National Institute for Health and Clinical Excellence

Prostate Cancer
Scope Consultation Table
28.11.11 – 16.12.11

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	UKHIFU	1.00	3.3.2 (f)	Re: High Intensity Focused Ultrasound. There is now a substantial amount of data to support the use of HIFU as a treatment option for appropriately selected patients. This data is taken from 1). The UK Sonablate HIFU Registry of 1417 patients 2004 – 2011. 2). Peer reviewed publications. 3). Registry Data from geographic locations other than UK. 4). New significant FDA HIFU Trials data.	The high level RCT search conducted as part of the initial review process did not identify anyhigh-quality, comparative data that would result in a change to the current guideline recommendations.Therefore we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	Novartis Pharmaceuticals	2.00	3.3.2 point j	We note that Bisphosphonates in the treatment of Prostate Cancer is not part of the current draft scope and NICE will be replicating the advice in CG58 within the new Prostate Cancer guidelines. We would like NICE to reconsider this decision as there have been a number of recommendations made in various guidelines since 2008 by the British Uro-Oncology Group (BUG), British Association of Urological Surgeons (BAUS):Section of Oncology,and British Prostate Group (BPG).[1] Guidance was also updated in 2011 by the European Association of Urology (EAU) in the most recentProstate Cancer Guidelines.[2]	We are aware of ongoing trials in this area but these are unlikely to publish during the timeframe of this update. Since we are not aware of any recently published high-quality, comparative data that would result in a change to the current recommendations we do not propose to update this topic.Recommendations from CG58 will be duplicated in the update to this guideline.

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SH	Novartis Pharmaceuticals	2.01	3.3.2 point j- Evidence 1	**Evidence for Bisphosphonates to be part of the scope** The MDT (Multi-disciplinary Team) Guidance for Managing Prostate Cancer 2nd Edition (November 2009) produced by British Uro-Oncology Group (BUG), British Association of Urological Surgeons (BAUS):Section of Oncology,and British Prostate Group (BPG) states:[1] Those patients who do not respond to hormone therapy are considered to have hormone-refractory prostate cancer (HRPC; i.e. unresponsive to all hormone therapies) or castrate-refractory prostate cancer (unresponsive to treatment with LHRH agonists) and are candidates for chemotherapy, novel therapies and/or symptomatic local treatments. The benefits of zoledronic acid, in combination with hormone therapy have been investigated in a study by Saad in men with HRPC and bone metastases.[3,4]This was a multicentre, randomised, placebo-controlled trial evaluating the efficacy of zoledronic acid 4 mg administered every 3 weeks in 422 patients with HRPC for 15 months, with an option to continue for an additional 9 months. • At the 2-year analysis, treatment with zoledronic acid was found to significantly reduce the percentage of patients with at least one skeletal-related event (SRE; defined as radiation for bone pain or to prevent pathological fracture/spinal cord compression; pathological fracture; spinal cord compression; surgery to bone; change in antineoplastic therapy) compared with placebo (38% versus 49%; p=0.028). All SREs were delayed. • Zoledronic acid also significantly delayed the time to first SRE by around 6 months (median 488 versus 321 days; p=0.009). Furthermore, patients in the zoledronic acid group had consistently lower incidences of all types of SRE than the placebo	The data you cite was already considered in the 2008 guideline. We are aware of ongoing trials in this area but these are unlikely to publish during the timeframe of this update. Since we are not aware of any recently published high-quality, comparative data that would result in a change to the current recommendations we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.

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				group. • Pain scores were consistently lower in patients taking zoledronic acid 4mg than placebo, and significantly at 3, 9, 18, 21 and 24 months ($p<0.05$).	
SH	Novartis Pharmaceuticals	2.02	3.3.2 point j- Evidence 2	**Evidence for Bisphosphonates to be part of the scope** The European Association of Urology (EAU) Prostate cancer Guideline 2011states:[2] Recently, bisphosphonates have been used to inhibit osteoclast-mediated bone resorption and osteoclast precursors in HRPC to provide effective treatment of skeletal complications and to reduce pain or provide total pain relief. In the largest single phase III trial,[3,4]. 643 patients who had HRPC with bone metastases were randomised to receive zoledronic acid, 8 mg or 4 mg every 3 weeks for 15 consecutive months, or placebo. • At 15 and 24 months of follow-up, patients treated with only 4 mg of zoledronic acid had fewer skeletal-related events compared to the placebo group (44% vs 33%, p = 0.021) and fewer pathological fractures (13.1% vs 22.1%, p = 0.015). • Furthermore, the time to first skeletal-related event was longer in the zoledronate group, so improving QoL. • Patients were initially randomised to 4 or 8 mg of zoledronic acid, but the 8 mg dosage was later modified to 4 mg because of toxicity. Currently, bisphosphonates can be proposed to patients with HRPC bone	We are aware of ongoing trials in this area but these are unlikely to publish during the timeframe of this update. Since we are not aware of any recently published high-quality, comparative data that would result in a change to the current recommendations we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.

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				metastases to prevent skeletal complications, even if the best dosing interval is unclear. At present, it is every 3 weeks or less. Pain due to osseous metastases is one of the most debilitating complications of HRPC:[5,6] • Bisphosphonates have been highly effective with a response rate of 70-80% in small, open trials, which, associated with a low frequency of side-effects, makes bisphosphonates an ideal medication for palliative therapy of advanced HRPC. • Bisphosphonates should be considered early in the management of symptomatic HRPC. • Critical issues of palliation must be addressed when considering additional systemic treatment, including management of pain,constipation, anorexia, nausea, fatigue and depression, which often occur (i.e. palliative external beam radiation, cortisone, analgesics and anti-emetics).	
SH	Novartis Pharmaceuticals	2.03	3.3.2 point j- References	<u>References</u> 1. MDT (Multi- disciplinary Team) Guidance for Managing Prostate Cancer 2nd Edition (November 2009) produced by British Uro-Oncology Group (BUG), British Association of Urological Surgeons (BAUS):Section of Oncology, and British Prostate Group (BPG) 2. Guidelines on Prostate Cancer, European Association of Urology,2011 3. Saad F, Gleason DM, Murray R, et al. A randomized, placebo-controlled trial of zoledronic acid in patients with hormone-refractory metastatic prostate carcinoma. J Natl Cancer Inst 2002;	Thank you for this information.

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				94:1458−1468. 4. Saad F,Gleason DM, Murray R et al. Long-Term efficacy of zoledronic acid for the prevention of skeletal complications in patients with metastatic hormone- refractory prostate cancer. J Natl cancer Inst 2004; 96:879-882 5. Heidenreich A, Hofmann R, Engelmann. UH The use of bisphosphonate for the palliative treatment of painful bone metastasis due to hormone refractory prostate cancer. J Urol 2001 Jan;165(1):136-40. 6. Heidenreich A, Elert A, Hofmann R. Ibandronate in the treatment of prostate cancer associated painful osseous metastases. Prostate Cancer Prostatic Dis 2002;5(3):231-5.	
SH	PCaSO Prostate Cancer Network	3.00	General	It is a shame that this document just deals with the here and now at a tactical level. The next guidelines from a NICE type organisation will be in 2016 therefore it would have been appropriate to detail a strategy for significantly reducing the deaths from prostate cancer and one way of undertaking this would have been from reviewing risk stratification. Earlier diagnosis would not only save lives it would save NHS money.	We believe that the implementation of this guideline will result in fewer men dying from prostate cancer.
SH	PCaSO Prostate Cancer Network	3.01	2.1..c	The following should be added to the sentence 'and also men with a familial history of the disease	Whilst we accept that this is factually correct the identification and management of men with suspected prostate cancer presenting to their general practitioner will be considered as part of the update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be

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					published in 2014. However, we will ask the GDG to consider your comments when we begin to develop this guideline. As the treatment of men with familial prostate cancer is the same as men without familial prostate cancer this group of men does not need to be highlighted.
SH	PCaSO Prostate Cancer Network	3.02	2.2.a	'and DRE' should be added	We think that the existing text accurately reflects current practice.
SH	PCaSO Prostate Cancer Network	3.03	2.2.c	NHS should be added before treatments as there are a greater number of treatments available through the private sector	The NHS setting is specified in section 3.2.a and we do not think this needs to be re-stated here.
SH	PCaSO Prostate Cancer Network	3.04	3.1.1.c	the following should be added "and men with a familial history of prostate cancer"	The identification and management of men with suspected prostate cancer presenting to their general practitioner will be considered as part of the update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be published in 2014. However, we will ask the GDG to consider your comments when we begin to develop this guideline. As the treatment of men with familial prostate cancer is the same as men without familial

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					prostate cancer this group of men does not need to be highlighted.
SH	PCaSO Prostate Cancer Network	3.05	3.2.a	It is shame that risk based screening has been left out of this section because by 2016 it will surely be a major factor in the early diagnosis of the disease	Risk based screening is outside the remit of this guideline as cancer screening is the responsibility of the NHS Cancer Screening Programmes.Risk assessment might be considered as part of the update to CG27.
SH	PCaSO Prostate Cancer Network	3.06	3.3.2.c	Nomograms should not be excluded from evidence reviews this would aid GPs in the question of whether to send a person for biopsy or not. This could save many unnecessary biopsies and catch many high grade cancers earlier.	The identification and management of men with suspected prostate cancer presenting to their general practitioner will be considered as part ofthe update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be published in 2014. However, we will ask the GDG to consider your comments when we begin to develop this guideline.
SH	PCaSO Prostate Cancer Network	3.07	4.1.1	The following should be added "risk based stratification"	The identification and management of men with suspected prostate cancer presenting to their general practitioner will be considered as part of the update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be published in 2014. However, we will ask the GDG

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					to consider your comments when we begin to develop this guideline.
SH	PCaSO Prostate Cancer Network	3.08	General	As a patient that was caught late and has therefore subsequently been treated, with many side effects of the regimes employed until becoming hormone refactory I feel that not having a NICE strategy to deal with a future male population who might at risk from the disease is both ethically and financially wrong. Population based screening is not the answer but risk stratification is and should not be left out of this review and scope	The identification and management of men with suspected prostate cancer presenting to their general practitioner will be considered as part of the update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be published in 2014. However, we will ask the GDG to consider your comments when we begin to develop this guideline.
SH	NHS Direct	4.00	General	NHS Direct have welcome the scope and have no comment on its content.	Thank you for your comment.
SH	Association of Chartered Physiotherapists in Women's Health &Chartered Physiotherapists Promoting Continence	5.00	4.1.1 h	Add: Access to specialist therapy services for instruction in pre-op pelvic floor exercises. Omit 'late' before specialist therapy services.	This list is not intended to be exhaustive so we have not made this change. We have, however, deleted the word "late".
SH	Sanofi	6.00	3.3.1	We are in agreement with the topics in the scope of the guideline update.	Thank you for your comment.
SH	Sanofi	6.01	4.4.1	We are in agreement with the topics in the scope of the Quality Standard	Thank you for your comment.
SH	Sanofi	6.02	4.4.1 – a)	We welcome the emphasis on patient information and decision-making and note that this is an overarching issue relevant to all of the stages of prostate cancer management (c – n in the Quality Standard). With regards to the specific questions on equality raised in the consultation, we	Thank you for your comment.

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				highlight that providing patients with the means to make informed decisions on treatment is important in promoting equality of opportunity in access to treatment.	
SH	Sanofi	6.03	4.4.1 – b)	As above, the area of multidisciplinary team (MDT) working is an overarching issue relevant to all of the stages of prostate cancer management. Efficient MDT working is critical to ensure appropriate and timely treatment decisions are made. The importance of MDT working is likely to increase as the range of treatments available for prostate cancer increases. We believe that guidance on MDT working will be an important part of the Quality standard, as getting this right will ensure patients receive the right treatment at the right time.	Thank you for your comment.
SH	Sanofi	6.04	4.4.1 – k)	Management of castrate resistant metastatic prostate cancer is an important issue. Docetaxel is the only treatment currently recommended by NICE for castrate resistant metastatic prostate cancer. The timing of docetaxel initiation is an important issue to be covered in the Quality Standard. There is increasing use of earlier chemotherapy in clinical practice, the benefits of which were highlighted in the original TAX327 trial (where patients who were asymptomatic on treatment initiation had greater survival than symptomatic patients). Earlier use of docetaxel chemotherapy ensures patients receive the maximum benefit from chemotherapy and also ensures more patients would be fit enough to benefit from further therapy. This is an increasingly important issue given that there are now a number of treatments either licensed or being trialled for use post-docetaxel (e.g. abiraterone and cabazitaxel, both of which are currently being assessed by NICE in this indication).	The use of docetaxel is covered by TA101 and we are not able to make changes to these recommendations.The TA recommendations will be incorporated into the guideline subject to a TA review proposal.
SH	British Association of Urological Surgeons	7.00	3.1.1 a)	It is really important that the NICE Guidance includes some referral guidelines for men with suspected prostate cancer. There is recent evidence obtained from a prostate cancer charity that many GPs are not complying with the NICE Guidance, often refusing men a PSA test when they request it. It is notable that a recent document from the College of General Practitioners indicated that such matters were now becoming a common cause of litigation for General Practitioners.The PSA level mandating a referral do seem to vary and they seem too low in the elderly asymptomatic patient and out of step with cancer target referral criteria. CG58 uses an age-specific range and this is the recommended range for referral in the 2WW guideline. Evidence for age-specific ranges should reviewed, as the evidence for this approach is limited. More recent data	The identification and management of men with suspected prostate cancer presenting to their general practitioner will be considered as part ofthe update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be published in 2014. However, we will ask the GDG to consider your comments

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				regarding PSA levels and individual risk analysis tools should be examined. The proposal that men referred from primary care for investigation of possible prostate cancer will be covered by the clinical guideline revision (3.1.1 a) is absolutely correct, and the suggestion in 3.3.3 a) that referral from primary care for men with suspected prostate cancer is a key issue that will not be covered makes no sense whatsoever.	when we begin to develop this guideline.
SH	British Association of Urological Surgeons	7.01	3.1.1 c)	Similar special consideration should be considered for men with a strong family history of prostate cancer	The identification and management of men with suspected prostate cancer presenting to their general practitioner will be considered as part ofthe update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be published in 2014. However, we will ask the GDG to consider your comments when we begin to develop this guideline. As the treatment of men with familial prostate cancer is the same as men without familial prostate cancer this group of men does not need to be highlighted.
SH	British Association of Urological Surgeons	7.02	3.3.1 c)	It is not clear why assessment of effectiveness is limited to surgery alone. There is no standardisation of radiotherapy technique or other less established therapies and if effectiveness is important (and to the patient that is paramount) then it would seem that all treatment modalities should be examined in the same way.	Although this document is not specifically evaluating the effectiveness of the different radiotherapy techniques for prostate cancer, national commissioning of radiotherapy is currently being considered. It is hoped this will include examination of all the available

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				The forthcoming HTA of lap versus robotic prostatectomy will inform the surgical discussion.	evidence for the use of different radiotherapy modalities for prostate cancer. The comparison of different radical treatments for prostate cancer was conducted as part of CG58. We are not aware of any newly published high-quality, comparative data that would result in a change to the current recommendations. Therefore we do not propose to updatethis topic. Recommendations from CG58 will be duplicated in the update to this guideline. Thank you for this information.
SH	British Association of Urological Surgeons	7.03	3.3.1 f)	The use of radical treatment for locally advanced prostate cancer with combined hormones and radiotherapy should be extended to an overview of how men with high risk prostate cancer are managed and whether there is enough evidence to recommend radiotherapy rather than surgery or whether NICE might wish to commend a future trial looking at such high risk men.	We believe the NCRI Prostate Group is currently addressing this issue. Therefore we have not made your suggested change.
SH	British Association of Urological Surgeons	7.04	3.3.2 d)	It is a mistake not to include guidance on active surveillance in this revision. The current NICE Guidance is not appropriate. Surveillance of localised prostate cancer remains poorly defined and varies greatly around the UK. The default position often seems to be "what would you like to do?" rather than an evidence based plan or protocol. AS is probably still an experimental treatment, unlike watchful waiting. The Guidance should include the role of template biopsy or registration software linking the output of multi-parametric MRI to ultrasound which again can be helpful.	We have added a topic about 'active surveillance' to the scope. A review of the evidence on multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy is planned as part of 3.3.1.a.

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					We will not be able to make recommendations until we have reviewed this evidence. Further interventions will be prioritised by the GDG for inclusion in the guideline based on criteria such as a) the likelihood that they have significant resource issues and b) there is variation in clinical practice.
SH	British Association of Urological Surgeons	7.05	3.5	There should be a specific section looking at the health economic disbenefits of late treatment. Men whose disease is not treated radically may require subsequent additional hormonal treatment with likely bone related complications and the need for secondary care for hip replacements etc if they develop metastatic disease when their primary is not treated. In a similar way the rates of positive margins and subsequent local relapse, if they are shown to be different between different forms of prostatectomy, should be reviewed.	We do not know at this stage which topics will be a high priority for health economic analysis. This will be determined following a review of published economic literature and completion of a health economic plan.
SH	British Association of Urological Surgeons	7.06	General	I think that the NICE Guidance should review the relationship between volume and outcome. If it is shown by a review of the literature that high volume centres have a decreased rate of positive margins then this is likely to be a proxy for subsequent biochemical recurrence and late surgical recurrence. I guess this could be included in section 3.4 where treatment related morbidity and biochemical free survival are looked at but I think a specific comment on this ie volume and outcome should be noted.	A review of the evidence on radical prostatectomy is planned as part of 3.3.1.c. We will not be able to make recommendations until we have reviewed this evidence.
SH	Advanced Medical Diagnostics	8.00	3.3.1	We would like to see the scope extended so that if the initial biopsy is negative (3.3.1 a ii) that ultrasound based tissue characterisation is included in the subsequent investigative tools.	A review of the evidence on multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy is planned as part of 3.3.1.a. We will not be able to make recommendations until we have reviewed this evidence. Further interventions will be prioritised

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					by the GDG for inclusion in the guideline. This prioritisation will based on criteria such as a) the likelihood that they will have significant resource issues and b) clinical need and variation in clinical practice.
SH	Advanced Medical Diagnostics	8.01	3.3.1	We would like to see the scope extended so that the role of imaging and in particular ultrasound based tissue characterisation in treatment planning is covered.	A review of the evidence on multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy is planned as part of 3.3.1.a. We will not be able to make recommendations until we have reviewed this evidence. Further interventions will be prioritised by the GDG for inclusion in the guideline. This prioritisation will based on criteria such as a) the likelihood that they will have significant resource issues and b) clinical need and variation in clinical practice
SH	Advanced Medical Diagnostics	8.02	3.3.1	We would like to see the scope extended so that the role of imaging and in particular ultrasound based tissue characterisation in patient monitoring is covered.	A review of the evidence on multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy is planned as part of 3.3.1.a. We will not be able to make recommendations until we have reviewed this evidence. Further interventions will be prioritised by the GDG for inclusion in the guideline. This prioritisation will

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					based on criteria such as a) the likelihood that they will have significant resource issues and b) clinical need and variation in clinical practice
SH	Advanced Medical Diagnostics	8.03	3.3.2 b	We would like it specified that ultrasound based tissue characterisation is included in the scope of the guideline review	A review of the evidence on multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy is planned as part of 3.3.1.a. We will not be able to make recommendations until we have reviewed this evidence. Further interventions will be prioritised by the GDG for inclusion in the guideline. This prioritisation will based on criteria such as a) the likelihood that they will have significant resource issues and b) clinical need and variation in clinical practice
SH	Advanced Medical Diagnostics	8.04	3.3.2d	We would like it specified that ultrasound based tissue characterisation for active surveillance and for its continued use thereafter is included in the scope of the guideline review	We have added a topic about 'active surveillance' to the scope.
SH	Advanced Medical Diagnostics	8.05	3.3.2.i	We would like it specified that that ultrasound based tissue characterisation for confirming and localising relapse is included in the scope of the guideline review	We do not consider this issue to be a priority for inclusion in the update.
SH	Advanced Medical Diagnostics	8.06	3.4	We suggest that diagnosis related morbidity and mortality is included	We have added this to the scope.
SH	NHS Cancer screening programme	9.00	3.1.1 (a)	Our comments are as follows …….CG27 uses an age-specific range and this is the recommended range for referral in the 2WW guideline. The PCRMP is referenced and the PCRMP web-site references the NICE guideline. Any evidence for age-specific ranges should be reviewed, as such evidence appears	The identification and management of men with suspected prostate cancer presenting to their general

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				somewhat thin to be included in a national guideline. More recent data regarding PSA levels and individual risk analysis tools should be reviewed.	practitioner will be considered as part ofthe update to the NICE guideline 'GP Referral For Suspected Cancer' that is due to be published in 2014. However, we will ask the GDG to consider your comments when we begin to develop this guideline.
SH	NHS Cancer screening programme	9.01	3.3.1(c)	Our comments are as follows …….There are little or no cost-effectiveness data on different approaches to radical prostatectomy, thus this approach is encouraged. It is unclear as to why a single treatment option has been singled out (namely surgery). If one is interested in looking at effectiveness and cost-effectiveness of treatment for localised prostate cancer, radiation therapies and active surveillance should also be examined in a similar manner – more data on the cost-implications of active surveillance have recently become available and should be included in the analysis.	We do not know at this stage which topics will be a high priority for health economic analysis. This will be determined following a review of published economic literature and completion of a health economic plan. The comparison of different radical treatments for prostate cancer was conducted as part of CG58. We are not aware of any newly published high-quality, comparative data that would result in a change to the current recommendations. Therefore we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	NHS Cancer screening programme	9.02	3.3.2(e)	Our comments are as follows …….The cost-effectiveness and effectiveness of radiotherapy should be reviewed against other treatments (see above).	The comparison of different radical treatments for prostate cancer was conducted as part

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					of CG58. We are not aware of any newly published high-quality, comparative data that would result in a change to the current recommendations. Therefore we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	NHS Cancer screening programme	9.03	4. 1.1 Quality standard	Our comments are as follows …….The rate of positive biopsy and adverse events of biopsy should be examined as a quality standard. There are data available that allow centres to be compared and this would represent a critical quality standard in the initial diagnosis of prostate cancer. There are more data that will be published in the BMJ in January 2012 that could be referred to. PCRMP comments re scope for CG58.msg	Diagnostic-related morbidity has now been added to the list of outcomes. Rates of positive biopsy will be included as part of the measurement criteria for the quality standard.
SH	NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST	10.00	3.3.1	Please also consider the following issues	Please see our responses below.
SH	NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST	10.01		Follow up by primary care vs secondary care following hormone sensitive relapse and newly diagnosed metastatic disease	We are not aware of any recently published high-quality, comparative data that would result in a change to the current recommendations. Therefore we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	NOTTINGHAM UNIVERSITY	10.02		Denosumab for cancer - skeletal related events	Denosumab is being investigated by a NICE

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	HOSPITALS NHS TRUST				technology appraisal and therefore will not be covered by this update.
SH	NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST	10.03		Following the 10yr update of MRC RT01 trial showing no survival benefit, the recommendation of 74 Gy (minimum) with external beam radiation needs to be revised	Survival was not the only important end-point in this trial – other significant benefits were shown. Although this document is not specifically evaluating the effectiveness of the different radiotherapy techniques for prostate cancer, national commissioning of radiotherapy is currently being considered. It is hoped this will include examination of all the available evidence for the use of different radiotherapy modalities for prostate cancer.
SH	NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST	10.04		Role of Sterotactic / Hypofractionated radiotherapy in prostate cancer needs NICE comment	Although this document is not specifically evaluating the effectiveness of the different radiotherapy techniques for prostate cancer, national commissioning of radiotherapy is currently being considered. It is hoped this will include examination of all the available evidence for the use of different radiotherapy modalities for prostate cancer.
SH	Society and College of	11.00	General	There is no mention of clinical trials (unless I missed it). Information regarding clinical trials should be given to patients when appropriate.	The scope defines what topics will be investigated by the

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	Radiographers				guideline. It does not make recommendations on what information patients should be given in relation to clinical trials.
SH	Society and College of Radiographers	11.01	3.1.1 (c)	Unsure about the term 'special consideration' – in view of the higher prevalence of prostate cancer among men of this ethnicity. We would prefer 'recognition of the higher prevalence and general socio-economic factors associated with this group'	We have removed the term "special".
SH	Society and College of Radiographers	11.02	3.3.2 (e)	It is very positive to see the updates relating to the use of Brachytherapy in localised prostate cancer which have been recommended for inclusion. However it is very disappointing that this review "NICE Clinical Guideline 58 review" will not review the evidence for Radiotherapy, aside from Brachytherapy. The original guideline pg xiii states Clinical Oncologists should use **Conformal Radiotherapy** for men with localised prostate cancer receiving external beam. Considerable developments have been implemented in the delivery of radiotherapy for prostate cancer, using IMRT/IGRT. Therefore - The SCoR believe that the wording in 3.3.2e, the current recommendation for 'conformal' radiotherapy MUST be updated to include IGRT/IMRT which we believe should be the standard of care in order to ensure that patients have access to the most optimum treatment for their prostate cancer. **Evidence review for IMRT** Extensive work was conducted by the UK Radiotherapy Development Board (Joint multiprofessional group RCR SCoR and IPEM) reviewing the evidence for the use of IMRT in Prostate cancer	Although this document is not specifically evaluating the effectiveness of the different radiotherapy techniques for prostate cancer, national commissioning of radiotherapy is currently being considered. It is hoped this will include examination of all the available evidence for the use of different radiotherapy modalities for prostate cancer. However we will revise the existing wording of this recommendation to bring it in line with accepted definitions.

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				http://www.clinicaloncologyonline.net/article/S0936-6555(10)00221-9/fulltext **A Review of the Clinical Evidence for Intensity-modulated Radiotherapy, Staffurth J,** on behalf of the Radiotherapy Development Board) **Clinical Oncology** Volume 22, Issue 8 , Pages 643-657, October 2010 We would like to recommend that the section on Radiotherapy is therefore updated and states IMRT/IGRT and that conformal is removed.	
SH	Society and College of Radiographers	11.03	4.1.1 (h)	Scope here for consideration of radiographer consultant practice. (also links to 3.3.2(h))	We have deleted the word "late" therefore radiographers could be involved in the management of complications.
SH	King George Hospital	12.00	3.1.2	Should be covered, significant proportion	We have re-worded 3.1.2.a for clarity. We anticipate that those men who have a raised PSA and have been referred for secondary investigation will be covered in 3.3.1.a.ii.
SH	King George Hospital	12.01	3.3.1 a to g	Effectiveness in a local centre more important than the publication	Apologies – we do not understand this comment.
SH	King George Hospital	12.02	4.1.1 e, f, g	Please see enclosed our proposed bullet points for an editorial  Early Prostate Cancer Treatment- N	Thank you for this information.
SH	Speciality European Pharma	13.00	4.1.1 j)	We would like to draw your attention to a recent publication: "New treatment paradigm for prostate cancer: abarelix initiation therapy for immediate testosterone suppression followed by an LHRH agonist" by Garnick and Mottet. This paper was accepted for publication on 9th August 2011 in the British Journal of Urology International. The objective of this study was to demonstrate the safety and endocrinological and biochemical efficacy of initiating treatment with the GnRH antagonist, abarelix, for 12 weeks followed by the administration of an LHRH agonist in	We could not find evidence of Market Authorisation in the UK for abarelix and therefore are unable to include it in the guideline.

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				patients with advanced or metastatic prostate cancer. This study shows that abarelix initiation therapy resulted in the desired effect of achieving immediate testosterone suppression and that testosterone surges after subsequent LHRH agonist therapy were greatly abrogated or completely eliminated. This treatment paradigm obviates the need for an anti-androgen.	
SH	Astrazeneca UK Ltd	14.00	3.3.1 - 3.3.2	Thank you for the opportunity to comment on the scope for updating this clinical guideline and quality standard. The draft scope indicates that there is no intention to review the use of hormonal therapies in the management of prostate cancer. In our view it is imperative that there be a review of this section (with particular focus on the clinical evidence supporting the recommendations in section 6.2 [Locally advanced prostate cancer – Systemic Therapy] and section 7 [Metastatic prostate cancer - Hormonal Therapy, Health Economic Evaluation] of NICE CG58. Within the current guideline, there is no differentiation between the available hormonal treatments and this is often interpreted to mean the LHRH analogues exhibit "a class effect". However, the most recent independent review of the evidence exploring this issue **[Gonzáles and Pijuan (2010)],**[1]concludes that the "current available evidence is not enough to support a presumed drug class effect of the various analogues in the treatment of carcinoma of the prostate in its different clinical situations." In addition to the lack of evidence supporting a "class effect", it is also of relevance to note the varying levels of supporting data which underpin the usage of the different members of this class of drugs. Firstly, the majority of reliable evidence on LHRH analogues is from randomized controlled trials of goserelin. This was highlighted by **Roach M III and Izaguirre A [2007]**[2]who reported that "of the 11 most important randomized clinical trials (RCTs) that have shown improved outcomes when androgen deprivation therapy (ADT) is added to EBRT, 10 have been performed with goserelin". Secondly, there are major differences in the licensed indications of the available hormonal therapies used in the management of prostate cancer [Please see table below]. For instance, goserelin is the only LHRHa that can demonstrate survival in all 3 stages of prostate cancer as reflected in its license.	The existing recommendations for hormone therapy do not exclude the use of Gorserlin for this indication. Prescribing guidance from the General Medical Council states that a licensed product should be used in preference to a non-licensed product. We therefore do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.

<table>
<tr><th>Type</th><th>Stakeholder</th><th>Order No</th><th>Section No</th><th>Comments
Please insert each new comment in a new row.</th><th>Developer's Response
Please respond to each comment</th></tr>
<tr><td></td><td></td><td></td><td></td><td>A full review of the available clinical evidence would therefore provide clarity and enable clinicians in making the most appropriate choice of treatment in the management of their prostate cancer patients.
<table>
<tr><th colspan="2" rowspan="2">Licensed indication</th><th colspan="3">LHRH Agonists</th><th>LHRH Antagonist</th><th>LHRH Analogue</th></tr>
<tr><th>Goserelin[1]</th><th>Leuprorelin[2]</th><th>Triptorelin[3]</th><th>Degarelix[4]</th><th>Histrelin[5]</th></tr>
<tr><td rowspan="2">High-risk localized prostate cancer</td><td>Neoadjuvant treatment prior to radiotherapy</td><td>✓</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
<tr><td>Adjuvant treatment to radiotherapy</td><td>✓</td><td>✓</td><td>✓3a</td><td>x</td><td>x</td></tr>
<tr><td rowspan="4">Locally advanced prostate Cancer</td><td>Alternative to surgical castration</td><td>✓</td><td>✓</td><td>✓</td><td>x</td><td>x</td></tr>
<tr><td>Neoadjuvant treatment prior to radiotherapy</td><td>✓</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
<tr><td>Adjuvant treatment to radiotherapy</td><td>✓</td><td>✓</td><td>✓3a</td><td>x</td><td>x</td></tr>
<tr><td>Adjuvant treatment to radical prostatectomy</td><td>✓</td><td>✓</td><td>x</td><td>x</td><td>x</td></tr>
<tr><td colspan="2">Metastatic prostate Cancer</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td colspan="7">Key: Licensed: ✓
Not licensed: X

Reference:
1. Zoladex 3.6mg & 10.8Mg SmPC.
2. Prostap 3 DCS & SR DCS SmPC
3. Decapeptyl SR 3mg & SR 11.25mg and 22.5mg SmPC
a. 3mg and 11.25mg only
4. Feirmagon 80mg & 120mg SmPC
5. Vantas 50mg SmPC</td></tr>
</table>

González SV, Pijuan XM. Evidence-based medicine: comparative analysis of luteinizing hormone-releasing hormone analogues in combination with external beam radiation and surgery in the treatment of carcinoma of the prostate. BJU Int 2011; 107: 1200–8.
Roach M III, Izaguirre A. Goserelin acetate in combination with radiotherapy for prostate cancer. Expert Opin Pharmacother 2007; 8: 257–64
</td><td></td></tr>
<tr><td>SH</td><td>Department of Health</td><td>15.00</td><td></td><td>Thank you for the opportunity to comment on the draft scope for the above clinical guideline update/quality standard.

I wish to confirm that the Department of Health has no</td><td>Thank you for your comment.</td></tr>
</table>

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
				substantive comments to make, regarding this consultation.	
SH	Dendreon Corporation	16.00	3.3.1 4.1.1	Suggest adding a section on identification of metastatic disease in men with castrate resistant prostate cancer, i.e., when to initiate evaluation with imaging and how frequently to image.	We are not aware of any recently published high-quality data that would result in a change to the current recommendations. Therefore we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	Dendreon Corporation	16.01	3.3.1	Suggest adding a section on sipuleucel-T (Provenge) for treatment of metastatic castrate resistant prostate cancer.	Sipuleucel-T will be scoped for consideration under thetechnology appraisal programme and as such it is not appropriate to investigate it in this guideline.
SH	British Pain Society	17.00	general	Specialist / interventional pain management should be considered whenever referral to palliative care for pain management mentioned	This issue will be covered by the NICE clinical guideline on "Strong opioids in palliative care", due to be published in May 2012.
SH	British Pain Society	17.01	4.1.1 o)	Specialist / interventional pain management. 1. It is well established that cancer pain is often under-recognised and under-treated; this applies to pain patients with prostate cancer, which can often be debilitating. 2. Adequate provision is to be made to provide appropriate analgesia not only to patients undergoing radical surgery for cancer prostate, but also for those undergoing prostate biopsy, pelvic brachytherapy including HDR (high dose radiation) prostate and multiple fractions of external beam radiation.	We feel that many of the issues you raise are covered in CG58, the 'improving supportive and palliative care for adults with cancer' guidance and other clinical guidelines and will be used when developing the quality standard. We have changed 4.1.1.n to "Supportive and palliative care".

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				3. Patients with difficult pains and previous complex pain issues should have input from specialist pain services and palliative care services. 4. Long-term survival prospects of patients with cancer of the prostate even with extensive bone metastasis have improved over the past few years and it is imperative that long-term pain management strategies have to be put in place early on for patient benefit and continuity of care. 5. Patients with intractable pain from metastatic bone disease or pelvic disease should be referred early for interventional pain management, particularly when there is little benefit and unacceptable side-effects from opioid analgesics. Often these pains can be adequately controlled by targeted neural or neuraxial blockade routinely practiced in most pain clinics. Some patients need specialist input for complex pain interventions like percutaneous cordotomy, neurolytic procedures, vertebroplasty and intrathecal/ epidural drug delivery using external catheters and fully implantable systems, depending on the prognosis and available resources. 6. Systems should be in place to identify and manage patients with spinal disease to prevent/ manage metastatic spinal cord compression.	
SH	Thames Valley Cancer Network	18.00	General	I attach a draft paper from a recent expert meeting of US National Cancer Institute on Active Surveillance in prostate cancer  ASPC Final Draft Statement[1].pdf  Untitled.msg	Thank you for this information.

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SH	NCRI/RCP/RCR /ACP/JCCO	19.00	General	The NCRI/RCP/RCR/ACP/JCCO are grateful for the opportunity to respond to the draft scope consultation. Our experts are generally happy with the content of the scope but would like to make the following comments.	Thank you for your comment.
SH	NCRI/RCP/RCR /ACP/JCCO	19.01	General	At times, there seems to be some overlap between issues that are to be covered and those not to be covered. This should be addressed. An example is whether or not radiotherapy for high-risk localised and locally advanced disease is to be considered. Some experts view this as very important because the SPCG7 and PR07 trials provide important new data. They feel that it should be considered in the guideline.	Thank you for drawing this to our attention. We have amended section 3.3.2.
SH	NCRI/RCP/RCR /ACP/JCCO	19.02	General	Given the long-term survival data emerging from RT01 (and from other trials) of dose escalation in early prostate cancer, we believe that consideration should be made to bring this into the scope.	Although this document is not specifically evaluating the effectiveness of the different radiotherapy techniques for prostate cancer, national commissioning of radiotherapy is currently being considered. It is hoped this will include examination of all the available evidence for the use of different radiotherapy modalities for prostate cancer.
SH	NCRI/RCP/RCR /ACP/JCCO	19.03	General	We note that the role of RT is established with hormones for locally advanced disease. With this in mind it might also be brought into the scope towards assessing the role of RT for M1 disease. This is currently being considering in STAMPEDE.	Thank you for this information.
SH	NCRI/RCP/RCR /ACP/JCCO	19.04	3.3.1	We believe that the timing of MRI in relation to TRUS biopsy needs addressing. Multiparametric imaging needs to be defined at the outset.Standardisation of techniques and how this is to be quality assured for readouts is also critically important here.	A review of the evidence on multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy is planned as part of 3.3.1.a. We will not be able to make recommendations until we have

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					reviewed this evidence. Further interventions will be prioritised by the GDG for inclusion in the guideline. This prioritisation will based on criteria such as a) the likelihood that they will have significant resource issues and b) clinical need and variation in clinical practice
SH	Ipsen Ltd	20.00	General	There is currently minimal information on the recommended follow-up for patients with prostate cancer. There is also minimal information on the role of primary care in the management of patients with prostate cancer and shared care. We would encourage a review of this area.	We are not aware of any recently published high-quality data that would result in a change to the current recommendations. Therefore we do not propose to update these topics. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	Ipsen Ltd	20.01	2.2 d) and General	We would encourage a recommendation to routinely measure testosterone levels for patients who are receiving hormone therapy - often done routinely by oncologists, but not by urologists who rely on PSA which is an indirect marker of the efficacy of hormonal therapy. Ideally testosterone should be measured whenever PSA is measured, but as a minimum, it should be measured in the event of rising PSA to check whether the patient is developing CRPC or is just not responding adequately to their current hormone therapy. Given the fact that there is not equal evidence for all LHRH agonists, in the event of inadequate treatment response it may benefit the patient to change products. This may also be relevant in the context of improving the definition of CRPC.	We do not consider this issue to be a priority for inclusion in the update.
SH	Ipsen Ltd	20.02	3.3.1 b)	We would encourage a review of the evidence and role of LHRHa's post radical prostatectomy plus stronger recommendation that these products be continued during castrate resistant prostate cancer alongside any other treatments that are initiated.	We are not aware of any recently published high-quality data that would result in a change to the current recommendations. Therefore

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					we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	Ipsen Ltd	20.03	3.3.3 and General	Localised and metastatic disease may be covered by hormonal treatment but localised advanced disease does not appear to be covered.	This is not correct. It is covered in 3.3.1.f.
SH	Ipsen Ltd	20.04	4.1.1 j) and General	We would encourage a review of the correct or standardised definition of castrate levels of testosterone. In light of recent evidence, should the threshold for castration be redefined as 0.2ng/mL?	We do not consider this issue to be a priority for inclusion in the update.
SH	Ipsen Ltd	20.05	4.1.1 and General	Clarification on use of LHRH agonists in CRPC - the current guidance indicates that LHRH agonists are usually continued during CRPC, but does not indicate whether this is the correct course of action. It would be good to get a stronger recommendation that these products should be continued during CRPC alongside any other treatments that are initiated.	We are not aware of any recently published high-quality data that would result in a change to the current recommendations. Therefore we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	Ipsen Ltd	20.06	General	We would encourage a standardisation of nomenclature and definitions of the various stages of prostate cancer.	Staging of prostate cancer is outside the remit of this guideline.
SH	Ipsen Ltd	20.07	General	There is no mention or inclusion of the longer acting LHRH agonists (6 and 12 monthly formulations.	The current recommendations do not specify what preparation should be used. We feel it would be up to the service provider and patient to determine what preparation is delivered to achieve suppression.
SH	Translucency Ltd.	21.00	§3.3.2	§3.3.2 lists key issues covered by NICE clinical guideline 58 for which the evidence will not be reviewed. This list includes high-intensity focused ultrasound. As noted in §6.2, IPAC is currently developing new guidance on the use if HIFU in prostate cancer. We assume that any IPAC guidance on HIFU in (localised) prostate cancer will be incorporated in some way in the revised	The IPAC guidance will not be incorporated into the guideline as it only looks at safety and efficacy of an intervention. We are not aware of any recently

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				guideline, even though the Guideline Development Group will not be reviewing the evidence.	published high-quality, comparative data that would result in a change to the current recommendations. Therefore we do not propose to update this topic. Recommendations from CG58 will be duplicated in the update to this guideline.
SH	Royal College of Nursing	22.00	General	The Royal College of Nursing welcomes proposals to develop this guideline and Quality Standard. The draft scope seems comprehensive.	Thank you for your comment.
SH	The Prostate Cancer Charity	23.00	General	As previously highlighted, we welcome the review of the clinical guideline CG58 - Prostate cancer: diagnosis and treatment. We support the practice of reviewing new evidence on a regular basis to ensure men with prostate cancer and clinicians have up-to-date advice about the most effective way to diagnose and treat prostate cancer.	Thank you for your comment.
SH	The Prostate Cancer Charity	23.01	General	We welcome the inclusion of the quality standard for prostate cancer as part of the prostate cancer update. This national standard will help to eliminate the regional variations that exist in prostate cancer services and men's experience of care across the country, as evidenced in the National Cancer Patient Experience Survey.(1) We understand that the relationship between the clinical guideline and the quality standard are symbiotic and that the content of the quality standard is wholly dependent upon the content of the clinical guideline. Therefore, the comments made in this response are intended to ensure that the clinical guideline fully reflects the comprehensive, holistic care that men with prostate cancer need on key issues, such as the identification and management of treatment side effects and the way health professionals communicate with them. This will ensure that the clinical guideline comprehensively covers each of the three dimensions of	Thank you for your comments. We will have patient representation on the Guideline Development Group to ensure that patient experience is considered for all topics.

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				quality defined by NICE: clinical effectiveness, patient safety and patient experience.(2) The experience of men is largely dependent upon the information and support they receive through their treatment and beyond, as well as the outcome of their treatment. If the key measures within the quality standard are to be drawn from the clinical guideline, then it is essential that the guideline provides detailed recommendations on each of the three above dimensions of quality. Patient experience is an important area of quality and due regard must be paid to it throughout the guidelines. We believe the recommendations in our response indicate where extra detail will enhance the current advice within the guidelines and ensure patients receive the best possible communication, support and follow up care – laying sound foundations for quality prostate cancer care. **Reference** (1) National Cancer Patient Experience Survey 2010. Report available at http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsStatistics/DH_122516 (2) NICE Quality standards. Available at: http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp	
SH	The Prostate Cancer Charity	23.02	3.3.1	We welcome the inclusion of the nine key issues included within the scope of the update.	Thank you for your comment.
SH	The Prostate Cancer Charity	23.03	3.3.1 (i)	We are particularly pleased to see an emphasis on reviewing the recommendations made in the guideline on "*identifying and managing late effects of long-term androgen suppression".* .We would like to draw your attention to the *Hampered by Hormones?* report The Prostate Cancer Charity produced in 2009. This highlights the frequencyand	Thank you for this information.

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				impact of the side effects of hormone therapy on men and their partners. This report is informed by a survey of over 300 men who had received hormone therapy and 100 of their partners. The survey showed that many men find the side effects of androgen suppression difficult to cope with and are not receiving the support they need to overcome or manage these effects. It also highlighted the interventions and support services men need. For example, our survey found that:[(a)] • Fatigue impacted on the lives of over 70 per cent of those who took part in the survey (affecting their ability to work, conduct household chores and pursue hobbies) and 1 in 4 men who experienced this side effect found the impact it had on their lives difficult to cope with. • 1 in 4 survey respondents said that hormone therapy affected their ability to work. • 8 out of 10 said that they experienced erectile dysfunction as a result of their treatment – with a quarter of these men reporting that they found it difficult to cope with the impact this had on their lives. • 1 in every 2 men reported serious issues related to their mental wellbeing, for example, feelings of depression, loss of confidence and cognitive problems. Despite these experiences, over half of the men who responded to the survey said that they received 'too little' information before they began hormone therapy and 'too little' support whilst they were on the treatment. Many did not receive verbal or written information on the potential side effects before they began treatment – nor were they asked by the healthcare professionals involved in their care about these side effects or	

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				their support needs. These problems in the care of men with prostate cancer occur despite existing NICE guidance setting out that[b,c]: • Men with advanced and metastatic prostate cancer should have all hormone therapy options and the associated adverse effects discussed with them. • Patients and their carers should have access to a range of high quality information about cancer and cancer services. • All patients should receive psychological assessments and have access to appropriate psychological support.	
SH	The Prostate Cancer Charity	23.04		A thorough review of new evidence about the incidence of side effectsfollowing androgen suppression and the support that men with prostate cancer should receivewould enable greater clarity within the guidelines and quality standard about how menexperiencing these effects should be managed. The Charity also recommends that NICE provides advice to all relevant clinicians regarding assessments of men with prostate cancer to identify any treatment side effects and their related support needs. **References:** **(a)** The Prostate Cancer Charity (2009). Hampered by Hormones? Available here: http://www.prostate-cancer.org.uk/media/49198/htcampaignreport.pdf. **(b)** NICE (2002). Improving Outcomes Guidance for Urological Cancers http://www.nice.org.uk/guidance/index.jsp?action=download&r=true&o=28771 **(c)** NICE (2004). Supportive and Palliative Care for Adults with Cancerhttp://www.nice.org.uk/nicemedia/pdf/csgspmanual.pdf	These issues will be discussed with the GDG when agreeing the clinical question (PICO) for 3.3.1.g and 3.3.1.i. CG58 already makes recommendations on these areas.Recommendations from CG58 will be duplicated in the update to this guideline.
SH	The Prostate	23.05	3.3.2 (a)	We are disappointed that guidelines on the communication, support and	We feel that CG58 and the

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	Cancer Charity		and 3.3.2 (g)	follow up care men should receive have been omitted from the scope of the update. The current clinical guideline provides limited advice on the support that men should receive to help them cope with or manage the life-changing side effects of prostate cancer treatment, as highlighted in section 4 above). We believe a thorough review of new evidence about the incidence of side effects for all treatments and the support that men with prostate cancer should receive may enable greater clarity within the guidelines about how men experiencing these effects should be managed. This includes the communication men receive from health professionals about potential side effects and the assessment and support men need, whether they are on active surveillance, long term androgen suppression or have completed treatment. We know from our own research that not all health professionals are asking men whether they are experiencing treatment side effects.[1, 2] Given the high incidence of side effects from prostate cancer treatments, identifying the effects of treatment should be an essential component of follow-up care for men with prostate cancer in both primary and secondary settings. Following a review of the evidence on radiotherapy [3.3.1 (h)] and the late effects of hormone therapy [3.3.1(i)], the Guideline Development Group will need to add recommendations related to the way health professionals communicate potential adverse effects of these treatmentsto men, assess them for adverse effects, and then support men to manage such effects. We recommend that the scope of the guideline update be amended to ensure that the relevant sections on communication, support and follow-	'improving supportive and palliative care for adults with cancer'guidance alreadymakes recommendations on these areas, and therefore do not propose to update the evidence for this topic. Recommendations from CG58 will be duplicated in the update to this guideline.However we will look at the order of these recommendations and where they appear in the guideline to see if they can be made clearer.

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				up can be updated toinclude new recommendations on the communication, support or follow up care that men with prostate cancer receive. **References:** (1) The Prostate Cancer Charity (2009). Hampered by Hormones? Available here: http://www.prostate-cancer.org.uk/media/49198/htcampaignreport.pdf. (2) The Prostate Cancer Charity surveyed 156 men diagnosed with prostate cancer between January and February 2010. The survey asked men about the support they had received to cope with urinary incontinence, as well as the sexual and psychological problems they experienced as a result of their treatment for the disease. The survey was conducted online.	
SH	The Prostate Cancer Charity	23.06	3.3.2 (a)	In addition to the comments made above regarding the need to include guidance on the minimum standard communication skills for health professionals and provision of effective support, we are also disappointed that NICE will not be updating section 3.3.2 (a) to advise health professionals on the use of the term 'castrate-resistant' prostate cancer. As highlighted in ourprevious responses to the consultationon the scope of the guideline review, we are aware that the term castrate resistant prostate cancer is distressing to some men.(1) Whilst we recognise that the term is medically correct, we are concerned that some men may be distressed by the term or put off treatment. We surveyed members of our Prostate Cancer Voices network(2) and found that 24 out of 27 respondents wanted clinicians to refrain from using the phrase "castration resistant" when describing this type of prostate cancer. 21 men reported that the term was "unhelpful" and three men described the term as "alarmist", "extreme" and "tactless".(1) For	We feel that the term 'hormone relapsed prostate cancer' would be more appropriate and will be discussed with the Guideline Development Group at the initial meetings to gain consensus.

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				example, one man wrote: *"The word 'castration' suggests a far more radical and unpleasant outcome of treatment. It also indicates a very permanent physical change."* In addition, ten men said the term would influence their decision to have the treatment. We are concerned that the term "castration-resistant prostate cancer" will cause some men distress and may adversely influence their treatment decisions. We believe that NICE should advise clinicians to be sensitive to patients' reactions to using the term and refrain from using it in conversations, unless absolutely necessary. For example, in our information materials for men we describe castration resistant prostate cancer as prostate cancer that is "no longer responding to your original type of hormone therapy, but may respond to other types of hormone therapy".(3) **References** (1) The Prostate Cancer Charity surveyed 27 people affected by prostate cancer between 6 and 22 August 2010 through an online and paper survey. (2) The Prostate Cancer Charity is committed to ensuring that people affected by prostate cancer are at the heart of all we do. Prostate Cancer Voices in a network of men diagnosed with prostate cancer, their partners, families and friends whose thoughts and experiences we use to shape our work. To find out more about Prostate Cancer Voices visit: http://www.prostate-cancer.org.uk/get-involved/prostate-cancer-voices. (3) The Prostate Cancer Charity (2010). Treating prostate cancer after hormone therapy. Available at: http://www.prostate-	Thanks for this definition – we will keep consider this when drafting background text.

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				cancer.org.uk/information/treatment/treatment-choices/treating-prostate-cancer-after-hormone-therapy	
SH	The Prostate Cancer Charity	23.07	3.3.2 (d)	We are disappointed that watchful waiting has not been included within the scope of the guideline update. In our previous response to the scope of the review, we raised concerns about the emphasis the current guideline places on a man's age as a deciding factor for the decision to undergo watchful waiting. We believe a small change needs to be made to the guideline to remove this emphasis. Men should be told about all the appropriate treatment options and should not encouraged to have a particular treatment simply because of their age. We believe that fitness to undergo active treatments such as surgery or radiotherapy may be better assessed by considering an individual's fitness, including co-morbidities. The current guideline may be interpreted to mean that older men should be offered fewer treatment options than younger men, regardless of their fitness for the treatment. We recommend that NICE acknowledges the need for this change to the wording of the guideline, to ensure health professionals discuss the full range of appropriate treatment options with men. We would like this important update to be included within the scope of the review.	We will review the guideline to ensure that it complies with NICE's duties under equalities legislation.
SH	The Prostate Cancer Charity	23.08	4 - General	We would like to draw your attention to a project The Prostate Cancer Charity is currently undertaking to consult with people affected by prostate cancer, health professionals and policy makers in order to identify the standards of quality prostate cancer care that they value. We are collecting these views through research including a questionnaire and focus groups for people affected by prostate cancer, one-to-one structured interviews with health professionals, and meetings facilitated by politicians with stakeholders in their areas.	Thank you for this information.

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				We will be producing a report of the findings in 2012 and would be happy to present these to NICE and the Guideline Development Group when they are complete. We hope that you will take the findings of this consultation into account when developing the prostate cancer quality standard. They should provide an excellent opportunity for NICE to consider a wide range of diverse and representative views of people affected by the disease and ensure that the quality standard seeks to facilitate not only high quality clinical outcomes but also high quality patient-reported outcomes.	
SH	Bayer HealthCare	24.00	3.3.1	An area of the clinical guideline which for which the evidence should be reviewed is section 7.11 Bone Targeted Therapies. Results from the Phase III ALSYMPCA (**AL**pharadin in **SYM**ptomatic **P**rostate **CA**ncer) trial were presented during the Presidential Session at the 2011 European Multidisciplinary Cancer Congress in Stockholm, Sweden, Saturday 24 September (Abstract No. 1LBA). http://stockholm2011.ecco-org.eu/Programme.aspx Based on results of the interim analysis, radium-223 (Alpharadin) significantly improved overall survival (OS) in patients with castration-resistant prostate cancer (CRPC) with bone metastases (two-sided *P* value = 0.00185; HR = 0.695; 95% CI, 0.552-0.875).The median OS was 14.0 months for radium-223 and 11.2 months for placebo.	We are aware that Bayer Healthcare issued a press release on 6th June 2011 with the results of an interim analysis of the ALSYMPCA trial, but the trial results have not been published so we cannot consider alpharadin at this time. This treatment is not licensed in the UK and would be more appropriate to be investigated by NICE Technology Appraisals rather than this guideline.
SH	Bayer HealthCare	24.01	4.1.1	**k)** An area of care that should be considered as part of the quality standard is management of symptomatic bone metastases	This will be discussed when the GDG discusses 4.1.1.k.
SH	Janssen	25.00	3.3.2.m)	Janssen suggests that the GDG explore how disease progression in metastatic castrate resistant prostate cancer (mCRPC) is assessed. Currently, clinical assessments include PSA, radiographic assessments as well as clinical symptoms. Future technologies may also include biomarkers or biomarker panels such with additional measures such as levels of circulating tumour cells (CTCs).	We do not consider this issue to be a priority for inclusion in the update. We believe this more appropriate to be investigated by NICE's Medical Technologies Evaluation

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					Programme rather than this guideline.
SH	Janssen	25.01	3.3.3.c)	Janssen asks that the GDG also explore the literature regarding pharmacological treatments for chemotherapy naive patients, such as abiraterone acetate.	This is the subject of a future NICE technology appraisal and therefore cannot be covered by this update.
SH	Ferring Pharmaceuticals	26.00	General	We would like to seek clarification in terms of where a review of GnRH antagonists would be included in the scope. Ferring previously highlighted in our response to the CG58 review consultation that we would welcome an in depth review of degarelix (Firmagon®), the only licensed GnRH antagonist in the UK for prostate cancer, for inclusion in an updated prostate cancer clinical guideline. Since the development of the first guideline, we have a much greater body of evidence; 11 published clinical papers which we have referenced for review and consideration. In addition, degarelix is currently being used throughout the UK and is included on 68 hospital formularies, with regional variation in prescribing. Degarelix is a product which fulfils a clinical need in the treatment of advanced hormone-dependent prostate cancer by providing rapid reduction in testosterone and avoiding clinical flare or use of anti androgens. Ferring believes the guidelines should reflect all new published data. This will allow NICE to support (safely) current clinical practice, recognising the prevalence and variation of current prescribing in the field of oncology.	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring Pharmaceuticals	26.01	2.1	Ferring pharmaceuticals would like to suggest, in the interest of patient safety, that attention is drawn to the parallel epidemiology of cardiovascular disease in patients with prostate cancer. The Eindhoven cancer registry found a high prevalence of hypertension and cardiovascular disease in correlation with advancing age and male gender (51% in prostate cancer)**Error! Reference source not found.**]. This raises the issue of the impact of treatment for prostate cancer on concurrent	This is a guideline on prostate cancer hence the epidemiology section focuseson this disease. We will not be able to make recommendations until we have reviewed the evidence.

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				cardiovascular disease and should be more specifically highlighted throughout the guidelines alongside treatment recommendations. This is particularly relevant to patient safety in view of the recognised contraindications adverse events and long term impact associated with both anti-androgens and LHRH agonists. Agents used for flare protection such as cyproterone or flutamide are advised to be used with caution when there is concurrent cardiovascular disease (SPCs attached)[**Error! Reference source not found.**,**Error! Reference source not found.**]. On October 20th 2010, the FDA updated their safety communication regarding LHRH agonists [**Error! Reference source not found.**]. The FDA found that patients receiving GnRH agonists were at a small increased risk for diabetes, heart attack, stroke, and sudden death. They advised that the following products should be relabelled to include updates in the Warnings and Precautions section about these potential risks - Eligard, Lupron, Synarel, Trelstar, Vantas, Viadur, and Zoladex. Ferring would like to request a review of the clinical paper Smith et. al. 2010 [**Error! Reference source not found.**] which suggests that In men with prostate cancer observed rates of cardiovascular disease events were similar before and after degarelix treatment. Events were largely confined to men with pre-existing cardiovascular disease and further modulated by age and modifiable risk factors. This is a positive result compared to the data surrounding current LHRH options for treatment.	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.

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SH	Ferring Pharmaceuticals	26.02	2.2 d)	Ferring pharmaceuticals would like "GnRH Antagonists" to be included in "Hormonal Therapy" as a treatment option. Recent recognition that locally advanced disease can be high risk and in some circumstances needs to be treated aggressively and quickly has led to an increase of the use of degarelix in the UK, in this setting. Degarelix is supported by literature and current UK practice as a medical alternative to surgical castration in high risk cases when there is a need for rapid reduction in testosterone / PSA and surgical castration is not palatable to the patient. A recent publication by Payne and Mason in the BJC 2011 [**Error! Reference source not found.**] further defines locally advanced prostate cancer into "high risk" groups which require the use of hormonal agents to rapidly reduce PSA and testosterone when there is aggressive disease. Degarelix is listed as a treatment option when there is a need for rapid reduction in Testosterone / PSA. The European Association of Urology 2011 [**Error! Reference source not found.**] recommends the use of degarelix for immediate castration of patients with high risk locally advanced disease (alternatives are surgical castration, stilboestrol and LHRH agonisists). The following clinical paper explains the evidence for efficacy of degarelix. Klotz et al. (BJU Int 2008) [**Error! Reference source not found.**] published data from the pivotal trial of degarelix supporting the important role of degarelix in patients in need of a rapid reduction in testosterone and thus PSA. It was established that testosterone surge with LHRH agonists can delay castration by up to 3 weeks and there was a total avoidance of testosterone surge with GnRH antagonists.Furthermore,52% and 96% of patients on degarelix achieve castrate testosterone by Day 1 & Day 3 respectively. In addition to this, supporting long term therapy continuation with degarelix Crawford et al 2011 [**Error! Reference source not found.**] published data to suggest that the hazard rate of PSA recurrence or death in the subgroup of	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.

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				patients with PSA>20 was 0.23 for patients treated with degarelix vs 0.38 leuprorelin. This would suggest degarelix is an appropriate choice of treatment for this subgroup – high risk.	
SH	Ferring Pharmaceuticals	26.03	3.3.1 i)	As mentioned in section 2.2. Ferring would like to request a review of the clinical paper Smith et al 2010 which suggests that in men with prostate cancer observed rates of cardiovascular disease events were similar before and after degarelix treatment. Events were largely confined to men with pre-existing cardiovascular disease and further modulated by age and modifiable risk factors. This is a positive result compared to the data surrounding current LHRH options for treatment.	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring Pharmaceuticals	26.04	3.3.2. h)	Ferring would like to draw your attention to the increased usage of degarelix to avoid unnecessary risk of the side effects of "standard" anti androgens or LHRH agonists, such as venous thromboembolism, cardiac events or liver failure. Steroidal Anti Androgens have been associated with an increased risk of VTE in patients with prostate cancer**Error! Reference source not found.**]. The recommendation to use degarelix in this circumstance has been adopted by the LCNDG, stating that it should be used when there is a need to avoid the pro-thrombotic risk of steroidal anti androgens. It was also stated that non-inferiority was demonstrated and improved patient experience was noted [**Error! Reference source not found.**].	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further

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					details.
SH	Ferring Pharmaceuticals	26.05	3.4 c)	We would like to highlight the time to PSA progression failure data for Degarelix shown in a study by Tombal et al 2010 [**Error! Reference source not found.**]; Additional Analysis of the Secondary End Point of Biochemical Recurrence Rate in a Phase 3 Trial (CS21) Comparing Degarelix 80 mg Versus Leuprolide in Prostate Cancer Patients Segmented by Baseline Characteristics.	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring Pharmaceuticals	26.06	3.4 d)	Ferring pharmaceuticals would like to highlight the recent publication by Smith et al, which suggests that In men with prostate cancer observed rates of cardiovascular disease events were similar before and after degarelix treatment. Events were largely confined to men with pre-existing cardiovascular disease and further modulated by age and modifiable risk factors [5]. In Addition to this, Schröder et al 2010 [**Error! Reference source not found.**] published data to suggest improved control of serum alkaline phosphatase (S-ALP) and a lower rate musculoskeletal adverse events compared with leuprorelin. Degarelix induced numerically greater reductions in S-ALP from baseline compared with leuprorelin at all time points over a 1 year period and there was a significantly lower reduction in S-ALP levels at 1 year in the Degarelix arm compared with leuprorelin (p=0.01). In addition degarelix did not display late rises of S-ALP back to baseline as observed at 1 year in the leuprorelin arm.	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring	26.07	3.5.	Ferring would like to highlight that the cost–utility analysis for the SMC was	Thank you for your comments.

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	Pharmaceuticals		And 4.2	accepted in 2011. It compared degarelix with goserelin in patients with advanced hormone-dependent prostate cancer, based on the assumption that there is a class effect for the LHRH agonists i.e. that no LHRH agonist had demonstrated superior efficacy to any other. The SMC classed degarelix as cost-effective with the inclusion of the Patient Access Scheme (PAS) approved by the PAS Assessment Group (PASAG).	We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring Pharmaceuticals	26.08	4	Ferring believes that degarelix should be made available as a treatment option. Therefore, the Quality Standards should include that clinicians and patients should all have access to degarelix as a treatment option.	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring Pharmaceuticals	26.09	4.1.1 a)	In line with patient centred prescribing, Ferring feel that the rapid reduction of testosterone to castrate levels and LHRH antagonist action of Degarelix offers greater patient choice especially when the only option is surgical castration and	Thank you for your comments. We have had discussions with the NICE Topic Selection team

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				there is a need to avoid biochemical flare associated with the use of LHRH agonists.	about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring Pharmaceuticals	26.10	4.1.1. j)	Ferring Pharmaceuticals would like to suggest that the role of hormone antagonists be reviewed and included as a viable treatment option for patients with advanced hormone dependent prostate cancer. To date there are 11 published clinical papers to support the safety and efficacy of Degarelix. Inclusion in the guidelines will also reflect and support current UK practice. Currently antagonists are not covered by current NICE guidance and as there is a large amount of regional variation in practice, Ferring believe guidance should be given to ensure patients get the most appropriate treatment to achieve the best patient outcomes. Ferring Pharmaceuticals believe that national guidance is needed to produce consistent evidence-based clinical practice with degarelix. Degarelix is on 83 formularies. It is on 14 unrestricted, 63 with restrictions and approved but not yet purchased on 6 (due to waiting for shared care protocol etc). While degarelix is approved on these formularies in line with licence, clinical practice and guidance varies widely between hospitals. Please find examples of these regional guidance documents illustrating this	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.

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				variation below: SMC (Scottish Medicines Consortium) - The Scottish Medicines Consortium (SMC) approved HTA model demonstrates degaralex as a dominant technology in the PSA>20 population and delays the need for additional, later-stage and costly treatments such as chemotherapy. http://www.scottishmedicines.org.uk/files/advice/degarelix_Firmagon_RESUBMISSION_ FINAL_DECEMBER_2010.doc_for_website.pdf - links straight through & opens on the attached pdf. LCNDG (London Cancer New Drugs Group recommends for use in subgroups of advanced prostate cancer with critical metastases: http://www.nelm.nhs.uk/upload/documents/Communities/London_CNDG/The_London_ Cancer_Drugs_Fund_list_September_2011.pdf - links through & opens on the attached pdf. NECDAG (North of England Cancer Drug Approval Group) - http://www.cancernorth.nhs.uk/hpSite/groups/AdvisoryGroups/NECDAG/Decisions/2011 - links through to a list of 2011 NECDAG decision pdf documents, where the top of the list is the attached pdf. ECN - Essex Cancer Network does not have formally adopted commissioning guidance published, though their ChemoBoard Meeting Minutes (attached) indicate a propensity towards single dosing. http://www.essexcn.nhs.uk/pro/documents/CrossCuttingGroups/CancerDrugs/Minutes/ ecn%20chemo%20board%20%20sub%20group%20minutes%20010311.pdf MVCN - Mount Vernon Cancer Network demonstrates a belief that Degarelix is should be initiated as single dose and then switched: http://www.mountvernoncancernetwork.nhs.uk/assets/Uploads/Microsoft-Word-List-of-Medicines-and-Indications-for-Funding-by-the-MVCN-ICD-Fund.pdf	

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				PBCN - Pan-Birmingham Cancer Network - linking through & opens on the attached pdf showing on pages 13 & 18 Degarelix's listing for Routine, Unrestricted' use: http://www.birminghamcancer.nhs.uk/uploads/document_file/document/4eb3f803358e982df70002c4/network_formulary_2011_v8.4.pdf -	
SH	Ferring Pharmaceuticals	26.11	4.1.1 l)	Ferring Pharmaceuticals would like to highlight the importance of the role of degarelix when there is impending or actual spinal cord compression. This is when clinical implications of rapid testosterone and PSA reduction without an initial "flare" is vital to avoid long term complications. The importance of flare avoidance has been highlighted in the recently published European Association of Urology (EAU) Guidelines – *initial rapid onset of action is particularly important and of benefit in symptomatic metastatic patients who present with bone pain, impending spinal cord compression and urinary outflow obstruction.* Degarelix rapidly suppresses serum testosterone levels. This is associated with a concomitant reduction in PSA, which indirectly demonstrates a tumour benefit. In a phase III study, degarelix suppressed testosterone to castrate levels (<0.5ng/mL) in 53% of patients at day 1 and 96% of patients at day 3 (Klotz L et al, 2008). In contrast, LHRH agonists cannot offer a similar efficacy. Testosterone suppression is not achieved over the first 7-14 days and PSA reductions are delayed in comparison to degarelix, which is suggestive of a delayed tumour response (Klotz L et al, 2008).	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Ferring Pharmaceuticals	26.12	4.2	Ferring would like to highlight that the cost–utility analysis for the SMC was accepted in 2011. It compared degarelix with goserelin in patients with advanced hormone-dependent prostate cancer, based on the assumption that there is a class effect for the LHRH agonists i.e. that no LHRH agonist had demonstrated superior efficacy to any other. The SMC classed degarelix as cost-effective with	Thank you for your comments. We have had discussions with the NICE Topic Selection team about where the inclusion of degarelix fits best within the NICE guidance producing

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				the inclusion of the PAS approved by the PASAG.  Ferring response to NICE Prostate Cance	programmes. The topic has been submitted into the Topic Selection process for Technology Appraisals and the outcome is that this topic is suitable to be scoped as a potential technology appraisal. Please see the technology appraisals webpage for further details.
SH	Royal College of Radiologists	27.00	3.3.1 a) ii	Our view is that multiparametric MRI (i.e. T2weighted sequences, diffusion weighted images and dynamic contrast enhanced images) is the best technique for localising cancer within the prostate and for guiding targeted biopsies of the prostate. We feel that MR Spectroscopy is a costly technique (in time and money) and is only really useful in a research setting. We therefore suggest that NICE guidance should emphasise the use of Multiparametric MRI in prostate cancer diagnosis.	A review of the evidence on multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy is planned as part of 3.3.1.a. We will not be able to make recommendations until we have reviewed this evidence. Further interventions will be prioritised by the GDG for inclusion in the guideline. This prioritisation will based on criteria such as a) the likelihood that they will have significant resource issues and b) clinical need and variation in clinical practice
SH	Cambridge University Hospitals NHS Foundation Trust	28.00	General	Terminology: clinically insignificant or indolent disease confused "low risk" - all lumped together which is misleading. It would be useful to try and separate patients within low risk into those with high chance of indolent cancer who would be suitable for active surveillance and those with lower chance of indolent cancer who would be less suitable for active surveillance. The 'low risk' group as per NICE guidance sadly has a huge variablility in terms of actual disease.	We have added a topic about 'active surveillance' to the scope.
SH	Cambridge University	28.01	General	'Men with low-risk localised prostate cancer who are considered suitable for radical treatment should first be offered active surveillance' - this statement is	We have added a topic about 'active surveillance' to the

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	Hospitals NHS Foundation Trust			deeply flawed, data to generate this is from American series (with PSA screening!) which does not translate to the UK population. Note that of the patients classified as per NICE recommendation with 'low risk' 30% had intermediate or high risk features on final pathology following radical prostatectomy (General application of the National Institute for Health and Clinical Excellence (NICE) guidance for active surveillance for men with prostate cancer is not appropriate in unscreened populations. Wong LM, Johnston R, Sharma N, Shah NC, Warren AY, Neal DE.BJU Int. 2011 Nov 11. doi: 10.1111/j.1464-410X.2011.10730.x. [Epub ahead of print] PMID: 22077729) Hence patients should be carefully counselled to all options rather than a blanket statement that All low risk patients should be first offered AS.	scope.
SH	Cambridge University Hospitals NHS Foundation Trust	28.02	General	Hormonal therapy is not routinely recommended for men with prostate cancer who have a biochemical relapse unless they have: symptomatic local disease progression, or any proven metastases, or a PSA doubling time < 3 months. - this should be changed to <12 months as <3months is too aggressive especially in otherwise healthy men (Loblaw et al., 2007)	We have added a topic about 'active surveillance' to the scope
SH	Cambridge University Hospitals NHS Foundation Trust	28.03	General	NICE does not specifically recommend biopsy protocol and currently most biopsies are done as TRUSPs. In pts with negative TRUSPs, but raised PSA and a high index of suspicion, given that that upto 20% of tumours may arise in ant PZ then consideration for targeting the Ant PZ 9 perhaps by transperineal route also.	A review of the evidence on optimal diagnostic strategy (including multiparametric magnetic resonance imaging, 3D ultrasound and template biopsy) is planned as part of 3.3.1.a. We will not be able to make recommendations until we have reviewed this evidence. Further interventions will be prioritised by the GDG for inclusion in the guideline

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					based on criteria such as a) the likelihood that they have significant resource issues and b) there is variation in clinical practice.
SH	Cambridge University Hospitals NHS Foundation Trust	28.04	General	1.3.22 Routine DRE is not recommended in men with localised prostate cancer while the PSA remains at baseline levels - the level of evidence for this is again poor, there are limitatons to PSA as NICE has already acknowledged and have recommended that PSA as a sole test should not act as a trigger for initial biopsy, but a DRE is recommended. On the same basis, pts on AS should have a PSA and DRE aside form a programme of rpt biopsy (protocols varied though!).	We have added a topic about 'active surveillance' to the scope.
SH	Cambridge University Hospitals NHS Foundation Trust	28.05	General	Update on Abiraterone and qualification of when it can be used.	This is the subject of a future NICE technology appraisal and therefore cannot be covered by this update.
SH	Cambridge University Hospitals NHS Foundation Trust	28.06	General	Worth putting forward a proposal that men in a curative age group who have been diagnosed with apparent low risk low volume disease who are wishing to consider active monitoring, should undergo repeat prostatic biopsy after 3T MRI to check that we are not undergrading or staging their disease.	We have added a topic about 'active surveillance' to the scope.
SH	Cambridge University Hospitals NHS Foundation Trust	28.07	General	With regard to intermittent androgen deprivation therapy we do not feel there is evidence to support this approach particularly in men who have no nodal or metastatic disease. Clearly it would be useful in men at risk of the metabolic syndrome also. We would personally have some concerns with adopting intermittent androgen deprivation therapy in patients with high risk metastatic or nodal disease.	A review of the evidence on this topic is planned as part of 3.3.1.g. We will not be able to make recommendations until we have reviewed this evidence.
SH	Cambridge University Hospitals NHS Foundation Trust	28.08	3.3.2.m	Why is 3.3.2 section m. hormone refractory prostate cancer is not being reviewed - is this because carbazitaxel and abiraterone are being appraised separately (3.3.3 part c)? There is some much change in this area it seems odd to not review the evidence.	Yes, this is due to the ongoing NICE technology appraisals.

These organisations were approached but did not respond:

Abbott GmbH& Co KG
Abbott Laboratories
Afiya Trust
African HIV Policy Network
Age UK
Airedale NHS Trust
Albyn Medical Ltd
All About Nocturnal Enuresis Team
Almac Diagnostics
American Medical Systems Inc.
Amgen UK
Aneurin Bevan Health Board
Anglesey Local Health Board
Arden Cancer Network
Arrowe Park Hospital
Arthritis Research UK
Association for Continence Advice
Association of Chartered Physiotherapists in Oncology and Palliative Care
Association of Clinical Pathologists
Astellas Pharma Ltd
Astrazeneca UK Ltd
B. Braun Medical Ltd
Bard Limited
Barnsley Primary Care Trust
Beating Bowel Cancer
Bedfordshire Primary Care Trust
Betsi Cadwaladr University Health Board
Boehringer Ingelheim
Bostwick Laboratories
Bradford and Airedale Primary Care Trust
Bradford District Care Trust
Bristol and Avon Chinese Women's Group
Bristol Cancer Help Centre
Bristol Myers Squibb Pharmaceuticals Ltd

British Association of Art Therapists
British Association of Urological Nurses
British Dietetic Association
British Geriatrics Society
British Lymphology Society
British Medical Association
British Medical Journal
British National Formulary
British Nuclear Medicine Society
British Prostate Group
British Psychological Society
British Society for Immunology
British Society of Interventional Radiology
British Uro Oncology Group
BUPA Foundation
C. R. Bard, Inc.
Calderdale Primary Care Trust
Camden Link
Cancer Black Care
Cancer Network Pharmacists Forum
Cancer Network User Partnership
Cancer Research UK
Cancer Services Co ordinating Group
Cancer Voices
Care Quality Commission (CQC)
Cariad Technologies Ltd
Central & North West London NHS Foundation Trust
Central South Coast Cancer Network
CHKS Ltd
Clatterbridge Centre for Oncology
Cochrane Bone, Joint and Muscle Trauma Group
College of Occupational Therapists
Coloplast Limited
Commission for Social Care Inspection
Community District Nurses Association
Countess of Chester Hospital NHS Foundation Trust
Covidien Ltd.
Dako UK Ltd

David Lewis Centre, The
Deltex Medical
Department of Health
Department of Health, Social Services and Public Safety Northern Ireland
Derby Burton Cancer Network
Dorset Primary Care Trust
Dudley PACT Patient Advisory Cancer Team
Dudley Primary Care Trust
Durham University
EDAP SA
Eisai Ltd
Endocare, Inc.
Equalities National Council
Essex Cancer Network
Faculty of Public Health
Fresenius Kabi Ltd
Galil Medical
General Practice and Primary Care
George Eliot Hospital NHS Trust
GlaxoSmithKline
Gloucestershire Hospitals NHS Foundation Trust
Gloucestershire LINk
Great Western Hospitals NHS Foundation Trust
Grunenthal Ltd
Guerbet Laboratories Ltd
Guildford & Waverley Primary Care Trust
Hayward Medical Communications
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Help the Hospices
Hull and East Yorkshire Hospitals NHS Trust
Humber and Yorkshire Coast Cancer Network
Imaging Equipment Ltd
Independent Healthcare Advisory Services
Institute of Biomedical Science
Intra Tech Healthcare Ltd
iQudos
Isabel Hospice

James Whale Fund for Kidney Cancer
JBOL Ltd
Johnson & Johnson
KCARE
KCI Medical Ltd
Kidney Research UK
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
Lesbian, gay, bisexual and trans domestic abuse forum
Lincolnshire Teaching Primary Care Trust
Link Pharmaceuticals
Livability Icanho
Liverpool Primary Care Trust
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
Ministry of Defence
National Cancer Action Team
National Cancer Network Clinical Directors Group
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Council for Palliative Care
National Institute for Health Research Health Technology Assessment Programme
National Kidney Research Foundation
National Osteoporosis Society
National Patient Safety Agency
National Public Health Service for Wales
National Radiotherapy Implementation Group
National Treatment Agency for Substance Misuse
Newcastle upon Tyne Hospitals NHS Foundation Trust

NHS Bath & North East Somerset
NHS Bournemouth and Poole
NHS Bromley
NHS Connecting for Health
NHS Cornwall and Isles Of Scilly
NHS Derbyshire county
NHS Improvement
NHS Kirklees
NHS Lothian
NHS National Cancer Screening Programmes
NHS Plus
NHS Warwickshire Primary Care Trust
NHS West Kent
Norfolk & Waveney Prostate Cancer Support
North East London Cancer Network
North East London Strategic Health Authority
North of England Cancer Network
North Trent Cancer Network
North Yorkshire & York Primary Care Trust
Nottingham City Hospital
Nottinghamshire Healthcare NHS Trust
Nucletron
Nutrition Society
Oncura Ltd
Orion Pharma
Ovarian Cancer Action
Oxford Nutrition Ltd
Oxfordshire Primary Care Trust
Pan Birmingham Cancer Network
PERIGON Healthcare Ltd
Pfizer
pH Associates Ltd
Pharmion Limited
Pilgrims Hospices in East Kent
Primary Care Pharmacists Association
Prostate Action
Prostate Brachytherapy Advisory Group
Prostate Cancer Support Federation

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 Pathologists
Royal College of Psychiatrists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Royal Society of Medicine
Royal Surrey County Hospital NHS Trust
Royal United Hospital Bath NHS Trust
Royal West Sussex NHS Trust
Sandwell Primary Care Trust
Schering Health Care Ltd
Scottish Intercollegiate Guidelines Network
Serono
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 East Wales Cancer Network
South Staffordshire Primary Care Trust
South West Yorkshire Partnership NHS Foundation Trust
Step4Ward Adult Mental Health
Stockport Primary Care Trust
Sussex Cancer Network
Sutton1in4 Network
Takeda UK Ltd
Taunton Road Medical Centre
Teva UK

The Association for Clinical Biochemistry
The Association of the British Pharmaceutical Industry
The British In Vitro Diagnostics Association
The National Association of Assistants in Surgical Practice
The National LGB&T Partnership
The Princess Alexandra Hospital NHS Trust
The Rotherham NHS Foundation Trust
UK Anaemia
UK National Screening Committee
UK NEQAS for Immunology and Immunochemistry
UK Specialised Services Public Health Network
United Kingdom Council for Psychotherapy
University College London Hospital NHS Foundation Trust
University Hospital Aintree
University Hospital Birmingham NHS Foundation Trust
University Hospitals Coventry and Warwickshire NHS Trust
University of Birmingham
University of Nottingham
Velindre Hospital, Cardiff
Walsall Teaching Primary Care Trust
Welsh Cancer Services Coordinating Group
Welsh Government
Welsh Scientific Advisory Committee
Wessex Cancer Trust
West Midlands Ambulance Service NHS Trust
Western Cheshire Primary Care Trust
Whipps Cross University Hospital NHS Trust
Wiltshire Primary Care Trust
World Cancer Research Fund
York Hospitals NHS Foundation Trust
Yorkshire & The Humber Specialised Commissioning Group