RANDOMISED CONTROLLED TRIALS IN SURGERY – HOW CAN WE DO MORE?

Thursday 1st September 2011

Barriers to Recruitment in Head & Neck Surgical Trials

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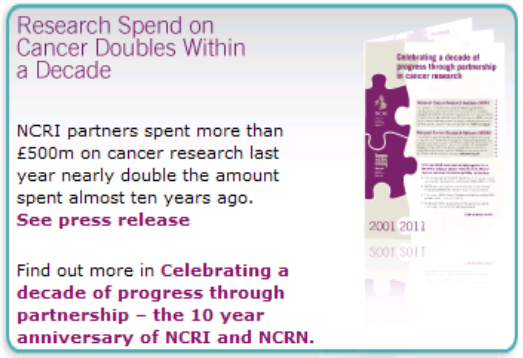
NCRI Head & Neck Clinical Studies Group
North West MRC Trials Hub

LIVERPOOL CANCER RESEARCH UK CENTRE

MRC Hubs for Trials Methodology Research
North West Hub

NCRI National Cancer Research Institute

Head Neck Research in UK



2010: 1158 (15%) patients recruited

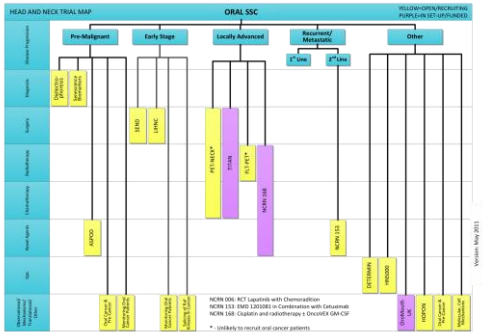
- 749 : RCTs
- 409 : non-RCTs

Compare 5.7% year before and ~2% year before that

20 studies on the H&N portfolio

CSG in Surgery & Localised Therapies

ISRCTN	Acronym & Title	Status	Type	Open to additional sites
	Alternative Splicing of Raf Kinases in Cancer - An investigation of the Role of Alternative Splicing of Raf Kinases in Head and Neck Squamous Cell Carcinoma (HNSCC)	Open	Observational	No
	ART DECO - A Randomised Multicentre Accelerated Radiotherapy Study of Dose Escalated Intensity Modulated Radiotherapy vs Standard Dose Intensity Modulated Radiotherapy in Patients Receiving Treatment for Locally Advanced Laryngeal and Hypopharyngeal Cancers.	Open	Interventional	Yes, within and outside lead country
31503555	**ASPOD** - Oral Topical Cyclo-oxygenase2 Inhibitors (COX2-1) mouthwash for the treatment of oral dysplasia - a proof of concept study	Open	Interventional	No
81772291	**COSTAR** - COchlear Sparing Therapy And conventional Radiation: A Multicentre Randomised Study Of Cochlear Sparing Intensity Modulated Radiotherapy Versus Conventional Radiotherapy In Patients With Parotid Tumours	Open	Interventional	Yes, within and outside lead country
	Determination of Quality of Life Instrument - Determination of Quality of Life Instrument most prefered by Head and Neck Cancer patients	Open	Observational	No
	Dielectrophoresis in oral cancer - Dielectrophoresis as a prognostic tool for potentially malignant and malignant disease of the mouth	Open	Interventional	Yes, within lead country only
97398362	**FLT PET to assess tumour proliferation during radical radiotherapy** - CT-18FLT- PET sequential imaging protocol to assess tumor proliferation during radical radiotherapy	Open	Interventional	No
71267356	**Head and Neck Cancer: molecular, cellular and immunological mechanisms** - Investigation of the molecular and genetic mechanisms promoting oral cancer development and progression	Open	Observational	Yes, within and outside lead country
	HeadandNeck5000 - Evaluation of centralisation in head and neck cancer	Open	Observational	Yes, within lead country only
39634732	**HOPON** - HOPON (Hyperbaric Oxygen for the Prevention of Osteoradionecrosis): A Randomised Controlled Trial of Hyperbaric Oxygen to prevent Osteoradionecrosis of the Irradiated Mandible	Open	Interventional	Yes, within lead country only
	Illness perceptions and imagery: Exploring the importance and usefulness of patients' images of canc - Illness perceptions and imagery: Exploring the importance and usefulness of patients' images of cancer (Phase 2).	Open	Observational	No
03712770	**Lugol's Iodine in Head and Neck Cancer Surgery** - A multi-centre, randomised controlled trial assessing the effectiveness of Lugol's Iodine	Open	Interventional	Yes, within and outside



 National Working Party for Recruitment to Interventional Trials		 Paula Williamson Catrin Tudur-Smith Geetinder Kaur	
Trial	SEND (CRUK)	PETNECK (HTA)	HOPON (CRUK)
C.I.	Iain Hutchison	Hisham Mehanna	Richard Shaw
Trials Unit	UCH Trials Unit	Warwick Trials Unit	Liverpool CTU
Trial Co-ordinator	Fran Ridout	Joy Rahman	Matt Bickerstaff
Date opened	2007	2007	2008
Recruitment / total	134/650 (20%)	291/560 (52%)	65/200 (33%)
Recruitment / proj.	134/400 (34%)	291/560 (52%)	65/90 (72%)
Special measures	Extension ? Metanalysis	Extended by 2 years	Not as yet

Method

- Online survey using Surveygizmo
- All Centres who have tried to recruit for 3 trials

surveygizmo

Summary Report - Aug 8, 2011

Survey: PET-NECK recruitment survey

Please rate the clinical team problems for PET-NECK from 0-3 as below: 0 not a problem 1 mild problem 2 moderate problem 3 severe problem

	0 (not a problem)	1 (mild)	2 (moderate)	3 (severe)	Totals
Inadequate time to complete administration around the trial (eg. emails, supplying CV, GCP training)	20 64.5%	8 25.8%	2 6.5%	1 3.2%	31 100%
Lack of time in clinic to accommodate research	12 38.7%	10 32.3%	5 16.1%	4 12.9%	31 100%
Lack of research experience in clinical team	22 71.0%	7 22.6%	2 6.5%	0 0.0%	31 100%
Clinical team does not regard clinical research as important	28 90.3%	1 3.2%	2 6.5%	0 0.0%	31 100%
Clinical team does not regard the research question as important	22 71.0%	8 25.8%	1 3.2%	0 0.0%	31 100%
Hesitation in involving oncology patients in randomised trials	26 83.9%	5 16.1%	0 0.0%	0 0.0%	31 100%
Consultant/surgeon's preference for one arm of the trial	14 45.2%	9 29.0%	6 19.4%	2 6.5%	31 100%
Other	16 100.0%	0 0.0%	0 0.0%	0 0.0%	16 100%

Method

0= no prob, 1=mild, 2=mod, 3=severe

- Roles, staff available, expectations
- Trial related (e.g. design, competition)
- Site related (e.g. research nurse, ETCs)
- Patient related (e.g. refuse consent, costs)
- Clinical team (e.g. lack of time or training)
- Trial documentation

- Free text

Results

- 141 complete and partial responses (approx. 200 possible)
- 45 centres

- Overlap, complex analyses & data cleaning is underway
- Differences between trials not emphasised here

Results – barriers to recruitment

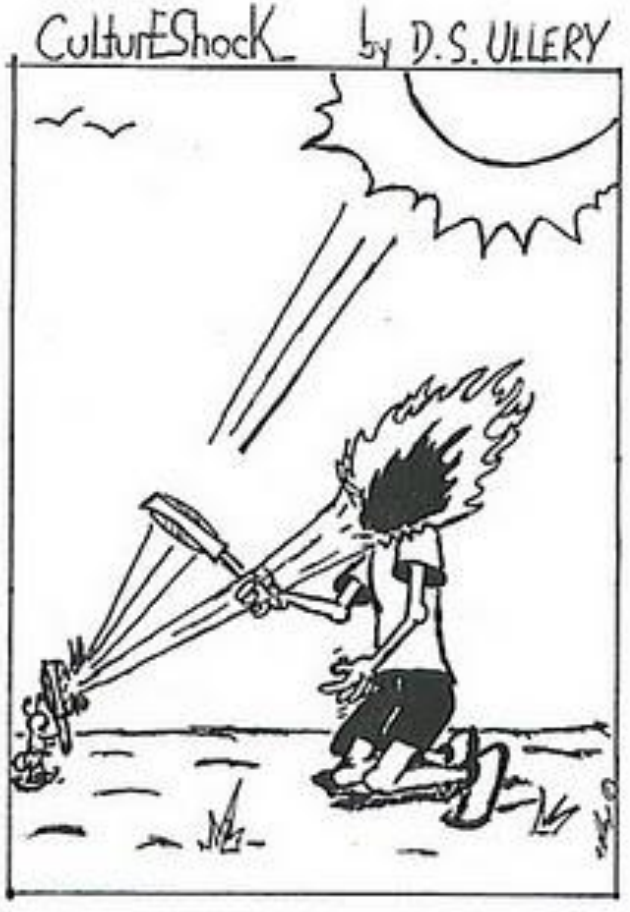
Common themes in 3 trials:

- Patients refuse consent - express a preference to one arm of the trial
- Lack of time in NHS clinic to recruit
- Consultant surgeon has preference for one arm of trial
- Educational Level of patients - dont understand the trial
- Lack of research nurse (excepting PETNECK (NIHR))
- Lack of funding from PCTs for ETCs (where ETCs needed i.e. HOPON / PETNECK)
- R&D Burden & Delay

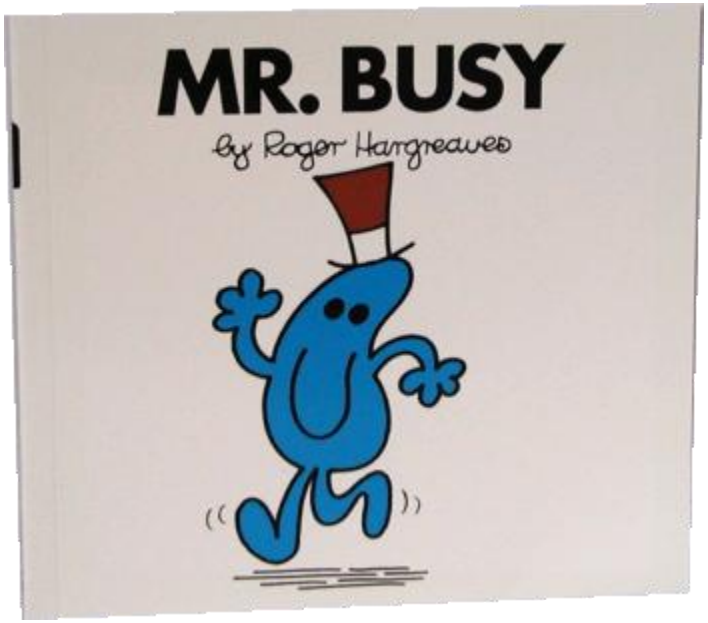
Results – barriers to recruitment

- Patients refuse randomisation
- Consultants prefer one arm of trial

= same problem?



Results – barriers to recruitment



- Lack of time

= low priority?

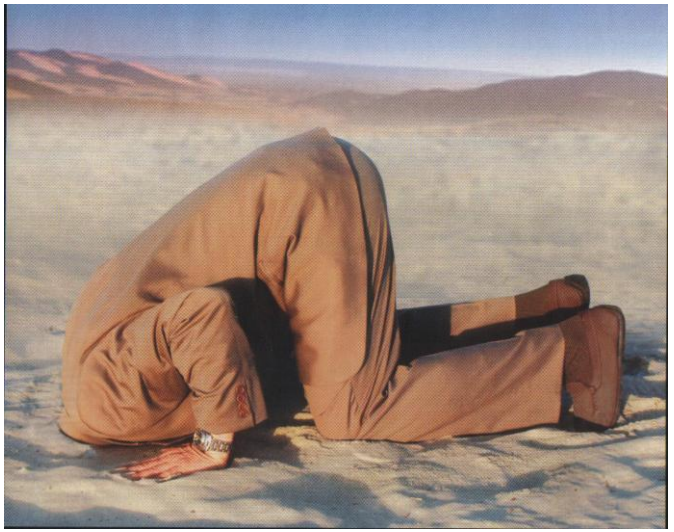
= not recognised?

= not rewarded?

Results – barriers to recruitment

- Lack of Research Nurses
- Lack of Excess Treatment Costs

= NHS failing to deliver DoH policy



West Midlands (South)
NIHR Comprehensive Local Research Network

NHS
National Institute for Health Research

West Midlands (South)
Comprehensive Local Research Network
Fourth Floor Rotunda (ADA 40017)
University Hospitals Coventry & Warwickshire NHS Trust
University Hospital
Clifford Bridge Road
Coventry
CV2 2DX
Tel. 02476 965031

Clinical Director: Professor Scott Weich
Hosted by: University Hospitals Coventry and Warwickshire NHS Trust

24 August 2011

Mr Matthew Bickerstaff
HOPON Trial Coordinator
Liverpool Cancer Trials Unit
University of Liverpool Cancer Research Centre
200 London Road
Liverpool
Merseyside
L3 9TA

Dear Mr Bickerstaff

Re: HOPON (Hyperbaric Oxygen for the Prevention of Osteoradionecrosis): A Randomised Controlled Trial of Hyperbaric Oxygen to prevent Osteoradionecrosis of the Irradiated Mandible

I write in response to your request for West Midlands (South) CLRN to obtain assurances from local PCTs that they will be willing to support the Excess Treatment Costs for patients randomised to the above trial. Unfortunately we have been unable to secure agreement from the relevant PCTs to cover the associated costs and as such, will be unable to progress applications for NHS Permission for the following sites:

- University Hospitals Coventry and Warwickshire NHS Trust
- Worcestershire Acute Hospitals NHS Trust

I understand that this must be disappointing news and I am sorry that I could not be of more assistance on this occasion. If you have any queries regarding this matter please do not hesitate to contact me either by email louisejones1@nhs.net or by telephone on 01564 711799.

Yours Sincerely

pp

Louise Jones
RM&G Manager
West Midlands (South) CLRN

cc: Mr RJ Shaw, University of Liverpool, Chief Investigator
Mr G Walton, University Hospitals Coventry and Warwickshire NHS Trust, Principal Investigator
Mr James Fox, Univeristy of Liverpool, Manager Contract Services
Mr Neil Whalley, Aintree University Hospitals NHS Foundation Trust, R & D Manager

Results – highest scoring

- Patients don’t understand trial
- H&N specific
- Negative effects of ethics committee requirements?

The Academy of Medical Sciences

Media Release

Embargoed until 00.01 GMT Tuesday 11 January 2011

Complex regulation system means UK not delivering vital health research for patients

"*We have found unequivocal evidence that health research in this country is being jeopardised by a regulatory and governance framework that has become unnecessarily complex and burdensome. Further, we received no evidence that this increased regulatory and governance burden has led to enhanced safeguards for participants in research. The changes we propose will streamline and improve the process to create a better environment for research, while protecting the interests of patients and the public.*"

Create a new Health Research Agency (HRA) to rationalise the regulation and governance of all health research.
Include within the HRA a new National Research Governance Service to facilitate timely approval of research studies by NHS Trusts.
Improve the UK environment for clinical trials.
Provide access to patient data that protects individual interests and allows approved research to proceed effectively.
Embed a culture that values research within the NHS.

Results – important negatives

- Problems:

trial design, NHS R&D, patients , PCTs, lack of nurses as a big problem

- No recognition of problems:

Lack of research experience

Lack of training

Paramasivan *et al. Trials* 2011, **12**:78
http://www.trialsjournal.com/content/12/1/78

TRIALS

RESEARCH Open Access

Key issues in recruitment to randomised controlled trials with very different interventions: a qualitative investigation of recruitment to the SPARE trial (CRUK/07/011)

Sangeetha Paramasivan[1*], Robert Huddart[2], Emma Hall[3], Rebecca Lewis[3], Alison Birtle[4,5], Jenny L Donovan[1]

(a) Investigators and recruiters had considerable difficulty articulating the trial design in simple terms;
(b) The recruitment pathway was complicated, involving staff across different specialties/centres and communication often broke down;
(c) Recruiters inadvertently used 'loaded' terminology such as 'gold standard' in study information, leading to unbalanced presentation;
(d) Fewer eligible patients were identified than had been anticipated;
(e) Strong treatment preferences were expressed by potential participants and trial staff in some centres

HTA – STEPS study

- Less than 1/3 trials recruit to schedule
- Success:
  - Dedicated trial manager
  - Cancer trial
  - Drug trial
  - Intervention only available in trial

Possible interventions

- Education and training, generic or trial specific
  - Trials workshop
  - Culture shift
  - Recruitment strategies
- Resource issues: ETC, Trust priority, Nurses
- Realism about trials of 700-1000 pts in HNSCC
- Focus group to test randomisation / PIS with patients
- Dismantle the R&D disaster - ? Health Research Agency better?