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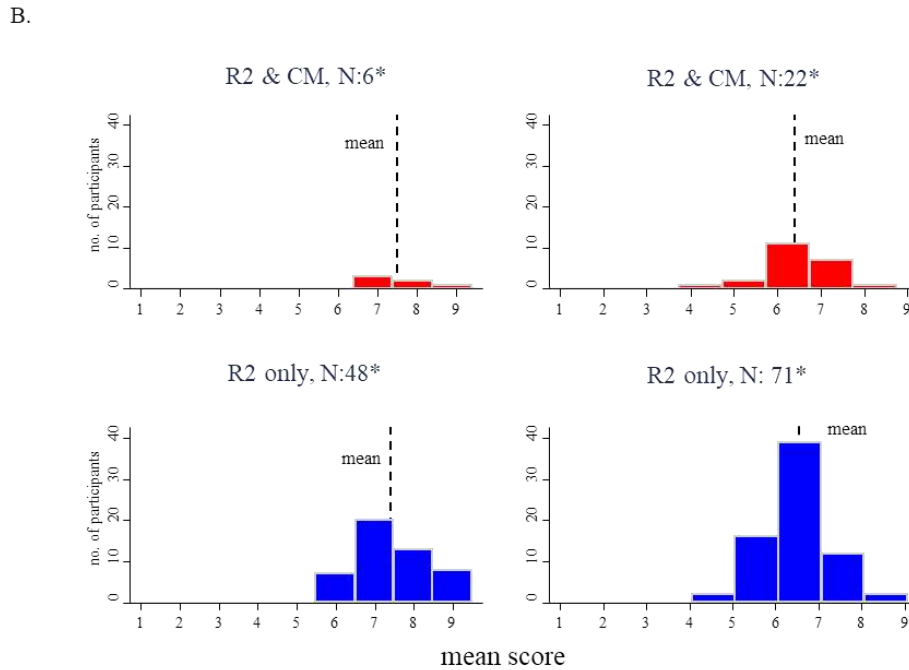
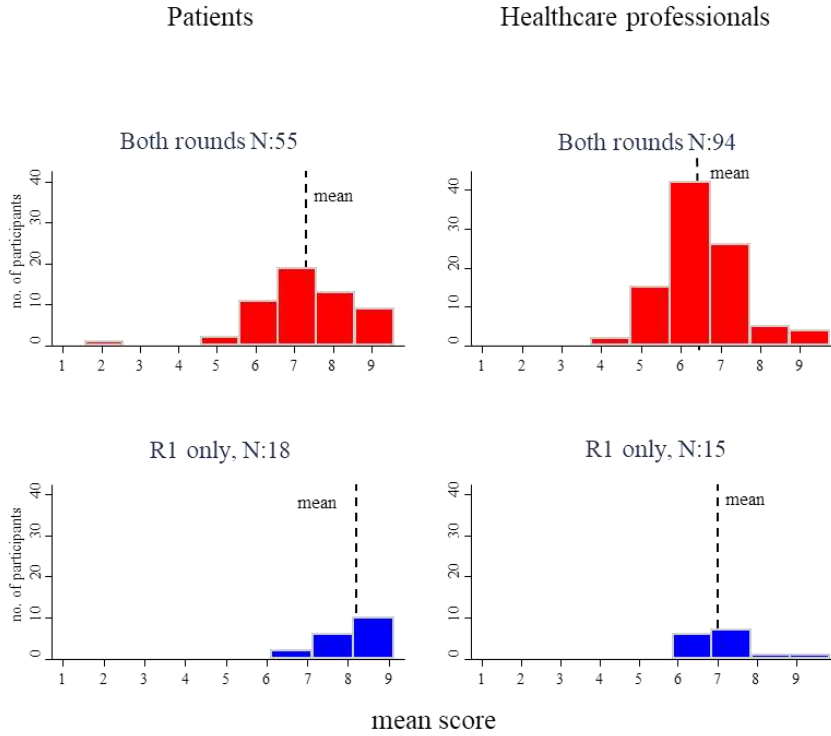
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Fig 2: Comparison of mean Delphi scores for analysis of Delphi attrition bias and consensus meeting participation bias.

(A). Comparison of mean scores per participant in Delphi round 1 (R1) according to whether participants completed Delphi round 2 (R2), for patients and healthcare professionals. (B). Comparison of mean scores per participant in Delphi round 2 (R2) according to whether participants partook in consensus meeting (CM), for patients and healthcare professionals. *The sums of the patients and HCP in Delphi R2 with eligible mean scores were 54 and 93, respectively: One participant in each group submitted 'unable to score' for every item.



Supplementary file S2: Patient and professional bodies contacted for Delphi recruitment

Patient advocacy groups contacted for Delphi recruitment

1. HPV and Anal Cancer Foundation;
2. International Anal Neoplasia Society;
3. Anal cancer- A bum rap;
4. Blog for a cure.

Professional bodies contacted for Delphi recruitment

1. The Association of Coloproctologists of Great Britain and Ireland;
2. The Colorectal Surgical Society of Australia and New Zealand;
3. The Trans-Tasman Radiation Oncology Group;
4. International Rare Cancers Initiative;
5. Nordic Anal Cancer Group;
6. The American Society of Colon and Rectal Surgeons;
7. The American Society of Clinical Oncology;
8. The European Society for Medical Oncology;
9. The European Society of Coloproctology



CORMAC

CORE OUTCOME RESEARCH MEASURES IN ANAL CANCER



Thank you very much for attending the CORMAC consensus meeting on 5th January 2018

We would value your feedback about the consensus meeting, to help improve future core outcome set work. If you could take a few moments to let us know your thoughts, it would be much appreciated

1. Please choose the option which describes you best:

Health care professional Patient

2. The information that the organisers provided me with in advance of the meeting was helpful.

Strongly agree Agree Neither Disagree Strongly disagree

Comments:

3. I was satisfied with the process used to agree the core outcomes set on the meeting day.

Strongly agree Agree Neither Disagree Strongly disagree

Comments:

4. I was satisfied with the way the meeting was facilitated.

Strongly agree Agree Neither Disagree Strongly disagree

Comments:

5. I felt able to contribute to the meeting.

Strongly agree Agree Neither Disagree Strongly disagree

Comments:

6. I felt comfortable in communicating my views.

Strongly agree Agree Neither Disagree Strongly disagree

Comments:

6. The workshop produced a fair result.

Strongly agree Agree Neither Disagree Strongly disagree

Comments:

7. Do you have any comments about the practical arrangements for the workshop (e.g. venue, timing of the meeting, catering, number of breaks, or anything else)?

8. Was there anything else that could have been done to improve the workshop?

(This example evaluation form is based on a form developed with the COMPACTERS COS Study team (Steven MacLennan, Thomas Lam, Linda Pennet, Paula Williamson) and Heather Bagley (COMET) and was adapted from a previous evaluation used by the James Lind Alliance Mesothelioma Priority Setting Partnership Workshop) The form was further developed with the input of Bridget Young and Rosemary Humphreys (co-chairs of the COMET PoPPiE Working Group).

Supplementary file S4 Minutes and outcomes following COMRAC Study Advisory Group meeting

Date: 22nd September 2016

Attendees:

Rebecca Fish	Richard Adams
Andrew Renehan	Rohit Kochhar
Paula Williamson	Julie Brewer
Caroline Sanders	Jill DeNardo
David Sebag-Montefiore	Sabine van der Veer

Outcome categories

RF presented the categories used by some other COS development projects to describe the rationale for the categories selected for presenting the CORMAC results. It was noted that categories could be revised if the group felt other categories would be more suitable, especially towards the end of the day after all the outcomes had been discussed. In the event, no revisions were made to the categories. Summaries of the day's discussions are therefore presented by category below.

Survival

The group agreed that overall survival and cancer specific survival were clearly understood terms and should be included in the Delphi.

Four composite outcomes were removed from the list as they were felt by the group not to be clinically or oncologically meaningful. These were: Event free survival, complication free survival, local recurrence free survival and inguinal relapse free survival

Disease Activity

This was one of the more involved discussions of the day as there is lack of clarity of definition for many of the terms in used to describe these outcomes.

Agreement was reached that the concept of 'treatment response' should be included as an outcome. The level of response (e.g. partial, complete) and the way in which the response is assessed (e.g. clinical, radiological) are not

specified at this stage, although there was broad agreement that it will include both clinical and radiological assessment.

The terms relapse, recurrence and failure were discussed. The group felt there was ambiguity around relapse/recurrence because they imply this includes disease that comes back after a period of remission rather than disease that is present continuously. This distinction was not felt to be accurate or meaningful clinically or biologically. D-SM described the concept of failure that is being adopted in the PLATO trial protocol. This is considered to be the presence of disease as assessed at a specified point in time, regardless of whether the disease has been present continuously or has gone away and come back. This term then avoids any the potential ambiguity around relapse/recurrence. The group felt it was important to capture the anatomical pattern of failure in terms of local, regional and distant. Therefore 3 failure outcomes will be included in the delphi: local failure; regional failure and distant failure.

Compliance

Whether compliance is an outcome or an effect modifier was discussed. No firm conclusion was reached on this however the feeling from the trialists and clinicians in the group was that it was information they would want to see reported in trials and therefore should be included in the Delphi. Chemotherapy and radiotherapy compliance were felt to be needed separately. Overall treatment time was felt to be the preferred term to describe radiotherapy compliance.

Summary of Survival, Disease Activity and Compliance decisions

Category: Disease Activity			
1. Disease progression	Progressive disease; Recurrence; Relapse Relapse free interval		IN
2. Treatment response	Tumour regression; Clinical response; Complete response; Complete clinical response; Partial response; Primary tumour regression; Stable disease; Treatment failure		IN
3. Distribution of disease	Local Use term local failure	Anal margin recurrence; Isolated local failure; Local control/failure; Local progressive tumour; Local recurrence; Local tumour relapse; Primary tumour control; Vaginal local recurrence	IN

	Locoregional Not felt to be necessary in addition to local and regional failure	Locoregional recurrence; Locoregional control/failure; Regional control./failure; Regional recurrence; Regional relapse; In field recurrence	OUT
	Nodal Use term regional failure	Inguinal node failure/recurrence; Nodal control/failure; regional disease activity	IN
	Distant (systemic) Use term distant failure	Distant control; Distant progression; Distant metastases; Distant recurrence; Metastases; Metastatic failure;	IN
Category: Survival			
4. Overall survival	Overall survival		IN
5. Cancer specific survival	Cause specific survival; Disease specific survival; Tumour specific survival		IN
6. Disease free survival	Disease free survival; Recurrence free survival; Relapse free survival; Tumour free survival		IN
7. Progression free survival	Progression free survival		IN
8. Event free survival	Event free survival Not felt to be clinically or oncologically meaningful		OUT
9. Inguinal relapse free survival	Inguinal relapse free survival Not felt to be a clinically or oncologically meaningful composite		OUT
10. Metastasis free survival	Metastasis free survival		IN
11. Colostomy free survival	Colostomy free survival		IN
12. Complication free survival	Complication free survival Not felt to be a clinically or oncologically meaningful composite		OUT
13. Local recurrence free survival	Local recurrence free survival Not felt to be a clinically or oncologically meaningful composite		OUT

Category: Compliance		
14. Compliance	Chemotherapy adherence; Compliance; Dose reduction; Interruption of treatment due to toxicity; Overall treatment time; Overall compliance; Radiotherapy adherence; Treatment according to guidelines; Treatment interruption; Unscheduled treatment break Requires specifying as chemotherapy compliance and total radiotherapy treatment time	IN x2
		13

Toxicities

General approach

Listing all the specific toxicity outcomes gathered from the literature and interviews in the Delphi was accepted as being impractical as such a long questionnaire would be likely result in participant fatigue and drop out. It was also agreed that listing toxicity outcomes simply in general terms (e.g. gastrointestinal toxicity) would be unsatisfactory as it is recognised that particular toxicity items that have significant impact on patients are poorly recorded and reported (e.g. faecal urgency).

RF presented a proposal for selecting which outcomes should be included specifically in the Delphi which was accepted by the group. Items arising from the literature and the patient interviews, or from the patient interviews alone, would be specifically included. Items arising only in the literature would be included in general terms only. All individual items were to be discussed however and if on discussion the group felt an item was sufficiently important it would be included.

The group agreed that the symptoms experienced by the patient, rather than the pathophysiological diagnosis (e.g. diarrhoea rather than radiation enteritis, dysuria rather than cystitis) should be used when describing toxicities. This is in keeping with the PLATO protocol which will be using patient reporting for toxicity outcomes after 3 months.

Toxicities by body system

Items in red were default out and items in yellow/white were default in. Where the group has taken the decision to alter this and for any items excluded, an explanation is given in bold.

Sub Category: Gastrointestinal toxicity	in/out
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15. Abdominal pain	Colic pain Felt to be covered by other items	out
16. Anal continence	Anal continence; Anal incontinence; Anorectal manometry; Bowel control; Faecal accident; Faecal incontinence; Flatulence; Functional anorectal sphincter; Impaired anorectal function; Inadequate sphincter function; Incontinence; Incontinence for gas; Insufficient sphincter function; Intact anal function; Light incontinence; Normal anal function; Partially incontinent; Preservation of sphincter function; Residual sphincteric incontinence; Slight incontinence; Sphincter function; Soiling; Stool incontinence	in
17. Anal/rectal fistula	Fistula; Ulceration/fistula; Anal fistula; Rectovaginal fistula	in
18. Anal pain	Anal pain	in
19. Anal ulcer	Anal ulcer; anal ulceration; anorectal ulcer Felt to be covered symptomatically by other outcomes	out
20. Anorectal scarring	Anal fibrosis; Anal stenosis; Rectal stenosis	in
21. Anorexia	Anorexia	in
22. Bowel obstruction	Bowel obstruction	in
23. Constipation	Constipation	in
24. Colostomy	Colostomy; Colostomy failure; Colostomy free interval Revise to include ileostomy	in
25. Colostomy complications	Hernia, prolapse etc	in
26. Dehydration	Dehydration Not felt to be specific enough to be meaningful	out
27. Diarrhoea	Diarrhoea; increased frequency of bowel movements	in
28. Dyspepsia	Dyspepsia Not felt to be a common problem encountered in this population	out
29. Faecal urgency	Faecal urgency	in
30. Mucositis (oral)	Mucositis Felt by the clinicians inc JB to be a frequent and troublesome problem for patients	in
31. Nausea/vomiting	Nausea; Nausea/vomiting; Vomiting	in
32. Gastrointestinal bleeding	Intestinal bleeding; Lower intestinal bleeding; Rectal bleeding	in
33. Gastrointestinal perforation	Perforation	in

	Acknowledged as rare but potentially extremely serious consequences for patient if occurs	
34. Radiation enteritis	Chronic haemorrhagic proctitis; Proctitis; Radiation enteritis; Radiation proctitis; Replaced by symptom descriptive items e.g. urgency, diarrhoea, gastrointestinal bleeding	out
35. Weight loss	Weight loss Move to constitutional symptoms	in
36. Prolapse	Pelvic floor descent/vaginal or rectal prolapse Felt to be a moderately frequent and potentially serious problem for patients	in
Total items included:		17

Sub Category: Dermatologic toxicity		in/out
1. Alopecia	Alopecia; Hair loss	in
2. Cellulitis	Cellulitis; Purulent cellulitis	in
3. Dermatitis	Dermatitis; Inguinal dermatitis; Radiation dermatitis; Radiation induced dermatitis; Radiodermatitis; Erythema; Oedema; Rash; Moist desquamation; desquamation To be re-termed skin loss/desquamation	in
4. Perianal/perineal skin toxicity	Anogenital mucosal damage; Anogenital skin damage; Cutaneous perianal necrosis and ulceration; Perianal desquamation; Perianal numbness; Perianal radiation dermatitis; Perineal dermatitis; Perineal skin ulceration; Perineal skin toxicity To be covered by skin symptoms, further specification of area effected not necessary. Some crossover with items in sexual/reproductive	out
5. Hand and foot syndrome	Hand and foot syndrome; Palmar/plantar syndrome	in
6. Oedema	Oedema	in
7. Stomatitis	Stomatitis Felt to be represented by mucositis in GI toxicity	out
8. Skin pain/buring	Not listed	in
9. Skin itch		in
Total items included		7
SUB CATEGORY: Renal and urinary Renamed 'urinary toxicity'		

1. Cystitis	Cystitis; Bladder toxicity Replaced by symptom descriptive items below	out
2. Dysuria	Dysuria	in
3. Haematuria	Haematuria	in
4. Urinary frequency	Urinary frequency	in
5. Urinary urgency	Not listed*	in
6. Urinary continence		in
		5

Sub category: Reproductive/sexual toxicity		
Categorised into gender specific items		
Men		
1. Erectile dysfunction	Impotence; Erectile dysfunction; Erective capability	in
2. Ejaculatory function	Not listed	in
3. Penile/scrotal toxicity	Genital dermatitis; Genital pain; Atrophy to perineal skin and external genitalia;	in
Women		
4. Menopause	Not listed	in
5. Vaginal toxicity	Atrophy of vaginal mucosa; Colpitis (vaginitis); Chronic genital mucosal toxicity; Vaginal fibrosis;	in
6. External genital toxicity	Atrophy to perineal skin and external genitalia; Genital dermatitis	in
All		
1. Anal/rectal toxicity	Not listed in this context	in
2. Dyspareunia	Dyspareunia; Painful sexual intercourse To be referred to as painful sexual intercourse to include men and women	in
3. Libido / arousal	Not listed*	in
7. Orgasmic function	Not listed*;	in
8. Sexual pleasure	Sexual enjoyment; Reduced enjoyment of sex; Intimacy	in
9. Infertility	Not listed*;	in
Total items included		12

Sub category: Musculoskeletal toxicity		
1. Bone injury	Insufficiency fracture; Hip/ pelvis fracture; Bone injury; Acute osseous toxicity To be referred to as fractures	in
2. Fibrosis	Inguinal fibrosis; Severe fibrosis Covered by pain and mobility	out
3. Radionecrosis	Soft tissue necrosis; Radionecrosis; Necrosis; Radionecrosis ulceration Avascular necrosis of femoral head covered by hip pain and mobility. Soft tissue necrosis felt to be dealt with by skin loss/desquamation in dermatological toxicity	out
4. Bone / joint pain	Not listed Specifically referring to hip back and leg pain	in
		2

sub Category: Haematological toxicity		
1. Anaemia	Anaemia	in
2. Coagulation effects	Arterial thrombosis; Thrombosis / embolism	in
3. Leukopenia	Leukopenia; WBC toxicity; Not felt to have sufficient clinical importance in addition to neutropenia	out
4. Neutropenia	Neutropenia; Neutropenic sepsis; Febrile neutropenia;	in
5. Thrombocytopenia	Thrombocytopenia; Low platelets; Platelet count	in
		4

Sub category: Generalised and constitutional toxicity		
1. Fatigue	Fatigue; General fatigue	in
2. Sleep disturbance		in
3. Fever	Fever Neutropenia sufficient (in haematological)	out
4. Pain	Pain Covered in specific body systems	out
5. Syndromes	Syndromes	out

	Unclear what this refers to	
		2

sub Category: Other toxicities		
1. Allergy/ anaphylaxis	Allergy	out
2. Cardiovascular	Arrhythmia; Cardiac toxicity; To include myocardial infarction as particular toxicity of chemotherapy	in
3. Electrolyte disturbances	Hyponatraemia; Hyperkalaemia; Magnesium wasting syndrome Uncommon	out
4. Endocrine	Endocrine toxicity Uncommon	out
5. Hepatic	Hepatic toxicity; Deranged gamma glutyltransferase; Uncommon	out
6. Lymphatic	Lymphoedema; Lower extremity oedema; Leg lymphoedema; Specifically referring to lower limb/pelvic lymphoedema	in
7. Neurologic	Neurological toxicity; Auditory changes; Encephalopathy; Ocular/visual Specifically referring to paraesthesia/altered sensation in the pelvis/lower limbs	in
8. Respiratory	Dyspnoea; Pulmonary toxicity To include chest infections and shortness of breath	in
9. Second malignancy	Second malignancy; Second primary	in
		5

Life Impact

The group accepted the term life impact as meaningful. The 6 items listed within this category were thought to be representative of how these concepts have been described elsewhere and to include all the key areas where patients' lives may be impacted. Further specification was deemed unnecessary as it will fall under the remit of deciding how best to assess the life impact and quality of life. There is already work being undertaken in this area with the development of the EORTC anal cancer specific quality of life module.

Category: Life impact	
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1. Quality of life	Quality of life; Global quality of life	in
2. Physical function	Imposed discreet/modest behaviour; Normality	in
3. Cognitive function	Concentration; Cognitive function;	in
4. Emotional wellbeing	Body image; Embarrassment Feeling alone; Emotional function; Future perspective; Stress;	in
5. Occupational/role function	Ability to perform normal role including work and family life. Including but not limited to financial difficulties, financial impact, return to work, duration of sick leave	in
6. Relationships and social functioning	Finding a partner; feeling mistrusted; changes in interactions with family and friends; intimacy; social functioning; social stigma; Imposed discreet/modest behaviour; Normality	in
		6
Total items to include in Delphi:		73

Supplementary file S5 Additional outcomes and action proposed after Delphi R1

Proposed additional outcome	Existing outcome mapped to	Existing outcome description	Add as additional outcome to round 2?
Long term inability to work due to side effects	Role function	The effect of cancer or its treatment on your role; for example, ability to look after children or to work or earn money.	No
PTSD type symptoms relating to fear of cancer returning	Emotional function	The effect of cancer or its treatment on thoughts and feelings for example, mood, self-esteem or feeling able to cope.	Add as additional outcome 'outlook' (although technically included under emotional function may have particular importance)
Anal fissures; tears in the anus that will not heal	Anal scarring / anal pain	Scar tissue causing tightness or fragile skin around your bottom/ Pain in your anus (bottom)	No
how people are mentally affected by treatment; PTSD for example	Emotional function	The effect of cancer or its treatment on thoughts and feelings for example, mood, self-esteem or feeling able to cope.	No
More attention needs to be focused on the aftercare of side effects. Not stop patient care once treatment has been completed.	not an outcome		No
Need for salvage surgery	? local failure	Cancer is found in the bottom (anus) after treatment has been completed, indicating that the treatment has not been successful.	Add as new outcome "Salvage surgery: Undergoing surgery for cancer that persists after treatment with chemoradiotherapy"

			Consider adding- inexact mapping
detailed questions about prior HPV testing outcome; if ever positive; how long prior positive variations of answer(for instance pelvic of oral testing)	not an outcome		No
mental health questions around reactions from family; friends; etc; as well as medical; (questions such as: you must have been very promiscuous; or had anal sex) which is commonly known not to be true; among female anal cancer patients.	social function	The effect of cancer or its treatment on relationships with partner, family and friends including ability to join in with social activities.	No but modify to “The effect of cancer or its treatment on relationships with people, including partner, family, friends, colleagues or health professionals. For example inability to join in with social activities or being treated differently (stigma).”
both of these questions must have an outcome on the spread and how everyone is vulnerable.	not an outcome		No
Proportion of patients who fail primary CRT who go on to have curative surgery	outside scope (COS for trials of chemoradiotherapy only)		No
Resons why paitents who fail primary CRT do not go on to have curative surgery	outside scope (COS for trials of chemoradiotherapy only)		No
Treatment outcomes for patients with positive inguinal nodes at presentation	not an outcome		No
Effect of radiation amount on pelvic bone density	? Fractures	Broken bones in the back, pelvis, hips or thighs	Suggest modifying existing outcome to ‘bone density changes; with description

			<p>“changes to the bones in the back, pelvis, hips or thighs that might lead to osteoporosis, broken bones or bone pain”</p> <p>Consider adding- inexact mapping</p>
Effect of radiation amount on hip movement issues	Physical function	The effect of cancer or its treatment on day to day physical activities; for example, walking, climbing stairs, driving	No
effects on patients with previous gastrointestinal issues (Celiac) and relation to Diarrhea	not an outcome		No
Radio/chemo therapy failed after 18 months and resulted in full APR with colostomy stoma	Local failure / colostomy / need for salvage surgery	Cancer is found in the bottom (anus) after treatment has been completed, indicating that the treatment has not been successful.	Covered under new outcome ‘salvage surgery’
Surgical treatment alone	outside scope (COS for trials of chemoradiotherapy only)		No
successful salvage abdominoperineal resection	outside scope (COS for trials of chemoradiotherapy only)		No
Having lifelong ongoing (high resolution) anoscopy /other surveillance for AIN to prevent second primary same site	not an outcome		No
Being unable to have insertive anal sex (possibly forever)	Anal/rectal toxicity in sexual toxicity	Changes to the anus (bottom) including narrowing or tightness, fragile or thinned skin, painful skin and changes in sensation (feeling) / Pain when having sex	<p>Consider adding- inexact mapping</p> <p>Additional outcome "inability to have anoreceptive intercourse”</p>
"Electric shocks" in legs or arms following treatment - nerve damage	Neurologic toxicity	Altered sensations in the pelvis or legs, including pins and needs and numbness	No
Clinical complete response at 6 months	treatment response	The assessment of how well the cancer is responding to treatment.	No

stigma perceived by patients during interactions with health care professionals.	social function	The effect of cancer or its treatment on relationships with partner, family and friends including ability to join in with social activities.	Modify description “The effect of cancer or its treatment on relationships with people, including partner, family, friends, colleagues or health professionals. For example inability to join in with social activities or being treated differently (stigma).”
need for post treatment biopsies	not an outcome		No
To be free of cancer and regain your fitness level before the cancer	Physical function/ disease free survival	The effect of cancer or its treatment on day to day physical activities; for example, walking, climbing stairs, driving. / How long someone is alive without any cancer	No
Overall and Disease Free Survival post Salvage Treatment	outside scope (COS for trials of chemoradiotherapy only)		No
Gastrointestinal pain and mucus discharge	?anal pain / anal continence	Pain in your anus (bottom) / Problems controlling the passage of stool (poo) or gas from your bottom	Consider adding- maps poorly 2 additional outcomes: Abdominal pain Anorectal discharge
Experience of anal sex previous to diagnosis	not an outcome		No
Approximate time of diagnosis from the first sign of blood in stools	not an outcome		No
Diagnosis of haemorrhoids previous to diagnosis of cancer	not an outcome		No

Supplementary file S6 Delphi question items

Disease activity

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
1	Treatment response: The assessment of how well the cancer is responding to treatment.		
2	Local failure: Cancer is found in the bottom (anus) after treatment has been completed, indicating that the treatment has not been successful.		
3	Regional failure: Cancer is found in glands in the groin or pelvis after treatment has been completed, indicating that the treatment has not been successful.		
4	Distant failure: Cancer is found in other parts of the body (outside the pelvis) after treatment has been completed, indicating that the treatment has not been successful.		
5	Disease free survival: How long someone is alive without any cancer		
6	Metastasis free survival: How long someone is alive without the cancer spreading to other parts of the body (outside the pelvis).		
7	Disease progression: After treatment, the cancer has got bigger, or has spread to other parts of the body, for example the lymph nodes (glands).		
8	Progression-free survival: The time until someone's disease either gets worse or they die from any cause.		
74	Salvage surgery: Undergoing surgery for cancer that persists after treatment with chemoradiotherapy		

Survival

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
9	Overall survival: The time until someone dies from any cause		
10	Cancer specific survival: The time until someone dies from anal cancer		
11	Colostomy free survival: How long someone is alive without a stoma (colostomy or ileostomy) bag.		

Delivery of care

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
12	Radiotherapy treatment time: How many days are taken to complete the course of radiotherapy. This shows whether there are any delays or interruptions to radiotherapy for any reason, for example because of side effects		
13	Chemotherapy compliance: Whether treatment with chemotherapy has to be interrupted or changed for any reason, for example because of side effects.		

Life impact

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
14	Health related quality of life: An overall measure how a person's health effects their general wellbeing		
15	Physical function: The effect of cancer or its treatment on day to day physical activities; for example, walking, climbing stairs, driving.		
16	Cognitive function: Ability to think clearly including concentration, understanding and remembering things		
17	Emotional function: The effect of cancer or its treatment on thoughts and feelings for example, mood, self-esteem or feeling able to cope.		
18	Occupation/role function: The effect of cancer or its treatment on your role; for example, ability to look after children or to work or earn money.		
19	The effect of cancer or its treatment on relationships with people, including partner, family, friends, colleagues or health professionals. For example, inability to join in with social activities or being treated differently (stigma).		
75	Outlook: Fear or anxiety about the cancer returning in the future		

Gastrointestinal toxicity (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
20	Anal incontinence: Problems controlling the passage of stool (poo) or gas from your bottom		
21	Pelvic fistula: An abnormal passageway connecting one internal organ in to another, for example between the bowel and bladder, or between the bowel and vagina.		
22	Anal pain: Pain in your anus (bottom)		
23	Anorectal scarring: Scar tissue causing tightness or fragile skin around your bottom		

24	Anorexia: Loss of appetite		
25	Constipation: Having difficulty passing stools (poo), which may be small and hard		
26	Colostomy/Ileostomy: An opening on the surface of the abdomen (tummy) which has been surgically created to divert the flow of stools (poo) into a bag. Also known as stoma.		
27	Stoma complications: Problems with a stoma, including a hernia or bulge in the tummy under the stoma, more bowel telescoping out of the stoma or narrowing of the stoma opening.		
28	Diarrhoea: Passing looser (sloppier) stools (poo) or passing stools more often than is normal for you.		
29	Faecal urgency: The sudden, uncontrollable urge to pass stool (poo)		
30	Mucositis (oral): Break down of the skin inside the mouth which can cause pain, difficulty swallowing or mouth ulcers		
31	Nausea/vomiting: Feeling or being sick		
32	Gastrointestinal bleeding: Bleeding on the inside of the stomach or bowels		
33	Gastrointestinal perforation: A hole in the wall of the stomach or bowels leading to leakage of contents into the abdomen (tummy). A medical emergency that can be life-threatening and needs immediate medical attention		
34	Bowel obstruction: Blockage in the bowel meaning that digested food and waste cannot get past.		
35	Pelvic organ prolapse: Bulging of the perineum (the area of skin between your legs behind your scrotum/vagina) or in the vagina, caused by the bladder or womb dropping from their normal position. Or the inner lining of the rectum (part of the large intestine)		
77	Abdominal pain: Pain in the tummy		
78	Anorectal discharge: Mucus discharge from the bottom (anus)		

Skin toxicity (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
36	Alopecia: Hair falling out		
37	Cellulitis: Infection of the skin, causing it to become tight, red and painful and needing treatment with antibiotics		
38	Hand and foot syndrome: Redness, swelling and pain on the palms of the hands and/or soles of the feet		
39	Oedema: Buggy swelling under the skin		
40	Skin pain/burning: Pain or burning sensation in the skin		

41	Skin itch: Itching of the skin		
42	Skin loss/desquamation: Blistering or peeling of the skin leaving raw areas.		

Urinary toxicity (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
43	Dysuria: Pain when doing a wee		
44	Haematuria: Blood in the wee		
45	Urinary frequency: Having to go to the toilet for a wee very often		
46	Urinary urgency: The sudden, uncontrollable urge to go for a wee		
47	Urinary incontinence: Difficulty controlling the passage of wee (wetting yourself)		

Sexual and reproductive toxicity (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
48	Anal/rectal toxicity: Changes to the anus (bottom) including narrowing or tightness, fragile or thinned skin, painful skin and changes in sensation (feeling)		
49	Painful sexual intercourse: Pain when having sex		
50	Libido / arousal: The desire to have sex or ability to feel sexually aroused		
51	Orgasmic function: Changes to the experience sexual climax or loss of ability to have sexual climax		
52	Sexual pleasure: The enjoyment of having sex		
53	Infertility: Becoming unable to have children as a result of treatment		
54	(In men) Erectile dysfunction: Difficulty getting or keeping an erection		
55	(In men) Ejaculatory dysfunction: Not producing semen or producing less or altered semen at sexual climax		
56	(In men) Penile/scrotal toxicity: Changes to the penis or scrotum, including fragile or thinned skin, painful skin and changes in sensation (feeling)		
57	(In women) Menopause: The ovaries stop producing eggs and hormones, meaning you no longer have periods and are unable to have children. The hormonal changes can also cause symptoms such as hot flushes, night sweats and mood changes.		

58	(In women) Vaginal toxicity: Changes to the vagina including narrowing or shortening, dryness, fragile or painful skin or changes to sensation (feeling)		
59	(In women) External genital toxicity: Changes to skin around the vulva and clitoris (the area near the opening of your vagina), including fragile or thinned skin, painful skin and changes in sensation (feeling)		
76	Ability to have sexual intercourse: Being unable to have receptive intercourse (penetrative/insertive sex) either via the vagina or via the anus		

Musculoskeletal toxicity (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
60	Fractures and bone changes: Changes to the bones in the back, pelvis, hips or thighs that might lead to osteoporosis, broken bones or bone pain		
61	Bone or joint pain: Pain in the back, pelvis, hips or legs		

Blood toxicity (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
62	Anaemia: Having fewer red blood cells than normal reducing the amount of oxygen that can be carried in the blood		
63	Clotting effects: Blood clots forming inside the blood vessels (arteries or veins) that can stop blood flowing properly		
64	Neutropenia: Having low numbers of white blood cells raising the risk of having a serious infection (sepsis)		
65	Thrombocytopenia: Having low numbers of platelets raising the risk of bruising and bleeding		

Generalised toxicity (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
66	Fatigue: Feeling more lethargic and tired than normal		
67	Sleep disturbance: Difficulty getting to or staying asleep		
68	Weight loss: Losing weight		

Other toxicities (side effects)

Outcome ID	Outcome Name	Round 1 Score	Round 2 Score
69	Cardiovascular toxicities: Effects on the heart including having an irregular heart beat or having a heart attack		
70	Second malignancy: A new cancer occurring in someone who has had a cancer in the past. It is different to recurrence, which is where the original cancer has returned.		
71	Lymphatic toxicities: Swelling in of one or both legs due to a build up of fluid in the tissues		
72	Respiratory toxicities: Problems with breathing including chest infections, cough and shortness of breath		
73	Neurologic toxicity: Altered sensations in the pelvis or legs, including pins and needles and numbness		

Supplementary File S7 Results after Delphi R1.

Outcomes highlighted green were 'consensus in'.

Outcomes	HCP (n = 94)			Patients (n = 55)			Delphi consensus
	1-3 (%)	4-6(%)	7-9(%)	1-3(%)	4-6(%)	7-9(%)	
Disease activity							
1. Treatment response	1	13	87	0	4	96	in
2. Local failure	0	5	95	1	0	99	in
3. Regional failure	0	4	96	1	0	99	in
4. Distant failure	0	8	92	1	1	97	in
5. Disease progression	2	20	78	1	17	82	in
Survival							
6. Disease free survival	0	15	85	0	20	80	in
7. Metastasis free survival	0	28	72	0	11	89	in
8. Progression-free survival	2	20	78	1	17	82	in
9. Overall survival	1	24	75	13	29	59	No consensus
10. Cancer specific survival	0	7	93	1	5	94	in
11. Colostomy free survival	12	42	46	3	25	72	No consensus
Delivery of care							
12. Radiotherapy treatment time	1	47	52	0	14	86	No consensus
13. Chemotherapy compliance	1	50	49	0	14	86	No consensus
Life Impact							
14. Health related quality of life	0	27	73	1	22	76	in

15.	Physical function	1	36	63	1	15	84	No consensus
16.	Cognitive function	2	52	46	2	15	82	No consensus
17.	Emotional function	0	50	50	2	23	75	No consensus
18.	Occupation/role function	2	40	58	2	22	76	No consensus
19.	Social function	1	44	55	2	26	72	No consensus

Gastrointestinal toxicity

20.	Anal incontinence	0	22	78	0	17	83	in
21.	Pelvic fistula	1	24	75	1	14	85	in
22.	Anal pain	1	35	64	1	15	83	No consensus
23.	Anorectal scarring	2	50	48	0	22	78	No consensus
24.	Anorexia	5	64	31	4	32	65	Borderline
25.	Constipation	5	59	35	2	28	70	Borderline
26.	Colostomy/Ileostomy	2	29	69	1	14	84	No consensus
27.	Stoma complications	4	52	44	3	10	87	No consensus
28.	Diarrhoea	1	53	46	0	29	71	No consensus
29.	Faecal urgency	1	40	59	0	19	81	No consensus
30.	Mucositis (oral)	7	59	34	3	28	70	Borderline
31.	Nausea/vomiting	6	63	31	4	28	68	Borderline
32.	Gastrointestinal bleeding	5	50	44	1	13	86	No consensus
33.	Gastrointestinal perforation	4	29	66	1	5	93	No consensus

34.	Bowel obstruction	4	28	68	1	9	90	No consensus
35.	Pelvic organ prolapse	6	50	44	1	14	85	No consensus
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Dermatological toxicity								
36.	Alopecia	11	63	27	10	34	56	Borderline
37.	Cellulitis	6	58	36	1	25	74	No consensus
38.	Hand and foot syndrome	8	58	35	4	32	64	Borderline
39.	Oedema	10	60	30	6	36	58	Borderline
40.	Skin pain/burning	6	56	38	1	27	72	No consensus
41.	Skin itch	15	56	29	5	33	62	Borderline
42.	Skin loss/desquamation	6	43	50	2	19	79	No consensus
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Urinary toxicity								
43.	Dysuria	4	63	33	5	23	72	No consensus
44.	Haematuria	6	58	36	3	24	73	No consensus
45.	Urinary frequency	5	55	40	6	31	63	Borderline
46.	Urinary urgency	4	50	45	4	27	69	Borderline
47.	Urinary incontinence	3	37	60	4	20	76	No consensus
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Sexual/reproductive toxicity								
48.	Anal/rectal toxicity	4	49	48	1	28	71	No consensus
49.	Painful sexual intercourse	3	44	53	5	24	71	No consensus
50.	Libido / arousal	4	55	41	5	37	58	Borderline
51.	Orgasmic function	4	54	42	7	31	62	Borderline

52.	Sexual pleasure	4	50	46	8	26	65	Borderline
53.	Infertility	8	39	53	12	16	71	No consensus
54.	(In men) Erectile dysfunction	2	42	57	6	23	72	No consensus
55.	(In men) Ejaculatory dysfunction	4	56	41	10	22	69	Borderline
56.	(In men) Penile/scrotal toxicity	4	53	42	2	24	74	No consensus
57.	(In women) Menopause	4	50	47	1	28	71	No consensus
58.	(In women) Vaginal toxicity	2	44	54	3	21	76	No consensus
59.	(In women) External genital toxicity	3	48	50	4	23	73	No consensus
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Musculoskeletal toxicity								
60.	Fractures and bone changes	3	36	61	1	19	79	No consensus
61.	Bone or joint pain	4	52	44	1	30	69	Borderline
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Haematological toxicity								
62.	Anaemia	4	58	38	1	23	76	No consensus
63.	Clotting effects	4	44	51	3	18	79	No consensus
64.	Neutropenia	4	31	65	1	14	85	No consensus
65.	Thrombocytopenia	4	47	50	3	19	78	No consensus
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Constitutional symptoms								
66.	Fatigue	8	55	37	2	37	61	Borderline
67.	Sleep disturbance	10	64	27	4	37	59	Borderline
68.	Weight loss	7	60	33	4	42	54	Borderline
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Other toxicities								

69. Cardiovascular toxicities	3	37	60	0	12	88	No consensus
70. Lymphatic toxicities	2	33	65	0	5	95	No consensus
71. Respiratory toxicities	2	44	54	0	17	83	No consensus
72. Neurologic toxicity	5	50	44	0	21	79	No consensus
73. Second malignancy	5	48	47	1	29	70	No consensus

Supplementary File S8

Results after Delphi R2. Outcomes marked with * were added after round 1. Outcomes highlighted green were 'consensus in'; and red 'consensus out', other outcomes were either 'borderline' or 'no consensus'

Outcomes	HCP (n = 94)			Patients (n = 55)			Delphi consensus
	1-3 (%)	4-6(%)	7-9(%)	1-3(%)	4-6(%)	7-9(%)	
Disease activity							
74. Treatment response	0	5	95	0	6	94	in
75. Local failure	0	3	97	0	2	98	in
76. Regional failure	0	3	97	0	0	100	in
77. Distant failure	0	7	93	2	2	96	in
78. Disease progression	0	8	92	0	0	100	in
79. Disease free survival	0	9	91	0	25	75	in
80. Salvage surgery*	0	18	82	0	14	86	In
Survival							
81. Metastasis free survival	1	23	76	0	16	84	in
82. Progression-free survival	1	18	81	0	18	82	in
83. Overall survival	1	29	70	10	47	43	No consensus
84. Cancer specific survival	0	4	96	0	10	90	in
85. Colostomy free survival	8	46	46	0	43	57	Borderline
Delivery of care							
86. Radiotherapy treatment time	1	53	46	0	17	83	No consensus
87. Chemotherapy compliance	1	56	43	0	21	79	No consensus

Life Impact

88.	Health related quality of life	0	18	82	0	29	71	in
89.	Physical function	0	34	66	0	17	83	No consensus
90.	Cognitive function	2	61	37	0	17	83	No consensus
91.	Emotional function	0	56	44	0	25	75	No consensus
92.	Occupation/role function	0	42	58	0	31	69	Borderline
93.	Social function	0	48	52	0	42	58	Borderline
94.	Outlook*	3	69	28	2	29	69	Borderline

Gastrointestinal toxicity

95.	Anal incontinence	0	13	87	0	12	88	in
96.	Pelvic fistula	1	13	86	0	8	92	in
97.	Anal pain	1	33	66	0	25	75	No consensus
98.	Abdominal pain*	4	72	23	0	45	55	Borderline
99.	Anorectal discharge*	8	74	18	6	37	57	Borderline
100.	Anorectal scarring	2	60	38	0	27	73	No consensus
101.	Anorexia	6	82	12	0	56	44	out
102.	Constipation	6	82	12	0	39	61	Borderline
103.	Colostomy/Ileostomy	2	24	73	0	14	86	in
104.	Stoma complications	3	61	36	0	13	88	No consensus
105.	Diarrhoea	0	73	27	0	31	69	Borderline

106. Faecal urgency	0	37	63	0	13	87	No consensus
107. Mucositis (oral)	6	76	19	0	42	58	Borderline
108. Nausea/vomiting	6	79	16	0	47	53	Borderline
109. Gastrointestinal bleeding	6	60	34	0	13	88	No consensus
110. Gastrointestinal perforation	2	34	63	0	0	100	No consensus
111. Bowel obstruction	2	31	67	2	0	98	No consensus
112. Pelvic organ prolapse	4	63	32	0	9	91	No consensus

Dermatological toxicity

113. Alopecia	12	80	8	12	53	35	Out
114. Cellulitis	9	71	20	0	34	66	Borderline
115. Hand and foot syndrome	7	76	18	2	51	47	Out
116. Oedema	9	77	14	5	55	41	Out
117. Skin pain/burning	3	73	23	0	39	61	Borderline
118. Skin itch	16	72	12	4	50	46	Out
119. Skin loss/desquamation	3	51	46	0	20	80	No consensus

Urinary toxicity

120. Dysuria	3	78	19	2	43	55	Borderline
121. Haematuria	10	73	17	0	37	63	Borderline
122. Urinary frequency	3	70	27	2	53	45	Out
123. Urinary urgency	3	58	39	4	38	58	Borderline

124. Urinary incontinence	3	38	59	2	29	69	Borderline
Sexual/reproductive toxicity							
125. Anal/rectal toxicity	1	61	38	0	33	67	Borderline
126. Painful sexual intercourse	2	53	44	4	25	71	No consensus
127. Libido / arousal	1	74	24	6	46	48	Out
128. Orgasmic function	3	70	27	6	46	48	Out
129. Sexual pleasure	2	69	29	6	37	57	Borderline
130. Infertility	6	49	46	18	30	52	Borderline
131. Ability to have sexual penetrative intercourse*	1	57	42	6	23	70	No consensus
132. (In men) Erectile dysfunction	1	43	56	0	38	62	Borderline
133. (In men) Ejaculatory dysfunction	3	78	19	13	46	42	Out
134. (In men) Penile/scrotal toxicity	3	69	28	0	35	65	Borderline
135. (In women) Menopause	3	69	28	5	46	49	Out
136. (In women) Vaginal toxicity	2	51	47	4	29	67	Borderline
137. (In women) External genital toxicity	3	62	34	5	30	66	Borderline
Musculoskeletal toxicity							
138. Fractures and bone changes	2	38	60	0	17	83	No consensus
139. Bone or joint pain	3	70	27	0	29	71	No consensus
Haematological toxicity							
140. Anaemia	6	76	19	0	33	67	Borderline
141. Clotting effects	4	51	44	0	15	85	No consensus

142. Neutropenia	4	36	60	0	8	92	No consensus
143. Thrombocytopenia	4	60	36	0	29	71	No consensus
Constitutional symptoms							
144. Fatigue	3	76	21	4	46	50	Out
145. Sleep disturbance	9	82	9	0	58	42	Out
146. Weight loss	8	78	14	4	73	24	Out
Other toxicities							
147. Cardiovascular toxicities	2	40	58	0	7	93	No consensus
148. Lymphatic toxicities	2	51	47	0	17	83	No consensus
149. Respiratory toxicities	9	63	28	2	36	62	Borderline
150. Neurologic toxicity	6	66	29	4	36	60	Borderline
151. Second malignancy	2	29	69	0	4	96	No consensus

Supplementary file S9 Consensus meeting participants

Stakeholder group	Name	Centre
Colorectal surgeon (10)	Andrew Renehan	Manchester
	Graham Branagan	Salisbury
	Martyn Evans	Swansea
	Nancy Baxter	Toronto, Canada
	Neil Smart	Exeter
	Nicola Fearnhead	Cambridge
	Peter Coyne	Newcastle
	Rachel Hargest	Cardiff
	Rick Saunders	Leeds
	Tamzin Cumming	Homerton
Oncologist (7)	David Sebag-Montefiore	Leeds
	Ian Geh	Birmingham
	Luc Dewitt	Amsterdam, The Netherlands
	Marianne Guren	Oslo, Norway
	Mark Saunders	Manchester
	Rachel Cooper	Leeds
	Victoria McFarlane	Southampton
Patient (13)	Angela Betsworth	Southampton
	Carol Sleith	Manchester
	Ian Curtis	Manchester
	David Crowe	Manchester
	Dean Nixon	Amherstburg, Canada
	Debbie Daley	Manchester
	Elaine Hughes	Bridgend
	Helene Hutchings	Ottawa, Canada
	Jill De Nardo	Manchester
	Lynne Atwood	Manchester
	Maggie Llewellyn	Manchester
	Sarah March	London
	Lindy Berkman (public representative)	London
Radiographer (1)	Lucy Davidson	Christie
Radiologist (2)	Catherine Grierson	Southampton
	Vicky Goh	London
Radiophysicist (1)	Ane Appelt	Leeds

Specialist nurse (1)	Julie Brewer	Manchester
Commissioner (1)	Julia Young	Newcastle
Facilitators (6, non-voting)	Rebecca Fish	Manchester
	Paula Williamson	Liverpool
	Caroline Sanders	Manchester
	Nasra Alam	Manchester
	Ruth Norris	Manchester
	Shira Baram	Manchester
Chair (1, non-voting)	Sara Brookes	Birmingham
Observers (2, non-voting)	Bilal Alkhaffaf	Manchester
	Andrew Harding	Lancaster
