Head and Neck Mucosal Melanoma Guideline – Comments from the consultation and replies for the Guideline Development Group

Note: All page, recommendation and line numbers refer to the consultation document not to the final document – the comments are sorted into page order of the full guideline.

#	Name	Organisation if applicable	Full Guideline Page #	Exec Sum Page #	Either Recommendation # /Line # in full guideline	Comment	Final Response
55.		BDA		General		Apart from the above requests, the BDA welcomes this as a helpful and well-researched guideline.	Thank you for your comment.
50		BAD	General	General		Our reviewers commented that they found this an excellent document overall.	Thank you for your kind words.
54.		BDA		General		Particularly because HNMM is a rare condition, we would urge the authors to include a recommendation to train both GPs and dental practitioners in its recognition and referral.	The aim is that the guideline will assist with training. Some photos have been added.
85	Carol Leonard		General			I am so sorry not to be in a position properly to respond to the excellent draft. It is not easy to read, given my own involvement. There is one thing, however, that Professor Harrington will of course be taking into account. Not infrequently, because research is still ongoing. new 'combinations" can prove useful. (1) For one example, example, from Oncology: SMR 2019: Lifileucel Therapy Leads to Durable Response in Heavily Pretreated,	Thank you for your comments.

						Refractory, Advanced Melanoma, for those with BRAF mutations. (2) For another, ""The axitinib (Inlyta)/nivolumab combination that was published in the Journal of Clinical Oncology this year for mucosal melanoma, we've been increasingly using in patients with [the disease]. That's a whole new type of target to bring to melanoma. It's really exciting. I'm treating a few patients with it now." From: https://www.oncnursingnews.com/web-exclusives/combination-therapy-is-the-future-for-metastatic-melanoma-treatment There should be some way to ask the NHS to keep this in mind and be open to experimentation that has proved feasible (low toxicity) and seemingly encouraging of progression free survival, even if the length of the trial is necessarily short and there is selection bias. Thank you so much for letting me see this document.	
25	Dr David N. Slater	RCPath	General			The comments made on the guideline relate primarily to histopathology . With reference to histopathology , the guideline is robust , sufficiently evidence -based	Thank you for your comments. We would expect most readers to refer to the Executive Summary or the Care Pathway and accept that the full guideline makes tedious reading. Ideally it should be hyperlinked but that is expensive and difficult.

						and well written , reflecting the expertise of the authors. It has used the current WHO tumour classification , the ICCR reporting guide for mucosal melanoma of head and neck and has applied TNM8 in a suitable nature and in particular supporting UICC8. It has not fallen into the not infrequent trap with Melanoma Focus trap of using AJCC8 ! The latter is not formally adopted in the UK (and indeed the rest of the world except the USA) and its use carries a licence fee! Accordingly necessary comments on the guideline are fortunately very limited Sadly, however, the guideline does make for very tedious reading and ' spot look-up' with the summary of studies being inserted in the main guideline rather than as evidence in a stand alone part or in the Appendix. It would be good if this format was altered to help readers but I appreciate there will be reluctance to do so.	
79	Dr Mehmet Sen		General			I read and reviewed the sent draft guidelines with a specific interest in radiotherapy section. I have no additional comments on its current	Thank you for your help

						format of the draft documents. I noted the literature search was limited to 2019 but new relevant large patient number papers published in 2019. I attached these references for the attention of Drs. Kent Yip and Pablo Nenclares. It may not be possible to use in these references but might be useful for future references.	
70	Dr Richard Simcock	Macmillan	General			The whole document is an impressive evidence review. Time for review has not allowed to check all of these references or search for potentially 'missing' references.	Thank you for your kind words!
24	Nimesh N Patel	Specialised Cancer Surgery CRG	General			**Commissioning Notes** HNMM should be commissioned with UAT Cancers HNMM Treatment should involve HN, melanoma and skullbase MDTs, An individual trained in advanced endoscopic rhinology should be a named member of the team caring for HNMM patients High quality prosthetic rehabilitation including osseointegrated implants needs to be available to patients where appropriate	Noted with thanks

						Patients need access to teams with skills in reconstruction of complex midfacial defects this includes microvascular reconstructive surgery Consideration needs to be given to specialist pathology especially molecular diagnostics Many patients have profound psychological distress and commissioning needs to include provision of psychological support Imaging follow up recommended here is onerous, although will certainly serve to provide evidence upon which to base future recommendations, but in the absence of proven locoregional control or survival benefit, this would need to be reviewed as evidence becomes available. Commissioning KPI recommendation?- all patients to be entered into a national database when/if this is implemented	
56.	Petra Jankowska			General		I have carefully reviewed the Executive summary and chapters 1-11 of the draft guidance. I made a point of especially reviewing all the	Thank you for your comment.

						clinical chapters relevant to my practice and expertise. The content is great, but there are just some grammatical errors and typos I noticed.	
68.	Prof Hisham Mehanna			General		Thank you for asking me to review these guidelines. They are timely and much needed. They have been written v I would like to congratulate you on an excellent document and considerable amount of work. They have been written very well and are very clear.	Thank you for your kind words.
28	Prof Mirimanoff	ESTRO	General			Thank you for asking to me to review the Executive Summary and Draft Guideline on Head and Neck Mucosal Melanoma (HNMM). Please find enclosed my comments on both documents. As a general comment, these documents represent a very comprehensive and well done overview on HNMM. However, as a radiation oncologist, I found that in general, the role of radiotherapy was underestimated and should be better stressed. I'd be happy to receive some feed-back from my own comments by the writing committee.	Thank you for your suggestions. We have taken on board your comments about the role for radiotherapy and have, we believe, adopted a more balanced position.

4.	Prof Speight				6	Add a recommendation 6: Do you think that we should make a n explicit recommendation that wherever possible and/or appropriate, all patients should be considered for entry into an appropriate clinical trial And give a link to where clinicians can search for open trials. This is mentioned in section 5	This information is available on the Melanoma Focus website.
38.	Prof Mirimanoff	ESTRO		8	Between 38 and 39	Between the chapters "Sentinel lymph node …etc" and "Adjuvant systemic therapy" , there should be, in my opinion, a chapter with a table entitled "Radical radiotherapy for medically or surgically inoperable patients". (this chapter should be separated from the chapter on "Post-operative radiotherapy"). Indeed, in case of inoperable HNMM, and in the absence of multiple metastases, (as for example, in locally advanced sino-nasal MM or in case of invasion of the base of skull), high-dose, high precision RT (HDHPRT), including particle therapy, should be a first choice, as the local control (LC) is between about 60% and 84 % with HDHPRT. (Please refer to the Draft Guidelines, pages 86-90, Table 20, and in particular to the following	Thank you for the suggestion, this has been added

						references: Combs 2009, Demizu 2014, Fuji 2014, Gilligan 1991, Zenda 2016, and a paper not quoted in the Draft by Gaze et al., in Clin. Oncol. 1990) In comparison, the "response rate" with chemotherapy (LC is almost never reported with chemo !) is only between about 15% and 25 % (see Table 28, pages 121 and 122), and the response rate with immune checkpoint inhibitors is only between about 20% and 25 %, with very few complete responses, when reported ! (see Table 29, page 123, 124).	
86	Dr Jonathan Leech Dr Gail Allsopp, Dr Richard Roope, Hannah Trippier	RCGP	2		General	It would be helpful to have the average UK incidence documented in the guideline. For example, mucosal melanoma accounts for 1-2% of all melanomas, which would suggest 160-320 cases per year in the UK.	Unfortunately, we couldn't find any definitive data for the UK.
1	Prof Speight		7		23	Replace "laryngo-pharyngeal" with "larynx and pharynx"	Changed thanks
51	Dr Richard Simcock	Macmillan	7		31	Missing full stop.	Corrected thanks
8	Nimesh N Patel	Specialised Cancer Surgery CRG (check OK)	7		37	*Former* should be *first*	Corrected with thanks

2	Prof Speight		7		37	Needs a full-stop after "guideline"	Corrected thanks
3	Prof Speight		7		38-40	I think it would be helpful to also state what the incidences rates are, and also the number of cases (registrations) per year in UK. Is there good UK data?	It proved impossible to find this information specifically for the UK.
4	Prof Speight		8		4	?across England. Are these guidelines only applicable to England. Are there similar guidelines for the devolved nations?	The GDG only represented England, however anyone is free to use them.
38		BAD	8		43	Did any of the adjuvant trials include any mucosal MMs, in particular HNMM?	These are noted where they are used in the evidence.
52	Dr Richard Simcock	Macmillan	9		25	Refers to "the latter" (retrospective studies) but then says "when HNMM have been included within prospective trials" which seems contradictory.	Have answered in separate email response
29	Prof Mirimanoff	ESTRO	9		5	Regarding medically or surgically inoperable disease, one should emphasize on the role of comprehensive, high-dose high precision radiotherapy (RT). Please refer to my detailed comments in "executive summary", page 8, recommendation 38 and 39.	This has been revised, thank you for your suggestions.
36	Prof Mirimanoff	ESTRO	9		5 6	Regarding medically or surgically inoperable disease, one should emphasize on the role of comprehensive, high-dose high precision radiotherapy (RT). Please refer to my detailed	This has been revised, thank you for your suggestions.

						comments in “executive summary”, page 8, recommendation 38 and 39.	
53	Dr Richard Simcock	Macmillan	10		1	The reference here to ‘tertiary centres’ here comes without preface as to the location of treatment/care and seems redundant (although this is then referenced again p17, line 20)	As the full guideline and recommendations are aimed at health professionals, we don’t think that this needs any explanation, but we will explain in the patient information.
39		BAD	10		28	Was it sent to the British Association of Dermatologists?	These comments were sent in on behalf of BAD.
40		BAD	10		39	Were conflicts of interest declared?	Declarations of interest from guideline development group members will be published with the guideline. Named reviewers (BAD comments submitted anonymously) were asked to submit a DOI form. These are available on request.
54	Dr Richard Simcock	Macmillan	13		6	“in qualitative evidence” should be “on qualitative”	Corrected thank you
55	Dr Richard Simcock	Macmillan	13		8	“while” is unnecessary here	Corrected thank you
56	Dr Richard Simcock	Macmillan	14		21	Supportive of this recommendation and aligns with managed self-care aims however what the guidance lacks is the instruction for treating units to establish these protocols. Our experience at Macmillan (particularly with Breast cancer and self-care protocols) has been that centres need to discuss internally and with CCG colleagues the mechanisms whereby a patient gets back into the system “quick and	The passage you are referring to is not one of our recommendations, but is illustrating what is in some of the NICE recommendations.

						easily" – for example services will be commissioned differently if patient request for review triggers a new of follow up out-patient appointment. In units where this is triaged by a CNS those CNS need to be empowered and enabled to book direct into appropriate clinics. Patient education clearly important but service redesign needs to precede it.	
9	Nimesh N Patel	Specialised Cancer Surgery CRG	14		25	Is this relevant in patients with mucosal melanoma?	This was quoting from the NICE cutaneous melanoma guideline. It is not reflected in the recommendations.
57	Dr Richard Simcock	Macmillan	14		37/38	"were written" repeated	Corrected thank you
10	Nimesh N Patel	Specialised Cancer Surgery CRG	14		41	Surgeon should be a "head and neck surgeon"	This is a direct quote from another guideline so cannot be changed.
58	Dr Richard Simcock	Macmillan	14		46	The term "cancer nurse specialist" used here	This is the review section which has summarised other guidelines which contributed to the formulation of the recommendations in this guideline. Therefore the term in this section is taken directly from the guideline
59	Dr Richard Simcock	Macmillan	15		1	The term "Clinical Nurse Specialist" used here – this is the preferred term and it would be better if the same term is used consistently throughout the document	This is the review section which has summarised other guidelines which contributed to the formulation of the recommendations in this guideline. Therefore, the terms in this section are taken directly from the guideline being discussed. The view of patient representatives on the guideline were that 'Cancer Nurse Specialist' was a better term as it avoided confusion with surgical Clinical Nurse Specialists. We have used this term consistently in the recommendations.

60	Dr Richard Simcock	Macmillan	15		21-23	This sentence is poorly written	Re-written
11	Nimesh N Patel	Specialised Cancer Surgery CRG	15		3	Is the groin a site for mucosal melanoma mets?	This is referring to guidance in the AUG guideline and is not advising on this guideline.
1.	Prof Speight		**16**	4		Line 13. Better to say "larynx and pharynx" rather then "laryngo-pharyngeal".	Changed thanks
2.	Prof Speight		**16**	4	1	"Information should be available at all stages ……." Not clear, ?stages of what.. Does this mean "…at all stages of the patient care pathway."?	This has been clarified.
74.	Dr Tom Roques	RCR	16	4	2	These patients are usually most effectively managed by a H&N MDT with support of the melanoma MDT rather than the other way round. This recommendation should make it clear that the lead H&N melanoma clinician could be in the H&N MDT (e.g. the H&N MDT chair)	The recommendation reflects the experience and view of best practice of the GDG. These are guidelines and can be adapted to the local situation which, on occasion, may favour management led through the H&N MDT.
5.	Dr David N. Slater	RCPath	**16**	5	2.6	See full guideline on multidisciplinary teams. Not repeated here as requested but requires correction as full guideline	Noted
75.	Dr Tom Roques	RCR	**16**	4	3	The first two bullet points duplicate each other as the CNS is usually the key worker	The view was that there could be exceptions.
28.	Ms Jane Henderson		**16**	5	3	Educational materials ++ contact details of CNS	Thank you

76.	Dr Tom Roques	RCR	**16**	5	6	This needs to reflect any changes to 2) based on the above comments. In my experience for sinonasal HNMM the HN MDT would usually take the lead on communication with other professionals rather than the melanoma MDT	This wasn't the view of the GDG
14.	Mr Stuart Winter	BAHNO	**16**	5	6	When referring to a specific melanoma pathologist is this a predetermined individual in all units with a head and neck MDT? Smaller units will have a merged melanoma team with their skin MDTs.	I see the point. There may not be a "melanoma pathologist" but all specimens should be reviewed by a pathologist who is experienced in melanoma diagnosis – in most path units we would refer to such a person as the "melanoma pathologist".
15.	Mr Stuart Winter	BAHNO	**16**	5	6	When referring to the specialist melanoma MDT is this synonymous with the skin MDT in smaller units or an additional arm of oncology?	The emphasis is on expertise in melanoma. We agree that in some hospitals, the expertise in melanoma will sit under the umbrella of a broader skin MDT.
16.	Mr Stuart Winter	BAHNO	**16**	5	6	Is there a risk of delays to treatment and discrepancies between MDTs with the multi-MDT structure here? Would it not just be better that all cases are simply run through the head and neck MDT with a melanoma oncologist present>	This is based on best practice and can be interpreted with regard to local structures. Appropriate streamlining of the service should avoid systematic delays.
29.	Ms Jane Henderson		16	5	6	Hard copies of results available to patient at patient request	This would be at the discretion of individual centres.
71	Mr Michael Ho - SSIG lead for Head and Neck Reconstruction	BAOMS	17		15	Replace 'extirpative' with 'resective'	The think that extirpative is more accurate.

41		BAD	17		19	Agree in principle, but might be difficult if elderly and have to travel a long way to access - what is their definition of a tertiary centre?	This would be the decision of the individual clinician
12	Nimesh N Patel	Specialised Cancer Surgery CRG	17		24	Specifying subspecialist is inappropriate as there are different practices nationwide- eg. In some departments all sinonasal cancers are under the remit of ENT surgeons others all under OMFS	Thank you, we have used a more generic term.
26	Dr David N. Slater	RCPath	17		5.3.1	Although pure specialist melanoma MDTs were listed by NICE , in reality only a very small number exist . Mucosal melanoma of Head and Neck is most frequently considered by the melanoma section of Specialist Skin Cancer MDTs (as per NICE for England and Wales) , in conjunction with the Head and Neck MDT. This should clarified or readers could be perplexed by the type of MDT to be used	This has been clarified.
93.		BASCSN	17	6	6	'Following the melanoma MDT discussion, a named consultant responsible for the patient's care' - on this part it could be the Skin cancer CNS or MDT coordinator that could share this information	We agree
77.	Dr Tom Roques	RCR	18	5	8	This could be qualified - 'if the person is well enough to consider systemic therapy'	This would be at the discretion of the clinician.

53.		BDA	19	19	8-14	The BDA is concerned that dentists should be explicitly mentioned as a source of referrals for head and neck lesions.	Thank you for pointing this out, we have added reference to dentists.
13	Nimesh N Patel	Specialised Cancer Surgery CRG	28		18	What screening is recommended for unknown primary melanoma nodal mets?	This will include a skin survey, direct visualisation of mucosal surfaces (flexible endoscopy), examination of the uvea and a PET-CT scan.
42		BAD	28		8	They refer to the diagnosis of cutaneous melanoma in some cases below page 32 and therefore should patients be sent for a skin check on diagnosis or wait until histopath results are back? How easy is it to distinguish? mucosa	Evidence does not support patients presenting with both mucosal melanoma and cutaneous melanoma so a skin survey is not required for patients mucosal melanoma.
97.	Dr Jonathan Leech Dr Gail Allsopp, Dr Richard Roope, Hannah Trippier	RCGP	29	6	10	Consider rewording this statement as nosebleeds and nasal obstruction do not feature in NG12 as suggested in the executive summary https://www.nice.org.uk/guidance/ng12/chapter/1-Recommendations-organised-by-site-of-cancer#head-and-neck-cancers In order to align fully with NG12, the recommendation should read: Patients with persistence or recurrence of any of the following symptoms or signs lasting approximately 3 weeks or more should be referred to a head and neck clinic via the urgent cancer	Our wording states this- no need to change.

						referral pathway (e.g. two-week wait pathway). o unilateral nosebleeds lasting 3 weeks or more o unilateral nasal blockage or obstruction (not responding to topical steroids) lasting 3 weeks or more o Bilateral nasal blockage not responding to topical steroids lasting 3 weeks or more o a non-healing mouth ulcer a lump in the mouth with or without pigmentation or bleeding lasting 3 weeks or more* o a lump in the mouth with or without pigmentation or bleeding* *as per NICE guidance NG12 https://www.nice.org.uk/guidance/ng12	
69.	Mr Donald Holt SSIG Lead for Skin Surgery	BAOMS	29	6	10	Indication for referral "A lump in the mouth with or without pigmentation or bleeding". These criteria would encompass many common place benign pathologies found within the mouth such as mucoceles, fibroepithelial polyps, epulides of any variety, pyogenic granulomas etc. I do not agree that this would not potentially overwhelm out patient clinics with benign pathology and potentially make access for	This has been reworded with thanks.

						significant pathology more difficult. I wonder if this criteria could be finessed to prevent this, for example requiring rapid growth or bleeding or stressing the common sites for melanoma are the palate or gingiva. The real challenge with mucosal melanoma is its rarity and very few practitioners will see such lesions which will often mandate biopsy. The guidelines as they are would require the fast track biopsy of every lump within the oral cavity which would be a significant drain on resource. Whilst 10 -30% of oral lesions may be amelanotic, the majority will have some pigmentation and I would have liked the guidance to guide the biopsy of oral pigmented lesions. My and many colleagues current practice is to biopsy virtually all pigmented lesions to ensure diagnosis of a melanoma is not missed. Are there any criteria of pigmented lesions within the mouth eg location, pattern, thickness, location, which could be used to guide practice, for example advising that all palatal or gingival pigmented lesions are biopsied unless part of a widespread pattern of	

						melanosis as seen in smokers. (D Holt)	
58.	Prof Hisham Mehanna		29	5	10	bilateral should be small letter	Corrected with thanks.
30	Prof Mirimanoff	ESTRO	29		10	Add the following relevant symptoms to the existing list: 1) neck lumps/ lymphadenopathy 2) sinus/facial pressure or tenderness 3) hoarseness 4) wheezing, hard breathing	Persistent neck lump added and hoarseness added.
31.	Prof Mirimanoff	ESTRO	**29**	5 &6	10	Add the following relevant symptoms to the existing list: 1) neck lumps/ lymphadenopathy 2) sinus/facial pressure or tenderness 3) hoarseness 4) wheezing, hard breathing	Persistent neck lump added and hoarseness added.
37	Prof Mirimanoff	ESTRO	29		10	Add the following relevant symptoms to the existing list: 1) neck lumps/ lymphadenopathy 2) sinus/facial pressure or tenderness 3) hoarseness 4) wheezing, hard breathing	Persistent neck lump added and hoarseness added.
14	Nimesh N Patel	Specialised Cancer Surgery CRG	29		51	Bilateral nasal obstruction resistant to steroids is not a viable 2ww referral criteria, the criteria here would totally overwhelm 2ww services	Agreed, we already removed this.
87	Dr Jonathan Leech Dr Gail Allsopp, Dr Richard Roope, Hannah Trippier	RCGP	29		6 table	Consider replacing "hoarseness" with "persistent hoarseness" See comment from page 6, comment 10 in executive summary	This has been changed with thanks.

43		BAD	30		1	Under the diagnosis section 6.2 they should include a total body skin examination. The reason is that primary cutaneous melanoma can metastasise to mucosal surfaces, and mimic HNMM. It's rare, but so is NHMM. I don't think the recently published evidence that patients with primary cutaneous melanoma have an increased risk of oral HNMM is terribly relevant since the absolute increase in risk is so small, but thought they should probably at least be aware if not mention it.	Thank you – this was beyond the scope of the guideline.
5	Prof Speight		30		10	Table 4: States that "The optimal order of diagnostic investigations: Fine Needle Aspiration Cytology (FNAC), Core Biopsy" This cannot apply to mucosal lesions, although it may be appropriate for nodal metastases. FNAC should never be used as a biopsy technique on a mucosal lesion (and some (often trainees) still do this!!). The optimal diagnostic intervention is a proper incisional biopsy, a punch biopsy can be used but is not ideal. An excisional biopsy may be OK on small lesions but is always risky because the biopsy is often too small.	Both the PICO question and the recommendation have been changed with thanks.

						See also recommendation 13. FNAC or core biopsies are for use on lymph nodes either after diagnosis of the primary tumor OR in the case of an unknown primary. BUT imaging first.	
44		BAD	31		1	How easy is it to distinguish between a primary HNMM or metastatic lesion with unknown primary? Is this just done on molecular profile? This isn't obviously discussed.	It is not possible to distinguish based on histology alone. This is part of the clinical investigations. There is lot of overlap between molecular diagnostics of mucosal and cutaneous melanomas, although the incidence of mutations in mucosal melanoma is less as compared to cutaneous counterpart. Hence one cannot completely rely on these techniques alone as well.
44.	Dr Bushra Awan	BSHNI	31	6	11	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.
98.	Dr Jonathan Leech Dr Gail Allsopp, Dr Richard Roope, Hannah Trippier	RCGP	31	6	11	The opening sentence does not make sense and should be rewritten avoiding the typos and repeated wording "Ideally, where practical imaging should or Ideally, where practical, imaging should precede …."	Noted with thanks
78.	Dr Tom Roques	RCR	31	6	11	The stem does not make sense	This has been changed thank you

92.	Miss Lisha McClelland		31	6	11	Sentence confusing – should it read: Ideally, where practical, imaging should precede biopsy.	Noted with thanks
70.	Mr Donald Holt SSIG Lead for Skin Surgery	BAOMS	31	6	11	The opening line has repetition and a typo after should	Corrected, thanks
10.	Mr Stuart Winter	BAHNO	31	6	11	Typo: Ideally, ~~where practical, imaging should pr ideally~~ where practical, imaging…….	Corrected, thanks
17.	Mr Stuart Winter	BAHNO	31	6	11	Imaging should "pr" ideally ……typo	Corrected, thanks
26.	Ms Jane Henderson		31	6	11	Clerical error – omit wording within brackets -after 'Ideally'	Corrected, thanks
59.	Prof Hisham Mehanna		31	6	11	first sentence should be corrected due to typos	Corrected, thanks
32.	Prof Mirimanoff	ESTRO	31	6	11	Remove the following words or letters on line one: "imaging should pr" and after ideally , remove "where practical" (redundant)	This has been corrected
3.	Prof Speight		31	6	11	Delete "Ideally, where practical, imaging should pr"	Corrected with thanks
45.	Dr Bushra Awan	BSHNI	31	6	12	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.

11.	Mr Stuart Winter	BAHNO	31	6	12	Option of MRI or CT is mentioned in point 20 whilst in point 12 “should be considered”(consistency required)	Corrected, thanks
18.	Mr Stuart Winter	BAHNO	31	6	12	What if any are the indications for PET scanning for mucosal melanoma cases in light of its tendency to be multifocal at presentation? Is PET any more sensitive than MRI?	PET-CT has a role if surgery is being considered. Otherwise it is unlikely to influence management. The primary is diagnosed clinically and histologically and locally staged with CT and/or MRI, which better depict the local extent than PET-CT. MRI is more sensitive for brain metastases than PET-CT
60.	Prof Hisham Mehanna		31	6	12	should the word potential orbital for skull base be inserted?	Evidence is limited regarding the relative advantages of CT vs MRI in the assessment of osseous invasion of the skull. In general, CT often better depicts cortical destruction/ permeation than MRI. MRI can better depict marrow infiltration. The modalities are complementary, but either is satisfactory in the assessment of osseous invasion. Intra-orbital disease and peri-neural invasion however are better on MRI
33.	Prof Mirimanoff	ESTRO	31	6	12	Line 3, after CT, add PET-CT (as this exam is mentioned in the Draft Guidelines)	The wording was agreed by the GDG.
71.	Mr Donald Holt SSIG Lead for Skin Surgery	BAOMS	31	6	13	Where excisional biopsy is carried out, should pre-biopsy photography be undertaken to assist with localisation of the primary should further excision be desirable?	This has been added to recommendation.
19.	Mr Stuart Winter	BAHNO	31	6	13	Regarding quality of biopsy is it worth specifying the clinical depth of the biopsy sample?	This has been changed, with thanks.
45		BAD	31		16	This relies on a high level of suspicion for it being a HNMM - do we know what the pathway is normally for	Agreed. Pre-biopsy imaging is ideal, to better investigate the invasive front of the tumour and to avoid confounding interpretation with post-biopsy artefact. The recommendations also allow for post-

						investigating the signs they allude to above?	biopsy imaging, as melanoma may not have been anticipated at the time of biopsy, and the order will as you say depend on the degree of suspicion. Existing pathways depend on local practice and local infrastructure and are not prescriptive
15	Nimesh N Patel	Specialised Cancer Surgery CRG	31		17	A punch biopsy is not usually performed in the nose/sinuses (simply incisional biopsy/representative sampling biopsies	This has been changed, with thanks.
46.	Dr Bushra Awan	BSHNI	32	6	14	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.
20.	Mr Stuart Winter	BAHNO	32	6	14	For failed FNA's what is the guidance? Does a failed core biopsy warrant open nodal sampling?	This has been clarified
27.	Ms Jane Henderson		32	6	14	If FNA fails to obtain cell retrieval then schedule core biopsy	We do recommend FNA but core biopsy is an alternative.
16	Nimesh N Patel	Specialised Cancer Surgery CRG	32		14	Core biopsy of a lymph node in potentially operable disease should be avoided if possible, advise fine needle aspiration cytology	We do recommend FNA but core biopsy is an alternative.
79.	Dr Tom Roques	RCR	32	6	15	How is this different from 19?	Thank you, this has been consolidated.
17	Nimesh N Patel	Specialised Cancer Surgery CRG	32		15	Does tumour depth mean tissue levels invaded?	No, it means measured depth

61.	Prof Hisham Mehanna		32	6	15	should there be a recommendation as desirable to immunostain for PD-L1.	This has been added to the recommendation under *additional features*, with thanks.
80.	Dr Tom Roques	RCR	32	7	16	Might be better worded as 'should seek a second opinion' rather than 'should be encouraged to seek a second opinion'	Agreed, the word 'encouraged' has been deleted.
30.	Ms Jane Henderson		32	7	16	Omit 'be encouraged'. Insert 'be mandatory'.	The wording has been changed.
46		BAD	32		17	I assume that this would be diagnosed on the histopath biopsy?	Yes, that is correct.
6	Prof Speight		34		23	This section address pathological staging and reporting (ICCR dataset guidelines). So the heading might be better as: "Pathological staging and pathology datasets." Or "Pathological staging and preparation of pathology reports".	The heading has been changed.
27	Dr David N. Slater	RCPath	34		7.2.1	The most important organisation to have adopted UICC8 is omitted! This was Public Health England for England and Wales and therefore importantly includes Cancer Registries. This must be added here as well as in the Appendix. It is not clearly stated that it is UICC8 has been adopted in the UK and not AJCC8	This has been added.

80	Miss Lisha McClelland		36		6	T4a: Should this also include extension into orbital contents?	This isn't included in the definition
81.	Dr Tom Roques	RCR	37	7	19	How is this different from 15?	This has been cross-referenced.
62.	Prof Hisham Mehanna		37	7	19	would be better placed in the section before on diagnosis.	This has now been cross-referenced.
6.	Dr David N. Slater	RCPath	**37**	8	2.18	This omits the vital advice that UICC8 should be used (accepting as stated that UICC8 and AJCC8 are identical)	This has been clarified.
72	Mr Michael Ho - SSIG lead for Head and Neck Reconstruction	BAOMS	38		1	Should the reference be superscripted at the end of the sentence?	Thank you
18	Nimesh N Patel	Specialised Cancer Surgery CRG	38		1	Typo: investigations	Corrected thank you
7	Prof Speight		38		1	This section addresses clinical staging and imaging. So the heading might be better as: "Clinical staging and imaging investigations."	This has been changed.
61	Dr Richard Simcock	Macmillan	41		3	Row 3 : SUV / MRI and CT would all usually be capitalised	Corrected with thanks
81	Miss Lisha McClelland		45		20	Orthopantomogram - would not be standard recommendation for sinonasal/ laryngeal tumours imaged by CT + MRI unless receiving radiotherapy.	This has been qualified.

						Should it be optional rather than recommended?	
47.	Dr Bushra Awan	BSHNI	46	7	20	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.
82.	Dr Tom Roques	RCR	46	7	20	This duplicates several of the earlier recommendations eg 14. Could they be consolidated.	These have been revised.
12.	Mr Stuart Winter	BAHNO	46	7	20	EUA is listed as a procedure that "should" be included – this is not always necessary and perhaps better phrased as "should be utilised where direct visualisation is not possible" or similar	This has been changed
48.	Dr Bushra Awan	BSHNI	46	7	21	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.
72.	Mr Donald Holt SSIG Lead for Skin Surgery	BAOMS	46	17	21	Currently states at presentation should be staging of thorax abdomen, pelvis. Should this be amended to at diagnosis?	Thank you. We agree. The guideline wording has already been altered appropriately
34.	Prof Mirimanoff	ESTRO	46	7	21	Add after CT " PET-CT", (as this exam is mentioned in the Draft Guidelines, page 45 , under 7.3.2.5,)	This has been changed
36.	Prof Mirimanoff	ESTRO	46	7	21 22	Recommendations 21 and 22 seem redundant	This has been changed
49.	Dr Bushra Awan	BSHNI	46	7	22	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.

73.	Mr Donald Holt	BAOMS	46	17	22	Could this be expanded?, what criteria for imaging of brain, clinical, eg headaches, focal neurology or stage of melanoma at presentation. Should all lesions above T2 or T3 be automatically imaged?	Thank you. This has been altered appropriately
21.	Mr Stuart Winter	BAHNO	46	7	22	MRI brain – specify whether the consideration is site specific eg maxillary, multisite, treatment modality (local/systemic) stage to guide MDT decision making in this context because of propensity for metastases to be located in the brain. Or consider merging 22 and 23. Ref Gorka 2016	Thank you. This has been altered appropriately
35.	Prof Mirimanoff	ESTRO	46	7	22	CT is mediocre for the detection of brain metastases (BM), so MRI only should be recommended unless contraindicated	The view of the GDG was that it was preferable to have a CT if an MRI wasn't available urgently.
62	Dr Richard Simcock	Macmillan	47			The GDG in discussion recommend MRI over CT for detection of intracranial metastases yet the guideline (p46) states: "Consider MRI or CT of brain. " Would it more helpful as guidance to add that MRI is preferred?	Thank you. We have changed this to contrast enhanced MRI of the brain
94.		BASCSN	48	7	21	Ct scan with or without contrast	Thank you. We have changed this to contrast enhanced MRI of the brain

95.		BASCSN	48	7	22	Ct scan with or without contrast	Thank you. We have changed this to contrast enhanced MRI of the brain
63	Dr Richard Simcock	Macmillan	49		10	What does 'triple negative' mean in this context? The term is not used at all throughout the rest of the document	A definition has been added.
19	Nimesh N Patel	Specialised Cancer Surgery CRG	55		16	Therefore, guidance should recommend fresh tissue specimens to be taken for molecular diagnostics	Molecular diagnostics can be performed on Formalin-Fixed Paraffin embedded tissues (FFPE) and our lab routinely uses FFPE. Many labs will not have facilities to store fresh tissue and hence would not be a viable recommendation to do so.
83.	Dr Tom Roques	RCR	58	8	28	Does this mean that microscopic PNI is a contraindication to curative surgery? The evidence for this seems weak.	Agree, have made changes
73	Mr Chi-Hwa Chan - SSIG lead for Oncology	BAOMS	58		28	Recommendation 28 • Unacceptable morbidity – this is relative depending on patients and cultural perceptions. Perhaps replace with: The benefits of surgical intervention when evaluated within the context of treatment related morbidity is limited, and unlikely to have a positive impact on survival and/or quality of life	This has been changed

						• When there is evidence of intracerebral or perineural disease – perhaps replace with: When there is evidence of intracranial metastasis or extracranial perineural disease where a negative resection margin is not achievable (M Ho) In this recommendation, surgery is contra-indicated 'When there is evidence of intracerebral or perineural disease'. What I think would be appropriate is to comment on the situation where the primary site is clearly in one of the head and neck subsites and operable, but distant metastases are present on the staging scans of CT, MRI or PET/CT. Is surgery to the primary melanoma still indicated provided that intracerebral or perineural disease is absent, and systemic therapy is also part of the treatment plan?	

63.	Prof Hisham Mehanna		58	8	28	should distant metastatic disease also be a contraindication to surgery?	This has been revised, thank you for your suggestions.
31	Prof Mirimanoff	ESTRO	58		28	Regarding contraindications to surgery: 1) the presence of single or even of oligo brain metastases (BM) should not be a contraindication to surgery, as radiosurgery (RS) , or stereotactic radiotherapy (SRT) are very efficient to eradicate brain metastases in this situation 2) In general, single or oligometastases elsewhere (ex :liver, lung) should also not be contraindications for surgery for the same reasons (efficacy of RS or SRT). 3) I would include "disseminated disease", or "multiple metastases" (like bone, lungs, brain etc) in the list of contraindication.	This has been changed, with thanks.
37.	Prof Mirimanoff	ESTRO	58	8	28	Line 3: 1) I disagree with this statement: the presence of single or even of oligo brain metastases (BM) should not be a contraindication to surgery, as radiosurgery, or stereotactic radiotherapy (SRT) are very efficient to eradicate brain metastases in this situation 2) In general, single or oligometastases elsewhere (ex liver, lung) should also not be contraindications for surgery for the same reasons (efficacy of SRT). 3) Finally, I	This has been revised, thank you for your suggestions.

						would include “disseminated disease”, or “multiple metastases” (like bone, lungs, brain etc) in the list of contraindications.	
20	Nimesh N Patel	Specialised Cancer Surgery CRG	59		12	Endoscopic resection is not possible once disease has involved certain structures eg. skin on nasal dorsum and orbit There is a place for radical open surgery if clear margins are possible and morbidity acceptable Endoscopic resections tend to be performed for more limited disease/ selection bias might influence outcomes data	This is suggested in the recommendation without being too prescriptive.
84.	Dr Tom Roques	RCR	59	8	29	Rephrase to avoid two uses of 'involvement'?	This has been correct thanks
21	Nimesh N Patel	Specialised Cancer Surgery CRG	62		1	To deliver this guideline an experienced Rhinologist with skills in anterior skull base surgery/tumour resection has to be clearly identified as an extended member of the Head and neck MDT	Agreed, we have said in the recommendations “Patients with HNMM should be seen by surgeons who practise in an MDT with an appropriate skill mix”. So this should do and we feel there is no need to specify it should be a rhinologist
22	Nimesh N Patel	Specialised Cancer Surgery CRG	62		1	Mosaic resection and margins need strict monitoring and protocol to ensure monitoring of clear margins/ there is a significant risk of sampling error in margin determination with endoscopic resections	In the follow up section, we have indicate a follow up protocol with examination of the area and monitoring

74	Mr Michael Ho - SSIG lead for Head and Neck Reconstruction	BAOMS	62		31	Recommendation 31 Where possible, surgical management should comprise trans-nasal endoscopic excision for sinonasal MM – this statement sounds repetitive as recommendation 30 has adequately clarified the main consideration in the choice between open vs endoscopic surgery. Perhaps replace with: In selection of the optimal surgical management of HNMM, consideration should be given to the value added by reconstruction and/or rehabilitation of the residual defect in the overall management of the patient, e.g. a patient who is likely to require combined modality treatment with a modest sinonasal defect with extension to the maxilla, whilst resectable endoscopically could be better served from functional and quality of life perspectives by open surgery, free tissue transfer reconstruction with potential for orofacial rehabilitation.	We think 30 and 31 are different recommendations and not repetitive. 30 is actually recommending open surgery and 31 says a different thing entirely for sinonasal disease.
32	Prof Mirimanoff	ESTRO	63			After the chapter on surgery, and before that on sentinel node, I suggest to add a chapter on :"radical (or comprehensive) RT for medically or surgically inoperable patients". As	This has been revised and there is now a section as you suggest.

						mentioned in my comments on the Executive Summary: "in case of inoperable HNMM, and in the absence of multiple metastases, (as for example, in locally advanced sino-nasal MM or in case of invasion of the base of skull), high-dose, high precision RT (HDHPRT) or particle therapy if available should be a first choice, as the local control (LC) is between about 60% and 84 % with HDHPRT. (Please refer to pages 86-90, Table 20, and in particular to the following references: Combs 2009, Demizu 2014, Fuji 2014, Gilligan 1991, Zenda 2016, and a paper not quoted in the Draft by Gaze et al., in Clin. Oncol. 1990). In comparison, the "response rate" with chemotherapy (LC is almost never reported with chemo !) is only between about 15% and 25 % (see Table 28, pages 121 and 122), and the response rate with immune checkpoint inhibitors is only between about 20% and 25 %, with very few complete responses, when reported ! (see Table 29, page 123, 124).	
64.	Prof Hisham Mehanna		64	8		The sentinel lymph node biopsy elective neck dissection section would benefit from a section detailing indications for	The staging system for H&NMM means that the majority of patients are Stage III+ and hence already currently eligible for adjuvant therapy without SLNB - so currently SLNB will not be needed to determine eligibility.

						adjuvant treatment secondary to elective neck dissection or sentinel node biopsy after doing sentinel node biopsy or elective neck dissection so that people are clear as to those indications.	
64	Dr Richard Simcock	Macmillan	64		4-13	I am aware that each chapter may be abstracted by interested parties and read separately and this may account for the large amount of repetition in each introduction to each section. This chapter is a good example of an introduction which once again recapitulates what has been stated in the document many times before. The authors may wish to consider having a standard introduction to each chapter.	Noted and changed the introduction but yes, each chapter has had a different author.
65	Dr Richard Simcock	Macmillan	65		28	The differences between macular and nodular melanoma are not specified anywhere in the document that I can find.	Definitions have been added with thanks.
85.	Dr Tom Roques	RCR	66	8	38	Could this be re-worded for clarity as on first reading it seems to contradict 37	Thank you for your suggestion but this was the best wording we could come up with.
22.	Mr Stuart Winter	BAHNO	66	8	38	If END is considered in the radiologically N0 setting what levels of dissection are recommended according to primary site?	The recommendation has been altered, although the GDG thought that is not feasible to go through all potential primary sites and therefore all the appropriate levels

66	Dr Richard Simcock	Macmillan	72		36	The opening line of the evidence review (p69 line 1) is that "the evidence base is generally of low quality" – it is therefore difficult to state that there is "Good" evidence for mucosal melanoma	There was an attempt to rate it relative to the other evidence.
86.	Dr Tom Roques	RCR	73	8	39	What is ICI?	This has been added to the abbreviations, with thanks.
67	Dr Richard Simcock	Macmillan	74		Section 1.1	This "introduction" appears to be the conclusion	This has been changed, thank you.
87.	Dr Tom Roques	RCR	82	9	41	There are no randomised controlled trials of either adjuvant radiotherapy or adjuvant systemic therapy. It seems a little odd that systemic therapy is recommended but radiotherapy is not (routinely). Your evidence review suggests RT improves local control which is of value in a disease that often causes significant local symptoms (eg sinonasal melanoma)	This has been revised.
8.	Mr Stuart Winter	BAHNO	**82**	9	41	The recommendation not to give adjuvant RT is at odds with NICE guidelines 2016. Cancer of the upper aerodigestive tract	The NICE guideline was not specifically addressing mucosal melanoma. However, this section has been revised to provide a more balanced assessment.
39.	Prof Mirimanoff	ESTRO	**82**	9	41	Although I agree that the data on post-operative RT (PORT) are not very strong, (like most other data on HNMM !), there is a reasonable evidence that	This has been revised to provide a more balanced assessment, thank you for your suggestions.

						PORT decreases the local or local-regional failure rate (see Draft, Table 18, pages 76-80, and papers not cited in the Draft by Benhyazid et al. in Arch.Otolaryngeal Head and Neck Surg, 2010 and by Pfister et al in JNCCN 2013). So I would rephrase the sentence as: "There is reasonable evidence to recommend PORT in patients with a high risk of local or local-regional recurrence, see recommendation 43."	
23	Nimesh N Patel	Specialised Cancer Surgery CRG	83		36	The guideline quite rightly allows consideration to be given for adjuvant radiotherapy on the basis that locoregional recurrence is often profoundly miserable in sinonasal malignancies (eg. Fungating and deforming tumour, bleeding and loss of vision)	Noted with thanks
88.	Dr Tom Roques	RCR	92	9	44	Do you mean in clinical trials? 'Research protocols' might imply using a protocol outside a trial	Agree, we should amend this to state "Proton beam and carbon ion therapy should only be used in the context of clinical trials."
33	Prof Mirimanoff	ESTRO	101	101	42	As stated in my comments on the Executive Summary, I would put some more emphasis on hypofractionation, because of radiobiological data and clinical data in *non*-HNMM. I would add a sentence like : "moderate hypofractionation should be	In recommendation 46, we recommend a dose-fractionation of 65 Gy in 30 fractions (2.167 Gy/fraction) and, in recommendations 48 and 49, we discuss the role of hypofractionated schedules. We believe that recommendation 50 (in which we advise that optimal dose-fractionation should be determined on a patient-by-patient basis) provides sufficient opportunity for selection of hypofractionated regimens, even in younger, good performance status patients.

						an option, (not only in elderly patients) provided that very high precision RT is used, and that no sensitive structure (like the optic nerve) is embedded in the target volume"	
65.	Prof Hisham Mehanna		102	18		Post operative adjuvant radiation therapy is good but may be clarified by moving No 49 to become No 47 and the original number 46 does appear strange as primary RT treatment is I believe done in very few circumstances and therefore it may be beneficial to mention it as the very last item and to put a caveat as to where or when it would be used.	We are grateful for these suggestions, but believe that the current order of the recommendations is sensible and should remain unchanged.
40.	Prof Mirimanoff	ESTRO	102	9	45 & 46	I basically agree with the total dose (as indicated for the post-operative and for the primary treatment setting) with conventional 2 Gy fractionation. However, even if a "biologically equivalent regimen" is mentioned, more emphasis should be put on hypofractionation, as there are radiobiological data showing that hypofractionation is better in a good proportion of melanoma, and that a number of clinical data on *non*-HNMM suggest the same. In HNMM, some studies indicate a superiority with hypofractionation, some do	We acknowledge the reviewer's desire to accentuate the emphasis on hypofractionation, but believe that we have provided a good balance in consideration of fractionation. In recommendation 46, we recommend a dose-fractionation of 65 Gy in 30 fractions (2.167 Gy/fraction) and, in recommendations 48 and 49, we discuss the role of hypofractionated schedules. We believe that recommendation 50 (in which we advise that optimal dose-fractionation should be determined on a patient-by-patient basis) provides sufficient opportunity for selection of hypofractionated regimens, even in younger, good performance status patients.

						not (see Table 22, pages 94-100). I suggest then to add a sentence regarding fractionation: “moderate hypofractionation should be an option, provided that very high precision RT is used, and that no sensitive structure (like the optic nerve) is embedded in the target volume”	
57.	Dr Richard Simcock	Macmillan	102	9	48	The term ‘elderly’ is not preferred by people living with cancer. ‘Older people’ is believed to be less pejorative. Furthermore the point made here is not the issue of age but of frailty and comorbidity. Work on cancer in older people at Macmillan and elsewhere has encouraged clinicians to move away from making decisions based on age but rather on physical fitness or its absence. We would therefore recommend that ‘elderly’ here is replaced with ‘frail’.	I’d like to change this.
23.	Mr Stuart Winter	BAHNO	102	9	50	For cases where adjuvant radiotherapy is deemed necessary, patients should undergo a full dental assessment and extraction of teeth with poor prior to starting radiotherapy to reduce the risk of osteoradionecrosis	We didn’t examine any evidence for this.
75	Mr Michael Ho - SSIG lead for Head and Neck Reconstruction	BAOMS	105		51	Recommendation 51. Patients should be referred to a specialist centre for ocular, nasal and	We agree with this view but did not want to delay initial treatment by suggesting that pre-treatment referral to these specialist services is mandatory.

						facial and dental prosthetic rehabilitation as appropriate. Suggest replace with: In patients who are likely to require complex ocular, nasal and orofacial prosthetic rehabilitation, the relevant specialty teams or centres should be involved from the beginning of treatment planning in order to optimise patient outcomes, care pathway and experience.	
13.	Mr Stuart Winter	BAHNO	**105**	9	51	consideration of primary prosthetic rehabilitation (osseointegrated implant placement etc) should be made at time of definitive resection	Based on local facilities and expertise, osseointegrated implants may or may not be used. But, we have added a new recommendation in the Rehabilitation section.
76	Mr Michael Ho - SSIG lead for Head and Neck Reconstruction	BAOMS	105		52	52. Consider referral to specialist endocrine services for patients at risk of thyroid, adrenal or pituitary dysfunction. Perhaps replace with: In patients at risk of thyroid, adrenal or pituitary dysfunction, early involvement of specialist endocrine services is recommended	Changed thank you
66.	Prof Hisham Mehanna		**105**	9	53	spell out CUADT as Carcinoma of the Upper AeroDigestive Tract guideline.	Changed thank you
47		BAD	109		6	There is a repeated typo at 13.3.1: “distal metastasis” should be “distant metastasis”.	Changed

88	Dr Jonathan Leech Dr Gail Allsopp, Dr Richard Roope, Hannah Trippier	RCGP	109		9 general comment	The importance of good and timely sharing of information with the patient's GP is essential and should be stressed in the follow up section. e.g. Treatment summaries, possible side effects of treatment, recommendations of symptoms that can be managed in the community and those that need referral to a CNS/other member of the Secondary Care Team or for palliative care pathways to be implemented. Whilst quick access to secondary/ tertiary care is essential, many patients will continue to see their GP for their other comorbidities and full knowledge is essential to ensure appropriate community treatment.	This has been added.
50.	Dr Bushra Awan	BSHNI	111	10	57	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.
51.	Dr Bushra Awan	BSHNI	111	11	58	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.
89.	Dr Tom Roques	RCR	111	11	58	This is a big change from current practice, which is usually imaging if there are symptoms rather than as a routine. Much of oncology is also moving away from regular follow up to seeing	This has been revised for more flexibility.

						patients when have symptoms or concerns. There does not seem to be strong evidence for regular clinic visits and imaging and there seems little point in regular routine imaging if there is no good treatment option for the recurrence or the patient is not well enough to consider more treatment. The table could be a suggested FU strategy for people who have further treatment options but I do not think it should be mandated for all patients	
24.	Mr Stuart Winter	BAHNO	111	11	58	Column 3 – fine "needle" aspiration correction	Corrected with thanks
48		BAD	111		58:	Just wondering if there is more evidence/need for cross sectional imaging in this group as they are at such high risk rather than just USS to pick up early lesions allowing for earlier treatment?	Cross sectional imaging is recommended to look for systemic disease.
68	Dr Richard Simcock	Macmillan	112			The recommendation that patients are discharged at Year 10 seems to me the least well evidenced and most controversial. The data presented shows high rates of metastatic failure but most of this happening within the first few years of therapy (justifying the intensive follow up regimens suggested). There is no	The wording of this has been changed to make it more flexible.

						referenced evidence supporting longer term follow up. Long term follow-up is resource intensive for service and expensive for patients. The Macmillan "Hidden Costs of Cancer" report showed that travel to and from appointments is a major financial burden affecting 69% of patients. It needs to be better justified.	
77	Mr Michael Ho - SSIG lead for Head and Neck Reconstruction	BAOMS	112		58	'From years 6-10 patients should be given an annual appointment for clinical examination or open rapid access if available.' The clinical value of annual follow-up is potentially questionable, I would be inclined that recommendation be considered for 6-monthly follow-up from years 6-10 then discharge or in suitable patients they are discharged and have lifelong rapid access for any HNMM related concern/query.	This has been reworded to make more flexible.
78	Mr Michael Ho - SSIG lead for Head and Neck Reconstruction	BAOMS	112		58 Last row in table	The benefit of early detection of recurrence with frequent clinical and radiological follow-up is balanced against the resource implication for a typical radiology or ENT department. Change to: The benefit of early detection of recurrence with	This reflects the discussion of the GDG at the meeting.

						frequent clinical and radiological follow-up is balanced against the resource implication for a typical radiology or head and neck department.	
82	Miss Lisha McClelland		116		14.6.65	Error reference not found	This is corrected with thanks
90.	Dr Tom Roques	RCR	116	12	59	I can't see the evidence for this statement. What systemic therapy is recommended and on what basis?	This is in the full guideline.
34	Prof Mirimanoff	ESTRO	116	116	59	14.6: recommendation 59. I fully disagree with this statement. As discussed previously, this clearly underestimates the efficacy of RT and greatly overestimates the effect of systemic treatments, (including novel therapies with immune checkpoint inhibitors), for the treatment of a local disease. Local disease needs first a local treatment, especially when the latter offers a much better LC than systemic treatments. (see data and references in my comments on Executive Summary, comments on page 8, 38-39 and page 12, 62). “Adjuvant systemic treatments could be discussed after RT, as the incidence of distant metastases is very high after local recurrence”.	More has been added about RT in order to provide a greater level of balance to the assessments, as per your suggestion.

41.	Prof Mirimanoff	ESTRO	116	12	62	Here again I disagree with this statement. Maybe it means that RT is "rarely indicated" in case of local or local-regional recurrence (LR) simply because LR alone is rare, with few published data. However, it doesn't mean that RT is inefficient in this setting. As for inoperable HNMM, (see my remarks above under "page 8, items 38 and 39") high dose, high precision RT (including particle therapy) offers a much better tumour control than chemotherapy or even immune checkpoint inhibitors. Of course the latter should be offered in case of concomitant disseminated disease, but again RT should be a first option in case of local/local-regional recurrence alone	This has been clarified and the sections on RT have been amended to provide a greater degree of balance to the assessments.
25.	Mr Stuart Winter	BAHNO	**116**	12	63	Is there ever a case for repeat DXT in late recurrence cases where previous DXT has been given? If so what minimum interval is recommended?	We didn't examine any evidence for this.
42.	Prof Mirimanoff	ESTRO	116	12	64	Same as above: RT should not be considered only "when systemic therapy is not an option". This sentence underestimates the efficacy of RT and overestimates the efficacy of systemic treatments. (see above). I suggest "Systemic treatments could be considered as adjuvant	We have clarified this.

						treatments after (or during) salvage RT."	
52.	Dr Bushra Awan	BSHNI	116	12	65	Accept in present form without any further changes as clinical/scientific reasoning appear adequate.	Thank you for your comment.
7.	Mr Stuart Winter	BAHNO	116	12	65	Would the team consider specifying the preference for PET CT over standard CT whole body in the context of recurrent disease.	Both are recommended. There was a discussion about this and the GDG did not want patients to have to wait for a PET if CT was available sooner.
83	Miss Lisha McClelland		117			Highlighted – see section	This is corrected with thanks
69	Dr Richard Simcock	Macmillan	120		3	'eb' should read 'be'	Corrected with thanks
49		BAD	125		33	Should there be a consider entry into trial somewhere here? Especially when they have failed CPI's or targeted therapies?	Entry into trials has been added.
67.	Prof Hisham Mehanna		125	12	66	spell out IiAE.	Changed thank you
35	Prof Mirimanoff	ESTRO	126			Regarding disseminated disease and/or palliative treatments, I would recommend to add a chapter on the role of RT in the palliative setting. In MM, as in many other disseminated cancers, RT plays a major role in situations like bone metastases, spinal cord compression, airway obstruction, and several others. There should also be a short chapter reminding the increasing role of SRT in	The management of palliative care for this condition is in line with that of other cancers of the head and neck. Therefore it was not within the scope of the guideline to research this. We cross refer to other guidelines.

						oligometastases (like in brain, lung liver mets).	
84	Miss Lisha McClelland		126		15.6	Discussion to be added	This has been corrected with thanks.
9.	Mr Stuart Winter	BAHNO	126	12	67	There is a general under appreciation for the presence of BRAF mutations in mucosal melanoma across Head and neck MDTs. Would the team consider adding the quoted "10-15% of patients have tumour harbouring BRAF mutation…" (full guideline line 18 page 120) to recommendation number 67 and also in the summary document.	We don't generally quote statistics in recommendations as we try to keep them as succinct as possible. The interested reader can drill down.
89	Dr Jonathan Leech Dr Gail Allsopp, Dr Richard Roope, Hannah Trippier	RCGP	127		2	When considering the palliative care of patient with head and neck cancers it is essential to include in the discussion and communication the primary care team who will look after the patient on a day to day basis until their death. The community team/ GP are not mentioned in the guidelines currently and consideration of adding this should be considered.	This has been added as a recommendation.
43.	Prof Mirimanoff	ESTRO	127	12 & 13	66-74	Nowhere under "advanced disease or palliative care" do I find any chapter on palliative RT. RT plays a major role in case of brain metastases, spinal cord compression, bone metastases, haemoptysis, in case of airway invasion, etc. I	A new chapter has been added.

						suggest that at least a short chapter should be dedicated to palliative RT, just as there is a chapter on systemic treatment for advanced disease. There should also be a short chapter reminding the increasing role of SRT in oligometastases (like in brain, lung liver metastases).	
99.	Dr Jonathan Leech Dr Gail Allsopp, Dr Richard Roope, Hannah Trippier	RCGP	129	13	70	When considering palliative care it is essential to fully inform the GP practice and ensure timely communication between secondary and primary care to ensure the on the ground day to day palliative care of the patient is maintained	We have added this to the first recommendation.
96.		BASCSN	130	14	46	Named Cancer CNS - This is too generic and should specify Skin Cancer CNS.	The wording reflects the views of the CNS on the GDG.
91.	Dr Tom Roques	RCR	130	14	Section 4.2	It would be helpful to have formal audit standards here	This would be up to the local unit.