporosis resulting from long term androgen deprivation. - **This recommendation is welcomed and considering that hip fractures have a high mortality and morbidity rate in men any intervention that will potentially reduce the risk of a fragility fracture and in particular hip and vertebral fractures is completely rationalised.**	Thank you..
Society and College of Radiographers	1	Full	306	2	Osteoporosis is common in the ageing man and may be present in men about to commence 2 androgen deprivation therapy. – **It should not be assumed that osteoporosis in men is a normal ageing process. Males with osteoporosis are more likely to have a secondary cause which must be investigated compared to females.**	Thank you for this information, we agree.
Society and College of Radiographers	2	Full	306	4	calcium plus vitamin D - **Supplementation needs to be added for clarification because this phrase could refer purely to dietary requirement**	We have made this change.
Society and College of Radiographers	3	Full	316		Offer bisphosphonates to men who are having androgen deprivation therapy and have osteoporosis. [new 2014] **- I would completely welcome this new addition – for so long men have been almost overlooked when it comes to treatment options and osteoporosis. There are more treatment options available for women with**	Thank you.

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					osteoporosis and few for males and so this new recommendation is certainly welcomes. **However I would suggest that more work is progressed into developing an osteoporosis treatment guidance document for male with ADT induced osteoporosis as is the case with females and breast cancer treatment induced bone loss. Such guidance provides the clinician with a fair and definitive treatment guidance that can be used for every patient.**	The guideline has made a research recommendation in this area on p339 line 1.
Society and College of Radiographers	4	Full	316		Due to the lack of evidence on the use of calcium and vitamin D to treat osteoporosis resulting from long term androgen deprivation, the GDG were not able to make any recommendations on these interventions. – **This should be assessed on a clinical basis and the patients vitamin D status should be assessed and if the patient is clinically deficient then supplementation should be considered**	The topic looked at the management of osteoporosis resulting from long term ADT, not specifically the management of vitamin D deficiency so we are unable to make recommendations on this.
The Lesbian & Gay Foundation	1	Full	100	14	Add sexual orientation and gender identity to the list of individual factors which may communication preferences and needs.	We have made this change.
The Lesbian & Gay Foundation	2	Full	100	N/A	General comment re. communication. We agree that communication should be tailored to an individual patient's needs. This should include a recognition of the specific issues facing gay and bisexual and men and trans women. Gay and bisexual men may find that their needs are not considered in provision of support (including peer and partner support groups) which are often centred on heterosexual people's experiences. LGB&T groups, including the only peer support group for gay and bisexual men affected by prostate cancer (Out with Prostate Cancer http://www.lgf.org.uk/news-articles/out-with-prostate-cancer/) should be consulted about the best engagement methods with this group.	We have amended the text to clarify that sexual orientation and gender identity may have an effect on communication needs and preferences.

Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
					Many trans women (i.e. women who have undergone a process to change their gender from male to female) will still have a prostate, and so will still be at risk of prostate cancer. The particular needs and sensitivities of this group with regard to screening and potential diagnosis, needs to be considered.	
The Lesbian & Gay Foundation	3	Full	101	N/A	Decision aids should take account of the needs of gay and bisexual men and trans women, and use inclusive language.	The development of decision aids is not within our control. However the text on p116, line 22 clarifies that decision aids should provide specific, individualised information, which we believe should cover this issue.
The Lesbian & Gay Foundation	4	Full	102	15	Consideration must be given to the impact of prostate cancer on gay and bisexual men's sense of masculinity, and with reference to above, to trans women's sense of femininity and relationship to their own gender identity history.	We have amended line 15 on p118 to include this.

Stakeholders who did not comment:

AAH Pharmaceuticals
Abbott GmbH & Co KG
AbbVie
Abertawe Bro Morgannwg University Health Board
Advanced Medical Diagnostics
Afiya Trust
African Health Policy Network
Age UK
Aintree University Hospital NHS Foundation Trust
Airedale NHS Trust
Albyn Medical Ltd
Allocate Software PLC
Almac Diagnostics
American Medical Systems Inc.
Amgen UK

Aneurin Bevan Health Board
APOGEPHA Arzneimittel GmbH
Archimedes Pharma Ltd
Arden Cancer Network
Arthritis Research UK
Ashford and St Peter's Hospitals NHS Trust
Association for Continence Advice
Association for Family Therapy and Systemic Practice in the UK
Association of Anaesthetists of Great Britain and Ireland
B. Braun Medical Ltd
Bard Limited
Baxter Healthcare
Bedfordshire Primary Care Trust
Betsi Cadwaladr University Health Board
beulah charity trust
Birmingham & Brunel Consortium
BME cancer.communities
Boehringer Ingelheim
Boots
Bostwick Laboratories
Bradford District Care Trust
Breast Cancer UK
Bristol and Avon Chinese Women's Group
Bristol Cancer Help Centre
Bristol-Myers Squibb Pharmaceuticals Ltd
British Association for Cytopathology
British Association of Art Therapists
British Association of Urological Nurses
British Dietetic Association
British Geriatrics Society
British Medical Association
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Nuclear Medicine Society

British Pain Society
British Prostate Group
British Society for Immunology
British Society of Interventional Radiology
BUPA Foundation
Calderdale Primary Care Trust
Calderstones Partnerships NHS Foundation Trust
Cambridge University Hospitals NHS Foundation Trust
Camden Link
Cancer Black Care
Cancer Commissioning Team
Cancer Network Pharmacists Forum
Cancer Network User Partnership
Cancer Phytotherapy Service
Cancer Research UK
Cancer Services Co-ordinating Group
Cancer Voices
Capsulation PPS
Care Quality Commission (CQC)
Cariad Technologies Ltd
Celgene UK Ltd
Central & North West London NHS Foundation Trust
Central South Coast Cancer Network
Chartered Society of Physiotherapy
CHKS Ltd
Clarity Informatics Ltd
Clatterbridge Cancer Centre
CLIC Sargent
Cochrane Bone, Joint and Muscle Trauma Group
College of Occupational Therapists
Community District Nurses Association
Countess of Chester Hospital NHS Foundation Trust
Covidien Ltd.
Croydon Clinical Commissioning Group
Croydon Health Services NHS Trust

Croydon University Hospital
Dako UK Ltd
David Lewis Centre, The
Deltex Medical
Dendreon
Department of Health, Social Services and Public Safety - Northern Ireland
Derby-Burton Cancer Network
Device Access UK Ltd
Prostate Action
Commission for Social Care Inspection
Dorset Primary Care Trust
Dudley Primary Care Trust
Durham University
East and North Hertfordshire NHS Trust
East Kent Hospitals University NHS Foundation Trust
East Midlands Cancer Network
EDAP SA
Endocare, Inc.
Equalities National Council
Essex Cancer Network
Ethical Medicines Industry Group
Faculty of Public Health
FBA and Brook
Five Boroughs Partnership NHS Trust
Fresenius Kabi Ltd
General Practice and Primary Care
George Eliot Hospital NHS Trust
GlaxoSmithKline
Gloucestershire Hospitals NHS Foundation Trust
Gloucestershire LINk
Great Western Hospitals NHS Foundation Trust
Greater Manchester and Cheshire Cancer Network
Greater Manchester, Lancashire, South Cumbria Strategic Clinical Network
Greater Midlands Cancer Network
Grunenthal Ltd

Guerbet Laboratories Ltd
Guildford & Waverley Primary Care Trust
Hammersmith and Fulham Primary Care Trust
Hayward Medical Communications
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Help the Hospices
Herts Valleys Clinical Commissioning Group
Hockley Medical Practice
Hull and East Yorkshire Hospitals NHS Trust
Humber NHS Foundation Trust
Imaging Equipment Ltd
Independent Healthcare Advisory Services
Institute of Biomedical Science
Integrity Care Services Ltd.
Intra-Tech Healthcare Ltd
iQudos
Isabel Hospice
James Whale Fund for Kidney Cancer
JBOL Ltd
Johnson & Johnson
KCARE
KCI Medical Ltd
Kettering General Hospital
Kidney Research UK
King George Hospital
King's College Hospital NHS Foundation Trust
Lancashire Care NHS Foundation Trust
Latex Allergy Support Group
Leeds Primary Care Trust (aka NHS Leeds)
Leeds Teaching Hospitals NHS Trust
Leicestershire County and Rutland Primary Care Trust
Leicestershire, Northamptonshire and Rutland Cancer Network
Leo Pharma
Lesbian, gay, bisexual and trans domestic abuse forum

Link Pharmaceuticals
Livability Icanho
London Cancer
Luton and Dunstable Hospital NHS Trust
Macmillan Cancer Support
Maidstone and Tunbridge Wells NHS Trust
Medicines and Healthcare products Regulatory Agency
Medway NHS Foundation Trust
Men's Health Forum
Merck Sharp & Dohme UK Ltd
Mid Cheshire Hospitals NHS Trust
Mid Yorkshire Hospitals NHS Trust
Milton Keynes NHS Foundation
Ministry of Defence (MOD)
National Association of Primary Care
National Cancer Action Team
National Cancer Intelligence Network
National Cancer Network Clinical Directors Group
National Cancer Research Institute
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Council for Palliative Care
National Institute for Health Research Health Technology Assessment Programme
National Kidney Research Foundation
National Patient Safety Agency
National Public Health Service for Wales
National Radiotherapy Implementation Group
Newcastle upon Tyne Hospitals NHS Foundation Trust
NHS Barnsley Clinical Commissioning Group
NHS Bath & North East Somerset
NHS Bournemouth and Poole
NHS Bromley
NHS Connecting for Health

NHS Cornwall and Isles Of Scilly
NHS County Durham and Darlington
NHS Cumbria Clinical Commissioning Group
NHS Derbyshire county
NHS Improvement
NHS Kirklees
NHS London
NHS Lothian
NHS Medway Clinical Commissioning Group
NHS National Cancer Screening Programmes
NHS Plus
NHS South Cheshire CCG
NHS Wakefield CCG
NHS Warwickshire North CCG
NHS Warwickshire Primary Care Trust
NHS West Kent
Nordic Pharma
Norfolk & Waveney Prostate Cancer Support
North and East London Commissioning Support Unit
North East London Cancer Network
North of England Cancer Network
North of England Commissioning Support
North Yorkshire & York Primary Care Trust
Northern Ireland Cancer Network
Nottingham City Council
Nottingham City Hospital
Nottinghamshire Healthcare NHS Trust
Nova Healthcare
Novartis Pharmaceuticals
NS Technomed
Nucletron
Numares Group
Nutrition Society
Oncura Ltd
Orion Pharma

Ovarian Cancer Action
Oxford Health NHS Foundation Trust
Oxford Nutrition Ltd
Oxfordshire Clinical Commissioning Group
Oxfordshire Primary Care Trust
Pan Birmingham Cancer Network
Parenteral and Enteral Nutrition Group
Peninsula Cancer Network
PERIGON Healthcare Ltd
Pfizer
pH Associates Ltd
Pharmametrics GmbH
Pharmion Limited
PHE Alcohol and Drugs, Health & Wellbeing Directorate
Pilgrims Hospices in East Kent
Primary Care Pharmacists Association
Primrose Bank Medical Centre
Prostate Brachytherapy Advisory Group
Public Health Wales NHS Trust
Queen Elizabeth Hospital King's Lynn NHS Trust
Rarer Cancers Foundation
Roche Diagnostics
Roche Products
Rotherham Primary Care Trust
Royal Berkshire NHS Foundation Trust
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners in Wales
Royal College of Midwives
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition
Royal College of Physicians and Surgeons of Glasgow
Royal College of Psychiatrists

Royal College of Surgeons of England
Royal Pharmaceutical Society
Royal Society of Medicine
Royal United Hospital Bath NHS Trust
Royal West Sussex NHS Trust
Sandoz Ltd
Sandwell Primary Care Trust
Schering Health Care Ltd
Scottish Intercollegiate Guidelines Network
Serono
Sexual Advice Association
Sheffield Primary Care Trust
Sheffield Teaching Hospitals NHS Foundation Trust
Shropshire & Mid Wales Cancer Forum
Siemens Medical Solutions Diagnostics
SNDRi
Social Care Institute for Excellence
South London & Maudsley NHS Trust
South Staffordshire Primary Care Trust
South Wales Cancer Network
South West Yorkshire Partnership NHS Foundation Trust
Speciality European Pharma
St Mary's Hospital
St Michaels Hospice
Staffordshire and Stoke on Trent Partnership NHS Trust
Step4Ward Adult Mental Health
Stockport Clinical Commissioning Group
Sue Ryder
Surrey, West Sussex and Hampshire Cancer Network
Sussex Cancer Network
Sutton1in4 Network
Takeda UK Ltd
Tameside Hospital NHS Foundation Trust
Taunton Road Medical Centre
Teva UK

Thames Valley Cancer Network
The Association for Cancer Surgery
The Association for Clinical Biochemistry & Laboratory Medicine
The Association of the British Pharmaceutical Industry
The British In Vitro Diagnostics Association
The Institute of Cancer Research
The National Association of Assistants in Surgical Practice
The National LGB&T Partnership
The Princess Alexandra Hospital NHS Trust
The Prostate Cancer Support Federation
The Rotherham NHS Foundation Trust
The Stefanou Foundation
Torbay and Southern Devon Health and Care NHS Trus
Translucency Ltd.
UCL Partners
UK Anaemia
UK National Screening Committee
UK Specialised Services Public Health Network
UKHIFU Limited
United Kingdom Council for Psychotherapy
United Kingdom National External Quality Assessment Service
United Lincolnshire Hospitals NHS
University College London Hospital NHS Foundation Trust
University Hospital Aintree
University Hospital Birmingham NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
University Hospitals Birmingham
University Hospitals Coventry and Warwickshire NHS Trust
University of Nottingham
Velindre Hospital, Cardiff
Velindre NHS Trust
Walsall Teaching Primary Care Trust
Welsh Cancer Services Coordinating Group
Welsh Government
Wessex Cancer Trust

West Midlands Ambulance Service NHS Trust
Western Cheshire Primary Care Trust
Western Sussex Hospitals NHS Trust
Westminster Local Involvement Network
Whipps Cross University Hospital NHS Trust
Wigan Borough Clinical Commissioning Group
Wiltshire Primary Care Trust
World Cancer Research Fund
York Hospitals NHS Foundation Trust
Yorkshire & The Humber Specialised Commissioning Group