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Friday 22nd March 2019

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Screening for and managing the late gastrointestinal effects of radiotherapy

Professor John Staffurth,

Professor in Clinical Oncology, Division of Cancer and Genetics, School of Medicine, Cardiff University

and

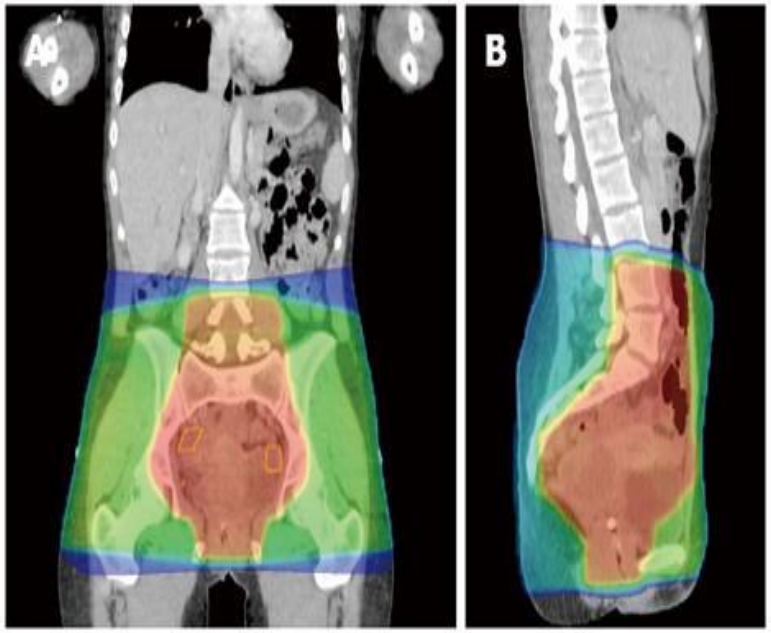
Consultant Clinical Oncologist, Velindre Cancer Centre, Cardiff

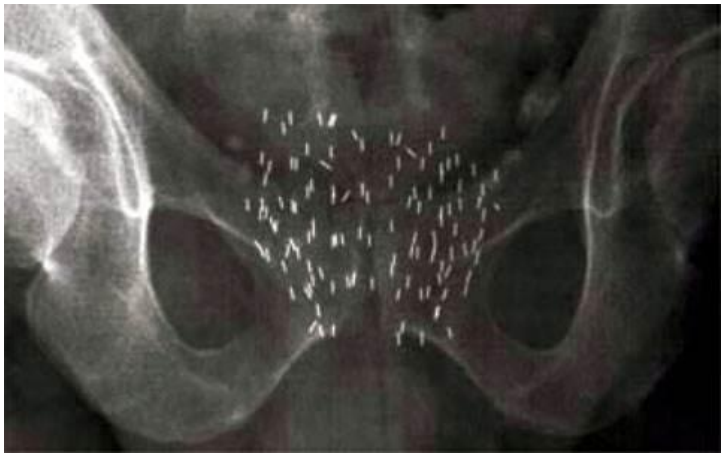
Talk structure

- Introduction
- Design of a patient-focussed screening tool – ALERT-B
- Implementation of a new service – EAGLE
- Extension project – TRIGGER
- Summary and questions

Background

- Macmillan estimate that there are currently 2 million cancer survivors in the UK
- NCRI are prioritising Living With and Beyond Cancer (LWBC)
- >17,000 patients receive radical pelvic radiotherapy each year in the UK
- Many patients are cured with minimal symptoms but some end up with long term symptoms





Late, Consequential Effects ('Pelvic Radiation Disease')

- Gast…
- …phoedema

Under reported

Under recognised

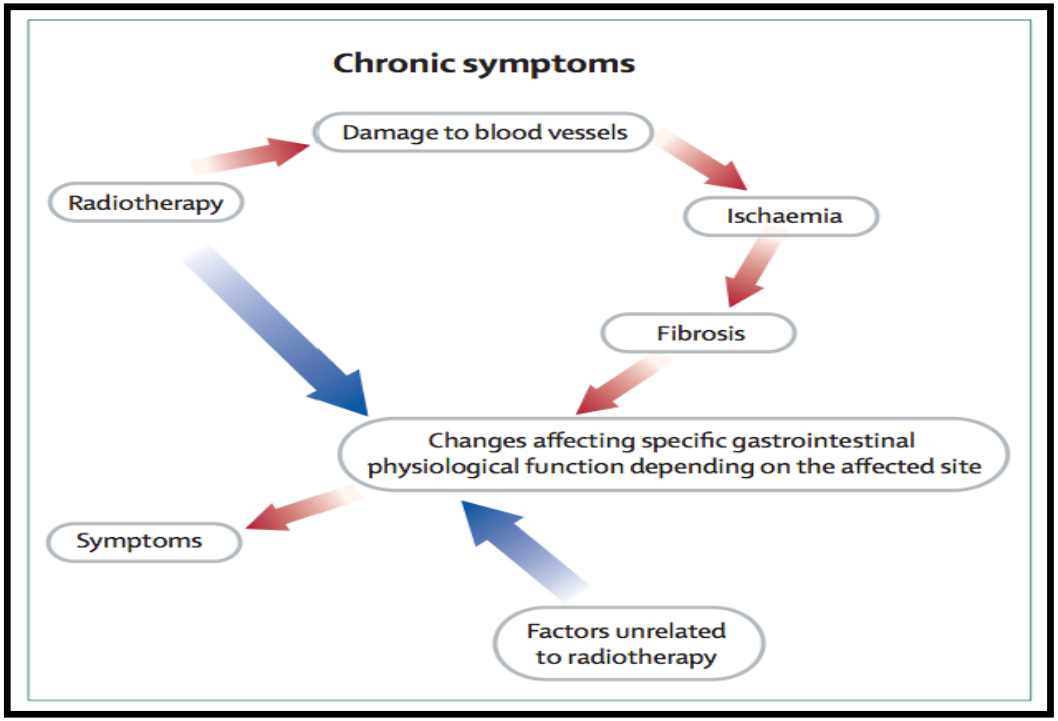
Under managed

www.PRDA.org.uk

2 phases of gastrointestinal toxicity with pelvic radiotherapy

Acute phase during radiotherapy

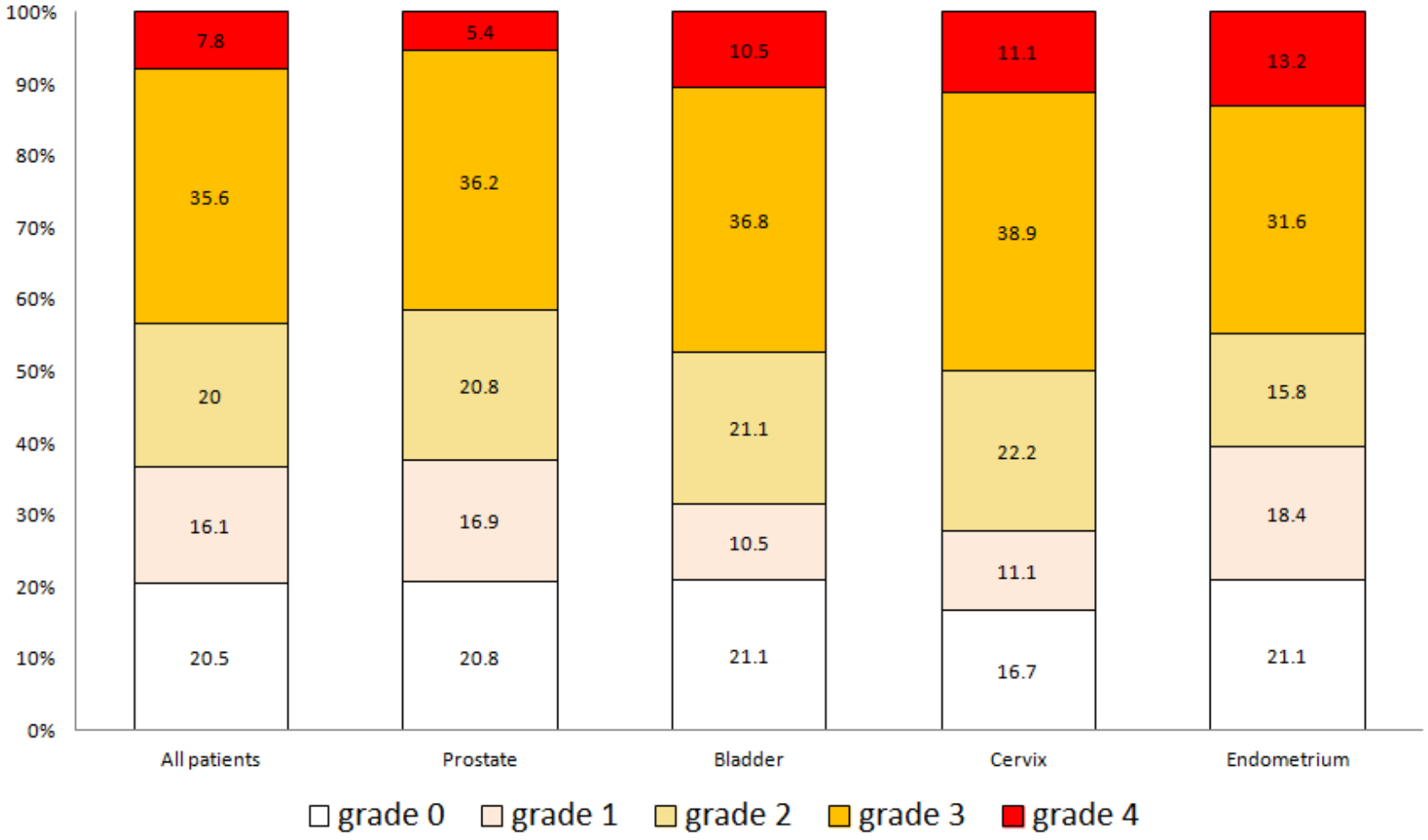
- Acute inflammatory response
- At its peak by 2nd week
- Resolved within 3 months



- It has been reported that 90% permanent change in bowel function (Olopade BJC 2005)
- Up to 40% patients report moderate to severe effects (Andreyev Lancet Oncol 2008)

Andreyev 2007

Our audit supports previous findings



Rashmi Jadon, 2015

Long list of reported symptoms

- Bleeding
- Bloating
- Borborygmi
- Constipation
- Diarrhoea
- Incontinence
- Flatulence
- Mucus
- Nausea
- Pain
- Urgency
- Vomiting
- Weight loss

It's really NOT all due to radiotherapy

Table 1. Causes of fresh rectal bleeding in patients with prior pelvic radiotherapy

Directly related to radiotherapy	Other causes
Acute radiation colitis	Anal fissure
Chronic radiation proctopathy	Haemorrhoids
	Diverticulosis
	Infection
	Inflammatory bowel disease
	Ischaemic colitis
	Polypoid lesions, that is, adenomas
	Rectal or distal colonic cancer

↑risk rectal cancer post prostatic radiotherapy
Wallis, BMJ 2016

Stacey & Green 2013

Causes of diarrhoea

- New/recurrent cancer
- IBD
- Microscopic colitis
- Coeliac disease
- Endocrine
- Infection
- Drug si
- P

- Bile acid
- S
- (eg
- malabsorption
- atic insufficiency
- Rapid transit / short bowel
- Strictures

Multiple diagnoses often coexist

- **Other treatments:**
  - Chemotherapy
  - Immunotherapy
  - Surgery
  - Psychological

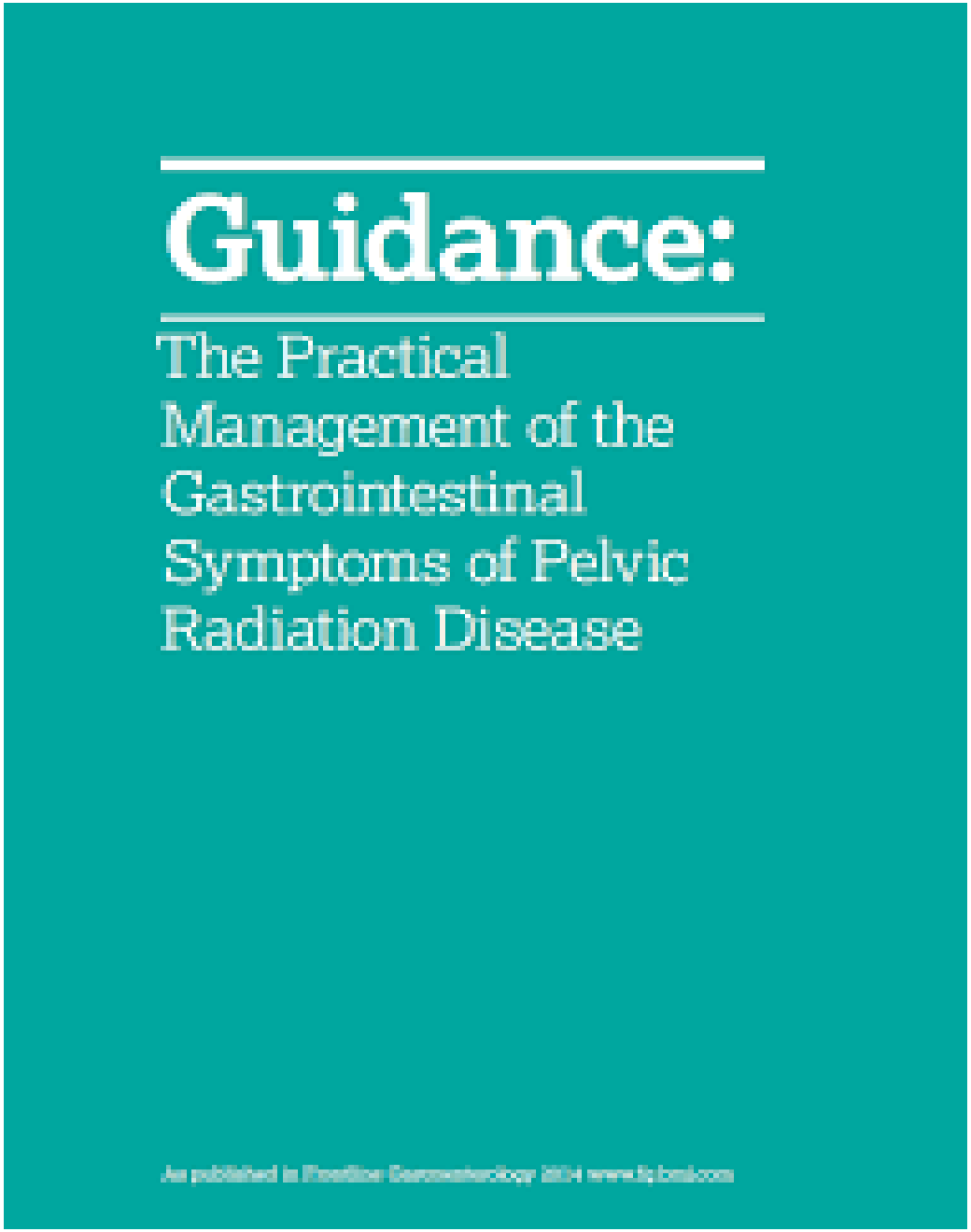
- As these can have identical symptoms you need an algorithmic approach to management

- Royal Marsden NHS Foundation Trust Guidance, led by Jervoise Andreyev

- Supported by Macmillan
- Published by BSG

http://www.prda.org.uk/wp-content/uploads/2016/10/Practical-Management-of-GI-Synptoms-of-PRD.pdf

MACMILLAN CANCER SUPPORT



The ORBIT study…

THE LANCET Oncology

Andreyev et al; 2013

Algorithm-based management of patients with gastrointestinal symptoms in patients after pelvic radiation treatment (ORBIT): a randomised controlled trial

Median 9m post RT

218pts with 'PRD'

70% urological

	68pts given supported self care booklet	70pts following algorithm seen by consultant gastroenterologist	80pts following algorithm seen by trained CNS
Change in IBDQ-B at 6m	4.9 (1.4-8.4)	10.4 (7.7-13.1)	9.1 (6.9-11.2)
Difference cf booklet		5.47 P=0.01	4.12 P=0.04

Considered 'clinically meaningful' difference

But…

- UK survey showed <20% patients are referred to gastroenterology (Clin Onc 2011)

- Reasons for non-referral include patients not been screened for late effects
  - Staff not knowing that appropriate referral and management can have a huge benefit to a patient's quality of life
  - Staff without the time or interest to ask about these symptoms
  - Patients not wanting to bother or embarrass their 'cancer' team about effects of their treatment
  - Tools in this space designed to assess toxicity or QOL for clinical trials and not to identify symptoms/ conditions that can be improved with intervention
- Lack of suitable services to refer to

Cardiff Group

GUIDELINES

Guidelines for the investigation of chronic diarrhoea, 2nd edition

P D Thomas, A Forbes, J Green, P Howdle, R Long, R Playford, M Sheridan, R Stevens, R Valori, J Walters, G M Addison, P Hill, G Brydon

Gut 2003;52(Suppl V):v1–v15

Late gastrointestinal effects of pelvic radiation: a nurse-led service

Helen Ludlow, John Green and Jeff Turner

British Journal of Nursing, 2017 (Oncology Supplement), Vol 26, No 4

SPiRiT

Grwp Sgil-Effeithiau Radiotherapi Pelfis De Cymru
South Wales Pelvic Radiotherapy Toxicity Group

Rhodri Stacey in Swansea

WE ARE MACMILLAN. CANCER SUPPORT

Canolfan Ganser Felindre
Velindre Cancer Centre

PROSTATE CANCER UK

ALERT-B

(Assessment of Late Effects of RadioTherapy-Bowel)

ALERT-B Screening Tool

Affix Patient Label Here

Date: _____

Your specialist has asked you to complete this screening tool to pick up any bowel or tummy problems you may have developed following radiotherapy treatment.

Please answer Yes or No to the following questions:

1. Do you have difficulty in controlling your bowels (having a poo), such as:
   - Having to get up at night to poo — Yes ☐ No ☐
   - Having accidents, such as soiling or a sensation of wetness ("wet wind") — Yes ☐ No ☐
2. Have you noticed any blood from your bottom recently? (any amount or frequency) — Yes ☐ No ☐
3. Do you have any bowel or tummy problems that affect your mood, social life, relationships or any other aspect of your daily life? — Yes ☐ No ☐

   (e.g., do you avoid any activities or situations – travel, work, social life or hobbies? Do you take continence supplies or spare clothing with you when you go out? Have you made any dietary changes? Do you need to allow for frequency or urgency of needing the toilet?)

If you have any other problems your doctor will be happy to discuss this with you.

Marie Curie Cancer Care

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Clinical Oncology xxx (2016) 1–9

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

The Three-item ALERT-B Questionnaire Provides a Validated Screening Tool to Detect Chronic Gastrointestinal Symptoms after Pelvic Radiotherapy in Cancer Survivors

S. Taylor *, A. Byrne *, R. Adams †, J. Turner ‡, L. Hanna †, J. Staffurth †, D. Farnell §, S. Sivell *, A. Nelson *¶, J. Green ‡¶

Funded by tenovus cancer care gofal canser

Dr John Green &
Prof Annmarie Nelson

'DESIGNER project':

Design a screening tool:

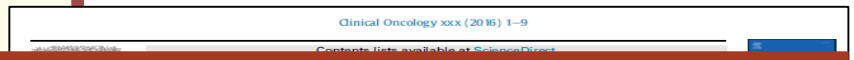
Rapid review of literature

Review by expert group clinical group

Involvement of patients to getting wording correct

ALERT-B

(Assessment of Late Effects of RadioTherapy Bowel)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THE IMPACT OF SPECIALISED GASTROENTEROLOGY SERVICES FOR LATE PELVIC RADIATION DISEASE: RESULTS FROM THE PROSPECTIVE MULTI-CENTRE EAGLE STUDY:

Improving the Wellbeing of Men by Evaluating and Addressing the Gastrointestinal Late Effects of Radical Treatment for Prostate Cancer

Professor John Staffurth,

Professor in Clinical Oncology, Division of Cancer and Genetics, School of Medicine, Cardiff University and

Consultant Clinical Oncologist, Velindre Cancer Centre, Cardiff

Co-authors:; S. Sivell, S. Ahmedzai, J. Andreyev, D. Farnell, J. Green, D. Sanders, C. Ferguson, S. Pickett, L. Smith, D. Cohen, R. O'Shea, S. Campbell, S. Taylor, and A. Nelson

EAGLE Study Overview

Screening
- Patients' ≥6 months attending urology/ oncology clinic from radical prostate radiotherapy (prostate/prostate bed/ nodal radiotherapy) will be screened by routine clinical staff with a three question screening tool (Alert-B).

Validation
- The Alert-B tool was validated in oncology clinics using the Gastrointestinal Symptom Rating Scale (GSRS).

Bowel Symptoms
- Patients identified as suffering from bowel symptoms referred to the new gastroenterology EAGLE service: RMH-trained CNS or gastro-STR and dietetic support

Gastro clinic
- Participants offered algorithm-dictated investigations and management using the Royal Marsden NHS Foundation Trust PRD algorithm

Data Collection
- Data (including qualitative interviews) collected at three time points over the study at baseline, 6 (±2 months) and 12 months (±2 months).

Study outcome measures

- Bowel specific Health related Quality of Life (HRQoL);
  - ALERT-B
  - GSRS
  - EPIC bowel Scale
  - EORTC QLQ PR25: Bowel Symptoms Scale
- Global HRQoL
  - EORTC QLQ C30: Global QoL Scale
  - EQ-5D-5L
- Prostate specific HRQoL;
  - EPIC: Urinary, Sexual and Hormonal scales
  - EORTC QLQ PR25:Urinary, Sexual and Hormonal scales
- Patient, carer and staff experience via qualitative interviews
- Healthcare resource utilisation

Centres and patients

All 3 centres set-up a specialist PRD service – 2 with a CNS-led model (Cardiff and Brighton), 1 with a medical model (Sheffield)

339 patients screened

91 (27%) patients had a positive symptom on screening

23 patients declined referral:
- Symptoms trivial
- Long standing symptoms
- Already full investigated
- Did not want further investigations at this stage

58 (64%) patients accepted referral to gastroenterology

Investigations, diagnosis and treatment

36 patients attended 6 month follow-up

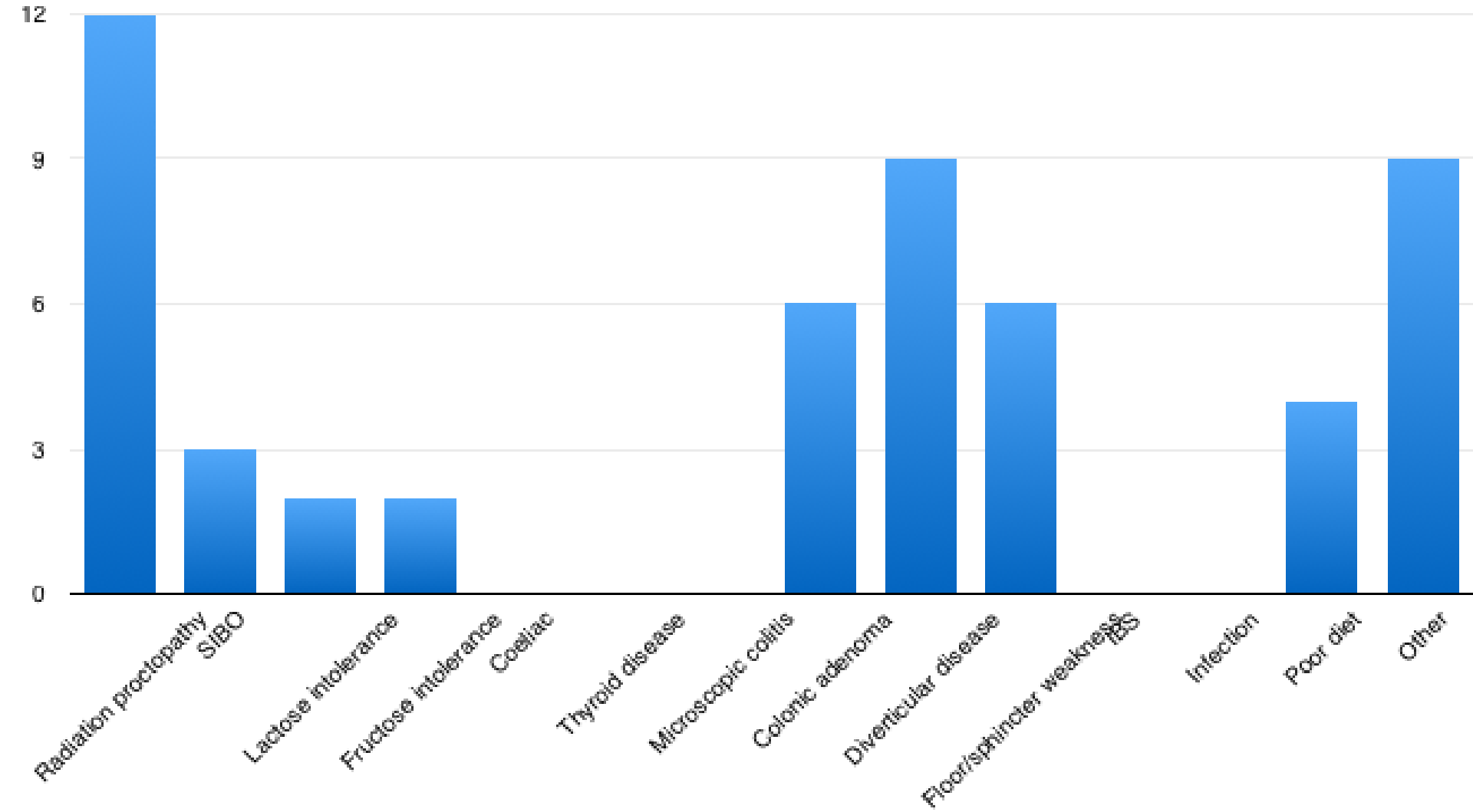
23 patients attended 12 month follow-up

51 interviews were held with patients, carers and healthcare professionals across three time points

Patients and treatment

Age (median)	68.3 years		
Site	Cardiff - 32	Sheffield - 21	Brighton - 3
Volume	Prostate - 49	Prostate + nodes - 9	
Treatment	EBRT - 57	EBRT + brachy - 1	
Fractionation	35-37 FR - 38	19-20 FR - 19	
ADT	Yes - 39	No - 15	
T Stage	T1 - 6	T2 - 27	T3 - 21
N stage	N0 - 52	N1 - 3	
Gleason Grade Group	2 = 36	3 = 15	4-5 = 2

Specific diagnoses

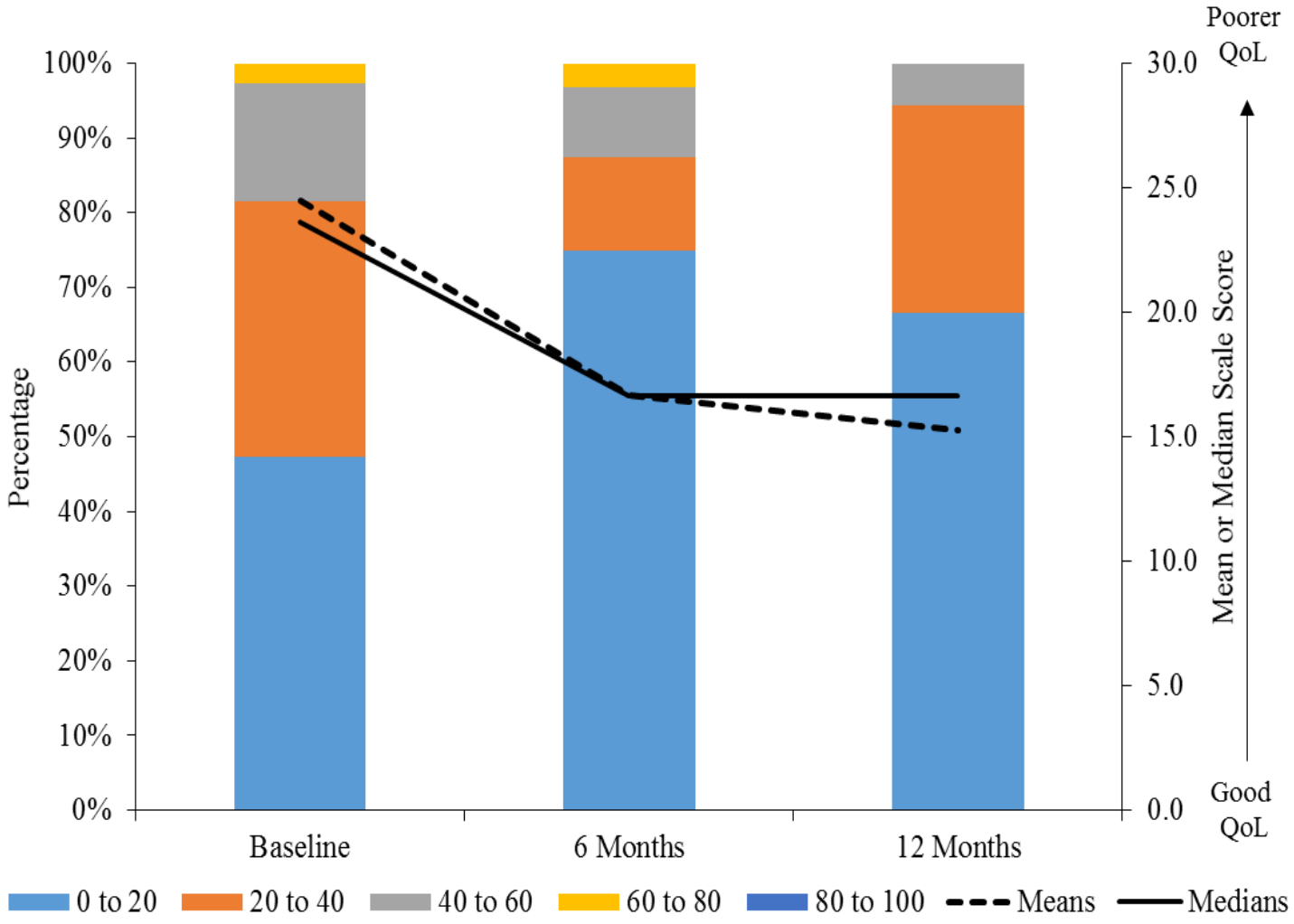


Changes in symptoms over time

Scale	Measure	(mean 6 months – mean baseline) ÷ SD baseline	(mean 12 months – mean baseline) ÷ SD baseline
EPIC	Bowel scale	0.44	0.53
GSRS	Diarrhoea scale	0.04	0.90
EPIC	Urinary Irritative / Obstructive scale	0.11	0.37
EPIC	Urinary Incontinence	-0.07	0.22
EPIC	Sexual Scale	0.16	0.23
EPIC	Hormonal Scale	0.14	0.37
EQ-5D-5L	Anxiety / Depression	-0.12	0.07
EQ-5D-5L	Pain	0.03	-0.06

Positive scores indicate an increase in QoL/ improved symptoms
Negative scores MEAN a decrease in QoL/ improved symptoms

EORTC QLQ PR25 Bowel Symptom Scale



Qualitative interviewing

Patient

"…Yes. A very definitely positive change. I mean, because it was getting to the stage where I was (pause) anxious not to, to eat, because I was afraid of, of bringing up the food … So, I'm eating much better now and I'm much ... and my appetite is back and, I'm not afraid to, to eat, if you know what I mean."

Staff

"… the man told me and his wife, for the very first time, he was actually really depressed.

He said he didn't feel like a husband should feel any more… He said it just destroyed him…"

Carer

- *"I cried on the way home ... just because I thought, 'Oh, my word,' you know? It wasn't the cancer – in fact, he found the cancer diagnosis easier to cope with, really, than what he's going through now…"*

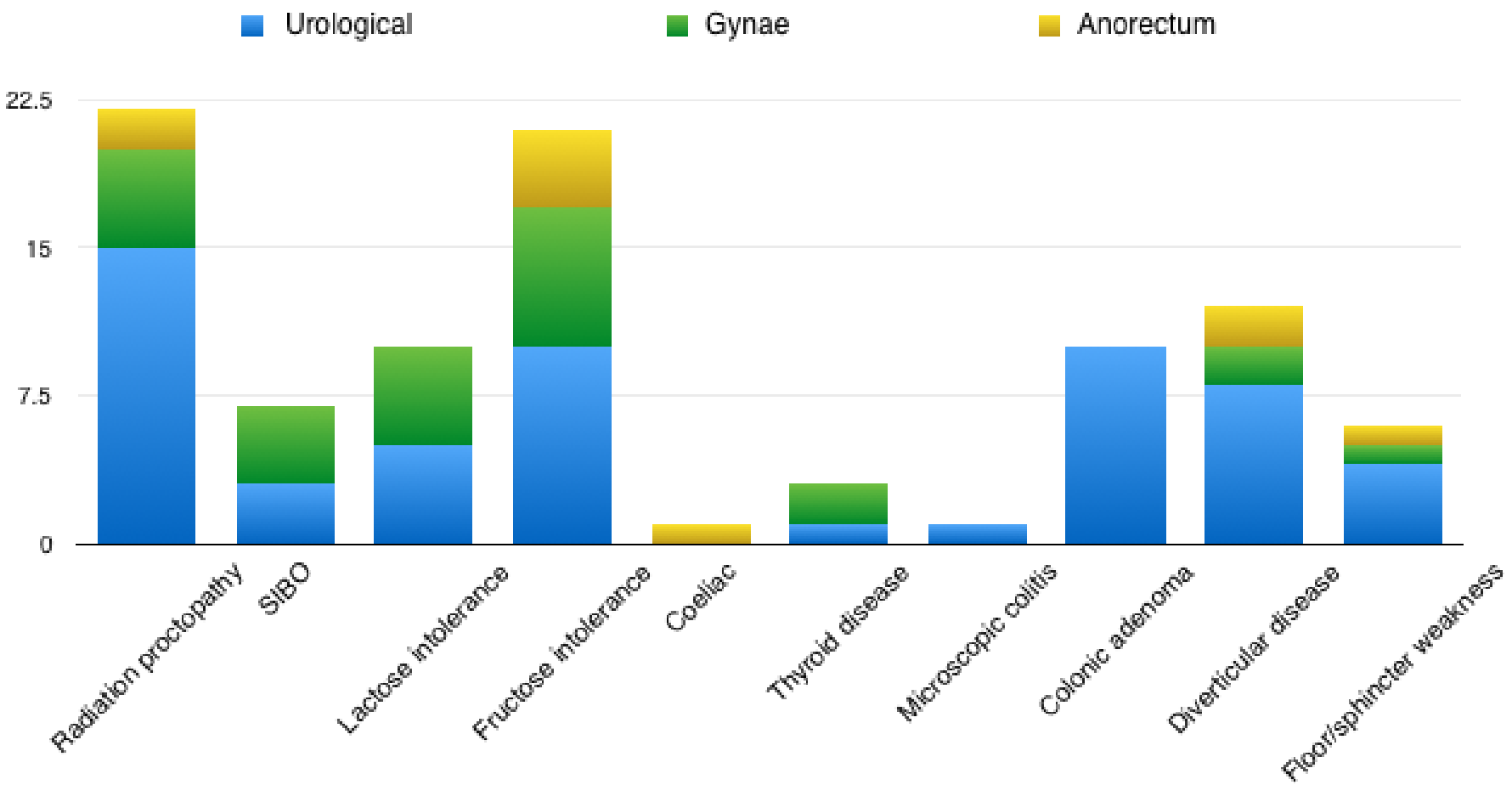
Healthcare resource utilisation

- Staffing and training costs per patient visit varied between the two delivery models
  - Nurse-led service (Cardiff): £117.04
  - Doctor-led service (Sheffield): £184.79
- Cost per patients for investigations and management = £2,390

- Training:
  - Royal Marsden online training course
  - Visits to Royal Marsden MDT and clinics
  - Email communication and support as needed

Results from parallel Macmillan funding in non-prostate cancers

Helen Ludlow, John Green, Jeff Turner, Steph Sivell, Annmarie Nelson, Lesley Smith, John Staffurth



Conclusions from EAGLE

- All 3 centres managed to set-up effective services, but they were fragile and dependent on individuals;
- We identified men with ongoing symptoms from a wide variety of diagnoses, but at a lower prevalence than expected
- The men that received this service were very pleased with the care that they received, many of them had no need for more than one or two appointments to resolve issues.
- Overall bowel related symptoms improved over time and there was also evidence of improved urinary and hormonal effects
- Qualitative interviewing identified strong patient, carer and staff support for the service with concerns around long-term funding paramount
- **We recommended a trans-pelvic, nurse-led model of care for management of Pelvic Radiation Disease**

Next steps

- Funding for the specialist gastroenterology services have not yet been secured
- Our service has continued using the CNS-led model embedded in IBD clinic
- Helen has joined a gynae/lower GI late effects clinic in Velindre
- Dietetic support is really important but currently lacking
- ALERT-B has been adopted within several UK trials including RAIDER (bladder cancer) and PIVOTAL boost (prostate cancer)

- Late PROs using ALERT-B collection is now part of NHSE Radiotherapy service specification
- ALERT-B is being used as a pilot within a Royal College of Radiologists and Macmillan Cancer Care funded project 'TRIGGER' tool to remotely collect PROs data from all patients having pelvic radiotherapy in three centres
- Hope to link results to the RTDS and to extend to an All-Wales program
- We are developing TRIGGER tools for other tumours sites e.g. for CNS tumours

TRIGGER

Archie Macnair and Matt Williams

- NHS England are creating a ‘Quality of life matrix’ which is in the process of being assessed in Pilot sites across the country
- This uses two PROM questionnaires EQ5D and EORTC QLQ- C30
- These are generic quality of life instruments and will not necessarily include items which differ according to the quality of treatment given. Also involved over 30 questions for each patient
- Instead we wanted to use a small screening tool that could be easily used in real life with minimal input from clinical staff
- Decided to choose ALERT-B in pelvic radiotherapy as a model that then could be generalised to radiotherapy for any tumour type

Vision

- Create an electronic platform that the patient signs up with only encouragement needed from the treating team either clinician or radiographer
- Patient would sign up with their demographic information, tumour type and length of radiotherapy
- Questionnaire would be asked just after treatment and automatically resent to the patient at defined time points initially 6 months later

- Aim to create an electronic platform that can be used in any hospital that needs minimal clinician intervention that can ask small trigger proms questionnaires
- This could highlight patients that could be potentially missed that need help
- Collect national data to ultimately improve radiotherapy services across the UK with the assumption that the rates of GI toxicity reflect quality of radiotherapy

Progress so far

- 3 pilot sites:
  - Imperial
  - Brighton
  - Velindre
- Clinicians or radiographers sign patients up
- Software used is MCO, but linked from RCR website:
- https://www.radiotherapyoutcomes.org

Progress so far

Activity

In November, across all cancer types, the percentage of eligible patients who have registered accounts with My Clinical Outcomes (MCO) was:

- Imperial: 18%
- Brighton: 20%
- Velindre: 33%

October

	Imperial		Brighton		Velindre	
	MCO patient registrations	% patients treated *	MCO patient registrations	% patients treated *	MCO patient registrations	% patients treated **
Colorectal	0	0%	0	0%	3	27%
Gynae	0	0%	1	17%	3	15%
Bladder	0	0%	0	0%	0	41%
Prostate	6	25%	9	25%	21	

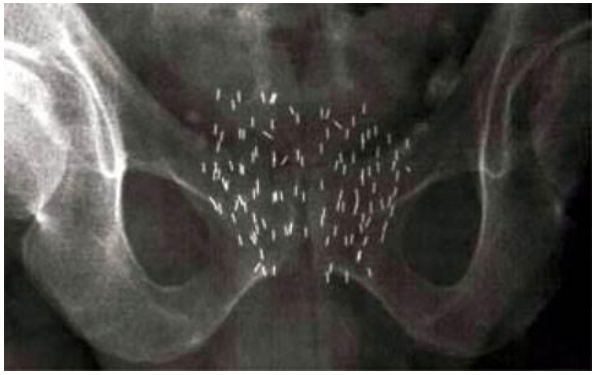
** Patients who have finished their treatment*

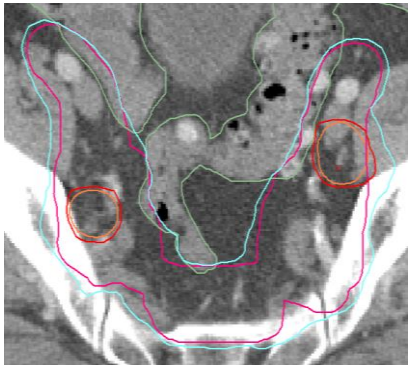
*** Proxy for patients completing data from previous months treatment start data*

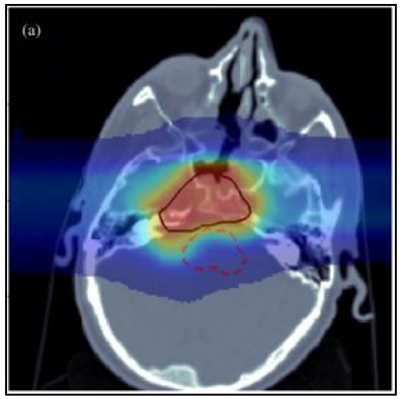
Conclusions

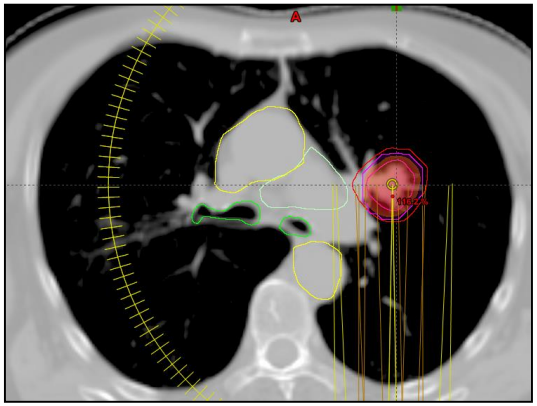
- Pelvic radiation disease is a real issue despite high quality radiotherapy
- It is under-recognised and reported but is often very treatable
- Services are appearing; currently this needs to be driven locally, but be aware of national interest groups
- We have confirmed the findings of the ORBIT study and are trying to implement the ALERT-B tool widely using an electronic platform

Radiotherapy is changing…









But this really isn’t going to go away

Thank you to the EAGLE team

Marie Curie Research Centre, Cardiff University

- **Prof Annmarie Nelson**
- Dr Steph Sivell
- Dr Fiona Morgan
- Sophia Taylor

Research Partners

- Father Raymond O'Shea
- Mrs Susan Campbell

Cardiff team

- **Dr John Green**
- Dr Jeff Turner
- Dr Jim Barber
- Dr Jake Tanguay
- Stephen Slade
- Claire Heymann

Sheffield and Brighton

- Dr Catherine Ferguson
- Angus Robinson
- Prof David Sanders
- Dr Susi Green

Co-investigators

- Prof Sam Ahmedzai
- Ms Ann Muls
- **Dr Jervoise Andreyev**
- **Dr Lesley Smith**
- Prof David Cohen
- Ms Sara Pickett

Our funders

- Movember – Paul Villanti
- Prostate Cancer UK – Kevin Rennie
- Macmillan Cancer Care – Lesley Smith

All investigations done

Blood tests

Scoping

- Anoscopy/Protoscopy
- Flexible Sigmoidoscopy
- Colonosopy
- OGD +/- duodenal aspiration

Special

- Transition study
- Glucose, hydrogen and methane breath tests
- Faecal Elastase
- SeHCAT scan
- Anorectal physiology
- Gut hormone (Chromogrannin A&B, gastrin, substance P, VIP, calcitonin, somatostatin, pancreatic polypeptide

Imaging

- MRI – small bowel, pelvis
- USS: abdominal, biliary tree, pelvis, hepatic and pancreatic, endo-anal
- CT Pneumocolon
- CT chest, abdomen and pelvis
- Abdominal X-ray
- PET scan

Other

- Urine analysis (metabolic abnormality, infection)
- Urinary 5-HIAA
- Stool test for microscopy, culture and Clostridium difficile toxin

Spearman's correlation coefficient between GSRS scales and items in the Alert-B.

		GSRS Scale				
		Abdominal pain	Reflux	Diarrhoea	Indigestion	Constipation
Alert-B	Get up at night to poo	0.295**	0.124	0.311**	0.232**	0.206**
	Accidents, such as soiling or wet wind	0.297**	0.183*	0.497**	0.455**	0.249**
	Blood from your bottom	0.253**	0.188*	0.157*	0.349**	0.257**
	Bowel or tummy problems affecting your daily life	0.357**	0.102	0.47**	0.339**	0.366**

(** Correlation is significant at the 1% level (2-tailed); * Correlation is significant at the 5% level (2-tailed).)

Work to confirm clinical validation i.e. PPV of ALERT-B symptom is ongoing

(Taylor Clin Onc 2016)

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