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Literature Review

How can the aetiological factors of rectal distension be managed to reduce interfraction prostate motion during a course of radiotherapy treatment

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Abstract

Aim: During radiotherapy of the prostate it is important to minimise interfraction prostate motion to allow dose escalation and reduce normal tissue damage. Rectal volume has been identified as playing a significant role in prostate motion with various methods used to reduce it. The aim was to systematically review published literature to allow evidence based recommendations to be made to current practice to reduce interfraction prostate motion.

Materials and methods: A systematic search of CINAHL, Medline, PubMed, Science Direct, NHS Evidence and The Cochrane Library was performed. Limited searches of The Society of Radiographers website, OpenGrey and COPAC were undertaken, alongside manual searches of cross references of eligible articles. The quality of included papers was measured using a pre-existing tool. The causes, consequences and solutions to manage rectal volume and its effect on prostate position were extracted, compared and evaluated to extract solutions to be implemented into clinical practice.

Results: Of the 2,339 unique articles systematically retrieved, 23 met the inclusion criteria, 15 of which discuss radiotherapy, five constipation and three flatulence.

Findings: A combined medicinal and dietary approach adaptable to departmental workflow is required to manage rectal volume, with special consideration to patients with pre-existing extrinsic factors.

Keywords: bowel gas; interfraction motion; prostate; radiotherapy; rectal distension; rectal volume

INTRODUCTION

Radical radiotherapy for localised prostate cancer is reliant upon the delivery of a tumourcidal dose of radiation to the prostate.[1] A conventional dose of 72 Gy is required,[2] however higher doses are desirable.[3] The introduction of conformal planning, image guided radiotherapy (IGRT) and intensity-modulated radiotherapy (IMRT) have enabled dose escalation to take place through increased accuracy and the ability to visualise prostate movement, while also reducing rectal and bladder toxicity.[4] However, variable rectal filling still appears as a hindrance to further reducing treatment margins.[3]

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The influence of rectal distension on prostate motion occurs due to their anatomical position. The prostate and seminal vesicles (SVs) are close to the mid rectum,[5] therefore reducing faeces and gas within the bowel is necessary to achieve increased accuracy of radiotherapy treatment, dose escalation and increased local control.[6] Recommendations to minimise the V_{70} and V_{75} rectal volumes, without compromising tumour coverage, has a significant impact on the predicted complication probability set out in the normal tissue complication probability model. A reduction in the V_{75} by just 5% should limit Grade $\geq$2 and Grade $\geq$3 late rectal toxicity to <15 and <10%, retrospectively.[7] With the aim to reduce the incidence of late effects such as rectal bleeding and faecal incontinence.[8]

The advent of IGRT and fiducial markers has enabled movement of the prostate to be observed. IGRT allows direct visualisation of soft tissue using onboard cone beam computerised tomography (CBCT), while fiducial markers may be used in addition for treatment verification.[9] Studies[10,11] undertaken using these methods have found that movement is greatest in the anterior–posterior direction, which can be attributed to bowel filling. This causes changes to the size and shape of the rectum particularly in patients treated supine.[12]

Radiotherapy centres throughout Europe use varying forms of bowel preparation to reduce prostate motion including: dietary advice alone,[9] or in conjunction with micro enemas[13] or mild laxatives[14,15] to regulate the bowels, or fixed treatment times and rectal balloons.[16] The measurement of fiducial marker movement, and therefore prostate position compared with pelvic bone[9] and the measurement of rectal distension at set levels of the prostate using IGRT[15] have been used to assess effectiveness.

METHODS

The systematic review was undertaken using PRISMA[17] to investigate how aetiological factors of rectal distension can be managed to reduce interfraction prostate motion during radiotherapy. The literature was analysed using SIGN checklists[18] relevant to study design. An outline of the search strategy is shown in Figure 1 with an overview of inclusion/exclusion criteria in Table 1.

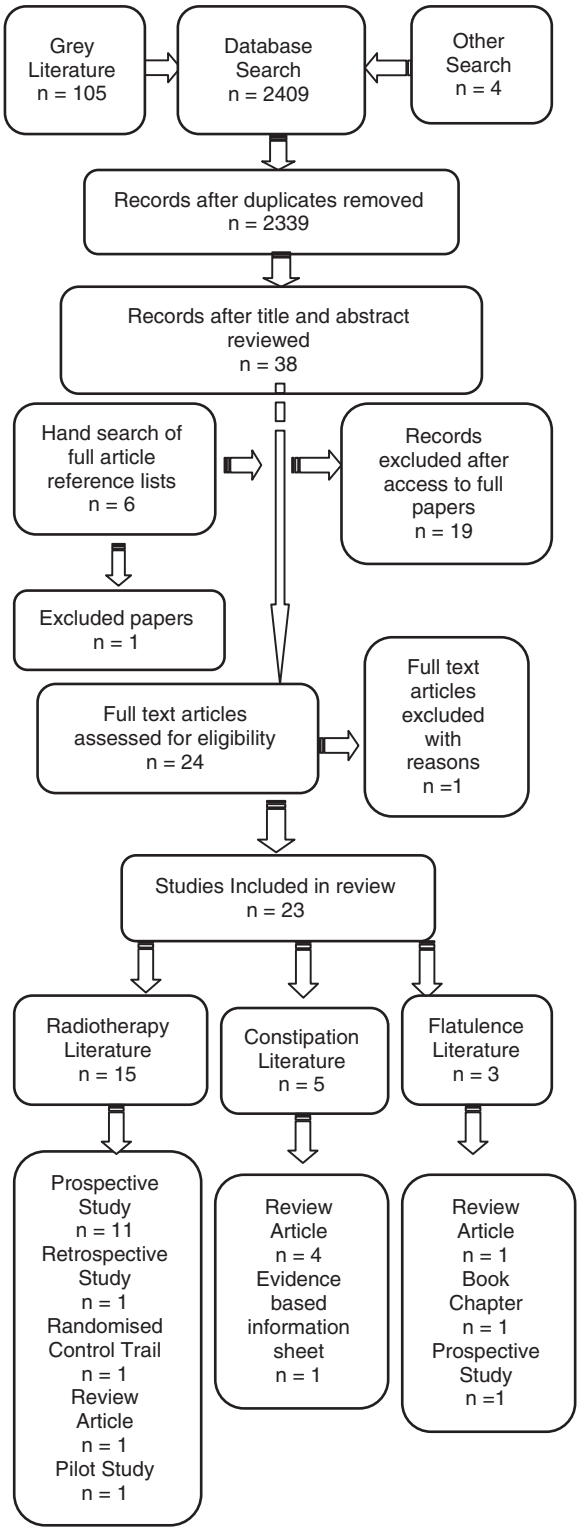

Figure 1. PRISMA flow diagram of the search and selection strategy used in the systematic review undertaken between January 2008 and December 2013. Databases searched: CINAHL, Medline, PubMed, Science Direct, NHS Evidence and The Cochrane Library.

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Table 1. PICOS used to define inclusion and exclusion criteria

PICOS	Inclusion criteria	Exclusion criteria
Participants	Older male population (45 years +) with increased bowel volume	Female only studies Infant studies
Interventions	Aetiology of rectal distension Use of physical/medicinal intervention to reduce bowel volume	Pre-existing bowel condition, that is, irritable bowel syndrome (IBS)
Comparators	Interfraction motion Bowel volume Prostate motion Effectiveness of medication	
Outcomes	Solution in practice to reduced rectal volume/prostate motion	Bowel late effects
Study design	Both prospective and retrospective Randomised clinical trails and population based cohort studies Pilot studies	Abstracts only Protocols Poster presentations Old or few references

RESULTS

Of the 2,339 citations obtained through database, grey literature and professional website searches, only 38 were selected for further evaluation following review of the title and abstract. For full results see PRISMA Flowchart (Figure 1).

The results of the review are presented by emerging themes seen throughout the included literature.

AETIOLOGY OF CHANGING RECTAL VOLUME

Bowel gas

Radiotherapy related literature[1,3,5,8,19–29] state that either gas and/or faeces are the cause of rectal distension and consequently prostate motion. Moving gas appears to be the main concern,[1] but there is little literature to explain the causes of bowel gas, making solutions to reduce it problematic. Two non oncology related papers[30,31] agree that both the physiology and pathophysiology of flatulence is poorly understood. However, all flatulence related literature[30–31] agreed that the volume of gas evacuated is determined by both diet and colonic microbiota,[31] also suggested[32] is that certain medications may impact on gastrointestinal motility and therefore intestinal gas.

The colonic microflora varies considerably among individuals with differences in activity, stability and composition[31] and can be determined by environmental factors, both early and later in life; antibiotics and dietary exposure.[30] A difference has been observed[31] in microbial and bacterial taxa in patients with excessive passage of gas per anus compared with healthy subjects. One pertinent taxon documented in the literature, with regard to the issues seen in prostate radiotherapy is *Bilophila wadsworthia*. This was shown to positively correlate with the volume of gas evacuated.[31]

The literature suggests that the amount of fermentation and colonic microorganism consumption is affected by gut transit time,[30,32] which can be influenced by pelvic muscle activity.[30,32] Faecal impaction reduces gut transit time, prolongs fermentation and therefore may increase gas production.[30] Highlighting that constipation should be treated effectively. Lipids are also stated to delay transit time, with transit of gas being more effective when stood than when supine.[30]

Constipation

It is documented[33] that healthy active older people have normal bowel function but the risk of constipation still exists, although it should not be seen as a physiological consequence of normal aging.[34] This and other literature reviewed[33–36] report that the medical definition of constipation is less than three bowel movements per week, although patient definition relates to stool consistency, feeling of incomplete emptying, straining and the urge to defecate, rather than frequency alone. Evidence[33–36] also suggests that the prevalence of constipation increases with

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older age, with a larger increase seen after the age of 70 years.[36] This is particularly relevant as a recently published UK paper[19] states that participants in three investigative groups had a median age at presentation for prostate cancer of 70·5, 62 and 71 years.

Two papers[33,36] describe the aetiological factors of constipation in older people, which include both extrinsic and intrinsic factors (see Table 2). A review[35] undertaken also describes the changes in the lower gastrointestinal tract that are associated with ageing. The existence of extrinsic and intrinsic factors,[33,35,36] can lead to slow colonic transit, low stool output and reduced bowel movement frequency[33] and should be considered further when applying bowel preparation in radiotherapy of the prostate.

CONSEQUENCES OF CHANGING RECTAL VOLUME

The prostate and SVs lie between the bladder and rectum and have shown to be affected by physiological changes in both bladder and rectal volume.[1,3,5,8,20–24,26] It has been shown that anterior–posterior prostate motion is influenced by a change in rectal shape and volume.[23,26] These changes can noticeably alter the position of the anterior rectal wall and consequently the prostate tumour volume in relation to the preplanned radiotherapy target,[23,26] causing both intrafraction and interfraction prostate motion.[5,25,26]

Due to the expansion in the use of IMRT there is an increased emphasis on decreasing treatment margins to reduce dose to organs at risk[1,8,23,26] without compromising dosimetric coverage of the clinical target volume.[25,26] With rectal gas being a significant predictor of interfraction motion due to rectal distension[1,26] this appears a large hindrance to reducing these margins. However, there is insufficient information on how to control rectal volume.[19,21]

Current solutions

A UK wide survey undertaken in 2009 has shown that 40% of responding centres use some form of bowel preparation,[19] with the aim to achieve consistency in rectal volume.[8,19–22,24,25,27,28,32]

Within the literature, bowel preparation takes on three distinct forms from varying countries, summarised in Table 3, alongside lifestyle modifications.[33,34,36]

DISCUSSION

The literature review[1,3,5,8,19–29] highlights the importance of managing rectal volume, although

Table 2. A summary of the aetiological factors of constipation discussed in the literature

Extrinsic factors	Intrinsic factors
Reduced fluid intake[33,36]	Pelvic floor dysfunction (PFD)[36]
Low fibre diet[33,36]	Slow colon transit time (SCT)[36]
Reduced mobility[33,36]	A combination of both PFD and SCT[36]
Environmental, that is, reduced privacy due to institutionalisation[36]	Neurodegenerative changes in enteric nervous system[36]
Endocrine/metabolic disorders, that is, diabetes[36]	
Neurological disorders, that is, dementia, Parkinsons disease[36]	
Psychological co-morbidities, that is, depression, anxiety[33]	
Concurrent medication, that is, opiates, iron supplement,[36] antidepressants[33]	

Table 3. A summary of methods discussed in the literature to manage rectal distension

Mechanical intervention	Medicinal intervention	Dietary manipulation	Lifestyle modifications
Endorectal balloon[25]	Antibiotics[30,32]	High fibre diet[1,3]	Increase fluid intake[33,36]
Interstitial biodegradable balloon[27]	Antiflatulents[30]	Low flatulent diet[30,32]	Increase dietary fibre[33,36]
Rectal emptying tube[21]	Micro enema[19,20,22]	Probiotics[24]	Exercise[33,36]
Manual gas removal[26]	Laxatives[8,19,22,33,34,36,37]		Reducing delays to defecation[33]

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the way in which this is undertaken is varied in both technique and levels of efficiency, in part, due to a lack of understanding of the aetiology of both bowel gas and constipation.[1] Despite some limitations this review highlights areas to be investigated further.

Mechanical interventions

Non UK papers discuss the use of interstitial biodegradable balloons,[27] endorectal balloons (ERB),[25] rectum emptying tube (RET)[21] and manual removal of rectal gas.[28] There is no UK data within the review regarding mechanical interventions.

The aim of mechanical interventions is to manage rectal volume and ultimately reduce rectal dose and toxicity.[21,25,27,28] Literature discussing this explain that the irradiated volume or cross-sectional area of the rectum is reduced. However, evidence in the literature regarding interstitial spacers[28] and ERBs[25] shows that neither completely pushes the rectal volume out of the field. ERBs have also been shown[25] to push the anterior rectal wall into high dose areas despite reducing dose to the posterior rectal wall. This in turn could lead to increased toxicities.

All mechanical techniques of managing rectal volume included in the review are documented to be reproducible.[21,25,27,28] Initial placement problems where highlighted.[21,25] Insertion of the RET[21] was incorrect on two occasions leading to a change in insertion technique. The use of an ERB[25] may give rise to interfraction motion due to stools present getting trapped upon initial insertion at the planning scan. This could lead to reproducibility problems during radiotherapy treatment.

Generally patient acceptance was high for what appear to be invasive techniques. However, one patient in the RET[21] study did not participate further due to lack of understanding of study purpose and repetitive examinations. Of all mechanical interventions the interstitial balloon[27] is the only semi permanent device. All others would need to be applied at each treatment fraction, meaning repetitive insertion would be required, possibly leading to further patient compliance issues and increased irritation of the rectum,[21] alongside increased treatment times.

Literature relating to interstitial balloons,[27] RETs[21] and manual evacuation of the rectum[28] concludes that they are reproducible techniques; however, the use of ERBs has shown that interfraction set up deviations were not significant between patients with or without the device in place.[25] Considering this and the possible increase in rectal dose, mechanical interventions may help to manage rectal volume but with some disadvantages. Therefore, consideration should be given to evidence based solutions that can be implemented into radiotherapy practice

Medicinal interventions

Many papers discuss the use of laxatives.[8,19,22,33,34,36,37] Laxatives take many forms including; bulk forming, stool softeners, osmotic agents, stimulants and chloride channel activators.[33,34,36,37] Little evidence exists to support the use of many laxatives in patients with chronic constipation, with the exception of lactulose and polyethylene glycol, which can improve stool frequency.[34] Of the two, polyethylene glycol was shown to be most effective,[37] in stool frequency and formation. It is also documented to have a faster effect[34] than many laxatives, other than stimulants[34] such as senna, which has a lack of placebo controlled evidence.[33] Despite this, none of the radiotherapy literature in this review discussing the use of diet and laxatives[8,22] specifies the use of this medication; no reasons are specified for the choice of laxatives used in the studies.

The use of enemas to manage rectal volume in prostate radiotherapy is common[19,20,22] and the suggestion has been made that in departments where access to CBCT is limited it may prove advantageous.[20] In a recent study[19] it was shown that the application of enemas reduced the number of geometric misses of >5 mm by half compared to no intervention, this was, however, not statistically significant due to a limited sample size of ten patients. In the context of prostate radiotherapy the use of daily enemas has been found to be easily implemented, highly efficient

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at reducing prostate motion, semi-invasive, inexpensive and well tolerated.[19,20] Enemas can be used to clear the rectum and restore normal function before commencing further bowel management,[33] although they are associated with greater risk of mechanical injury.[33] It is also recommended that enemas should only be for short term use,[34] something to consider during a course of radiotherapy.

A reduction in rectal volume has been observed in studies undertaken using CBCT where interfraction motion was seen to be larger in patients who attended computed tomography (CT) planning with a full rectum.[8,23] Although more recent information[5,8] suggests that such time trends were not observed in patients following diet and laxative bowel preparation before they attended CT planning. Due to time constraints within radiotherapy the possibility of using enemas at the initial planning scan should be considered to reduce rectal distension, and therefore time trends, that have previously been observed.[23]

The presence of gas in the bowel has been shown in the literature to cause interfraction prostate motion.[1,26] Two papers[30,32] discuss the use of Rifaximin, a non absorbable antibiotic. This has been shown[32] to be of value in patients who have small bowel bacterial overgrowth, to reduce intestinal gas production.[30] Despite this claim, decreased rectal excretion has not been demonstrated.[30] Considering this and the problems associated with long-term antibiotic therapy, no clear benefit is seen in the manipulation of flora in flatulent patients[30] and should be disregarded for use during a course of radiotherapy of the prostate.

A second medicinal approach to managing rectal volume are antiflatulents, namely β-galactosidase,[30] designed to enhance the digestion of oligosaccharides. Simethicone[30], which has defoaming properties, and peppermint oil,[35] which has an antispasmodic effect on the gastrointestinal tract. Each one of these is discussed with caution in regard to the evidence base surround their effectiveness.[30]

The literature surrounding medicinal intervention for constipation is wide ranging and, in the most part, conclusive. However, evidence regarding bowel gas reduction was less so, despite different approaches,[30,32,35] emphasising the difficulties in managing rectal volume.

Dietary interventions

Dietary intervention to manage rectal volume during prostate radiotherapy treatment has been investigated by a number of authors.[1,3,5,8,24,29] Many discuss the use of high fibre diets, alone[1,3] or in conjunction with a mild laxative.[5,29] The use of such diets is also outlined in non radiotherapy literature with the aim to encourage stool propulsion.[34] Evidence[5,8] exists that the implementation of a high fibre diet has shown to be effective in reducing rectal motion throughout a course of prostate radiotherapy, although one paper[1] did not prove this to be effective in achieving a reproducible rectal dimension. However, consensus[1,5,8] is that diet groups, when versus non diet groups, showed decreased feaces, moving gas and reduced rectal volume. Despite the reductions in gas and rectal volumes observed in these studies it has been suggested that a high fibre diet does not have an immediate effect[34] and can worsen bloating and flatulence, although this usually resolves through time.[32,34] Patients with normal transit constipation typically respond well to a trail of dietary fibre, those with a poor response may have other disorders[34] and may benefit from a suggestion made in one paper[32] of the FODMAP diet[32], which should be investigated further.

The literature[30] explains that dietary intake may cause an increase in colonic gas, for reason including; fermentation of sorbitol by colonic bacteria, malabsorption of lactose and the interference of nutrient absorption by components of everyday meals. Examples of such components include fibre, which increases starch malabsorption, and also a pancreatic amylases inhibitor, which is found in beans, and can slow starch digestion and absorption.[30] It may be that consideration needs to be given; not only to the exclusion of individual foods, but that some combinations of food in a single meal may lead to an increase of colonic gas production. It has also been suggested that further investigation into the role of gut microbiota may allow development of future

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treatment strategies rather than restrictive diets, which lack long-term patient compliance.[31]

The influence of diet on colonic gas is discussed in three papers[30–32] and consensus is that a diet rich in fermentable residue encourages excessive flatulence; this includes resistant starch, oligosaccharides and plant fibres. It has been[30] suggested that most patients note a dramatic decrease in gas evacuations when they consume a diet without the above food groups. This has not shown to influence stool frequency or consistency.[31]

The aetiology of constipation may provide evidence to support the need for an adaptive approach to individual patients, taking into consideration both intrinsic and extrinsic factors.[33,36] There is little that can be done regarding some extrinsic and intrinsic factors of constipation in the time frame for radiotherapy treatment, due to the specialist nature of potential problems such as diabetes, neurological disorders and anxiety.[34,36] One suggestion is that patients who have a predisposing factor for constipation may trigger the need to prescribe a form of bowel preparation automatically assigned to this 'high risk' group.

Solutions can be put in place to eliminate as many extrinsic factors as possible, through clear patient information, evidenced in a paper[3] that discusses the successful implementation of a fluid and fibre diet to manage rectal volume. This could help to manage rectal volume in the majority of patients undergoing prostate radiotherapy. Effectively treating constipation may also decrease rectal gas caused by prolonged colonic fermentation.[30] Further consideration to dietary information is required to establish a workable solution for all but the 'high risk' group.

The use of probiotics has been investigated in relation to radiotherapy of the prostate,[24] and was found to have benefits including reduction of radiation toxicities and interfraction set up errors. Although probiotics vary greatly in formulation,[32] and should be used with caution as excessive amounts can increase flatulence[24] and therefore rectal distension, further investigation could be advantageous.

In a number of papers[33,34,36] it was found that lifestyle issues can be associated with constipation. Aspects such as fluid intake,[33,36] dietary fibre,[33,36] history of laxative usage,[33] exercise[33,36] and delaying the urge to defecate[33] are thought to impact upon constipation. Although they are unsubstantiated in their contribution to constipation, it is common place for it to be discussed by both health professionals and consequently the public,[36] without harm.

In studies[1,3,24] evaluating the introduction of a dietary protocol, as with all interventions, patients were accepting of this with little deviation. It is presumed[1] that this acceptance illustrates the determination of patients to continue with interventions when they have perceived benefits.

Patient compliance is difficult to manage and assess to ensure instructions have been understood and followed correctly.[9] There is no specific data in the review papers to quantify patient compliance and this may have a bearing on study outcome.

LIMITATIONS OF THIS REVIEW

(1) Traditional synthesis methods were not appropriate due to the range of articles acquired.
(2) Unable to make strong evidential recommendations to reduce bowel gas as only three included papers focused on this area.
(3) The definition of rectal volume was not consistent in all studies, some compared cross-sectional rectal area, others rectal diameter, which is evidenced to have a strong correlation with anterior–posterior prostate motion.[38] In the analysis it was assumed that reduction in each was a positive result.
(4) Difficulty in comparison of the dietary literature, as few studies include specifics.
(5) Work was undertaken for a dissertation project therefore papers were screened and selected by one investigator only. This may introduce bias from the author.

CONCLUSION

The desire to dose escalate utilising new radiotherapy technologies requires consistent rectal

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filling to minimise toxicity from interfraction prostate motion.[25] It is evident from the literature that intervention before CT planning to manage rectal volume throughout the entire course of treatment is advantageous. Whether this is dietary advice, requiring pre CT contact and long-term patient compliance or enema based, also requiring compliance but more adaptable to the whole radiotherapy workflow.

What has also become apparent is that one bowel preparation regime will not benefit all patients, and that some individuals with complex extrinsic conditions should be identified and receive an approach appropriate to their needs. Investigation of how to highlight these patients in a timely manner should be undertaken on a departmental basis due to variation in workflow.

Importantly, further research is required into probiotic use, and investigation into the FODMAP diet, to assess if they may be of benefit to managing rectal volume in patients undergoing radiotherapy to the prostate.

RECOMMENDATIONS

- Individual centres would benefit from the introduction of bowel preparation in the form of enemas at CT planning.
- Patients would benefit from dietary information developed with consideration to the findings in this review.
- Identification of patients who are 'high risk' to enable effective bowel interventions to be established throughout the whole treatment process.
- The use of three-dimensional CBCT imaging is recommended to monitor rectal volume throughout treatment with or without the addition of daily enemas.
- Working collaboratively would allow UK centre to share practice and develop working guidelines to facilitate the formation of an effective bowel preparation regime. This would be adaptable to individual departmental practice, but established using a shared knowledge and evidence base. Allowing for comparability of effectiveness over a wider population.

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Conflicts of Interest

None.

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