EEPRU

Economic Evaluation of Health and Social Care Interventions Policy Research Unit

RESEARCH REPORT

Follow-up strategies in cancer: Comparing national clinical guidelines and current clinical practice across the UK using exemplars in bladder, breast, colorectal, and prostate cancer

Rafia R, Ara R, Ward S, Richardson G, Barbieri M, Paisley S & Sculpher M

Correspondence to: Rachid Rafia, ScHARR, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA

Email: r.rafia@sheffield.ac.uk

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Steven Brown, Consultant colorectal surgeon at Sheffield Teaching Hospital. Prof Brown has been in Sheffield since 2002 and is principally involved in benign disease. He is honorary secretary to The Association of Coloproctology of Great Britain and Ireland, was secretary to the RSM section of coloproctology. He has been involved in guideline development although not for colorectal cancer.

Mark Emberton, Consultant prostate surgeon at University College Hospital London. Mark Emberton is Professor of Interventional Oncology at UCL, an Honorary Consultant Urologist at University College Hospitals NHS Foundation Trust and Founding Pioneer of the charity Prostate Cancer UK.

John Griffith, Consultant colorectal surgeon at Bradford (City) Teaching Hospitals. Mr Griffith has over 17 year experience in the area, was the clinical lead for the old Yorkshire Colorectal Cancer Network, and a MacMillan colorectal expert consultant to NHS England for 3 years.

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John Kelly, Consultant Urological Surgeon at University College Hospital London. Professor John Kelly is a consultant urological surgeon specialising in robotic surgery for bladder and prostate cancer. He is the lead for the London Cancer Urology Surgery Centre and the robotic surgery programme at UCLH. John is the Professor of Uro-Oncology at UCL and his research group explore how new therapies for bladder and prostate cancer can improve outcomes for patients.

Andrew Miller, Consultant colorectal surgeon at University Hospital Leicester since 2001. Mr Miller is chair of the regional colorectal cancer board (since 2007), where strategies for clinical practice are agreed annually. He sits on the East Midland Cancer Network Advisory Group which agrees the minimum follow-up practices for the East Midlands.

Clare Rogers, Consultant breast surgeon at Doncaster & Bassetlaw NHS Foundation Trust for the last 10 years. Ms Rogers has been the clinical lead for breast cancer over the last 2 years

and clinical lead for Yorkshire and the Humber Clinical Network for cancer for the last 4 years. Ms Rogers is also interim lead for Doncaster and Humber Cancer Alliance until March 2017.

Vijay Sangar, Consultant Neurological Surgeon at University Hospital South Manchester and The Christie. He is Director of surgery at The Christie and also chairs the Specialist Cancer Surgery Group

Lynda Wyld, Consultant breast surgeon since 2002 (recently moved to Doncaster & Bassetlaw) and is a clinical academic at Sheffield Hallamshire Teaching Hospital. Ms Wyld's research interests relate to evidence-based clinical practice.

EXECUTIVE SUMMARY

Objectives: We aimed to establish the awareness of guidelines for the follow up of certain cancers and whether this guidance was being followed on a local/regional/national level. We also aimed to establish where there was likely to be variation in practice and where further research might be best targeted.

Methods: A series of semi-structured interviews was conducted with leading clinicians in the follow-up of four specific cancers. Bladder, breast, colorectal and prostate, cancer were identified as being a priority in discussions with policy experts from the DH.

Results: Nine interviews were conducted, three in breast cancer follow-up and two in each of the other three cancer types. In general, interviewed clinicians were aware of relevant guidelines for the follow-up of cancer. Perceived quality of the guidelines and adherence to guidelines varied considerable by type of cancer. In breast cancer, evidence to support guidance was considered relatively poor and follow-up strategies probably varied considerably by region. In colorectal cancer, guidance was deemed vague and varied by geographical area. However, in bladder cancer, there were several guidelines issued and the perception was that most clinicians would follow either NICE or European Association of Urologists guidance and there would be little divergence from this. In prostate cancer, while guidelines were available, follow-up was largely determined by local constraints (availability and ability of GPs to accept discharge to primary care) and patient preferences (whether they wanted to have a hospital follow-up). In the case of prostate cancer, unlike the others, the role of follow-up was questioned. There is a very good test for recurrence (PSa level) and follow-up was largely to manage the adverse events associated with radical intervention (incontinence, impotence) rather than to assess cancer status.

In terms of future research, audits of existing practice were highlighted, reflecting a lack of consensus about optimal follow-up. Subject to evidence availability, clinicians thought it would be informative to consider alternative models of follow-up (who should conduct follow-up, where and how often). There was also a suggestion that trials using adaptive designs would be useful and that a wider range of outcomes (e.g. potential reduction in anxiety) could be included.

Conclusions: In general, awareness of guidance was good, but adherence varied by type of cancer, perceived quality of the guidance and geography.

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1. INTRODUCTION

1.1 Background

The research described in this report was commissioned following discussions (8th November 2016) between colleagues at the Department of Health (Jane Allberry, Anna Garratt, Tim Elliott), NHS England and members of EEPRU (Mark Sculpher, Sebastian Hinde, Marco Barbieri, Gerry Richardson, Rachid Rafia, Paul Tappenden, Roberta Ara).

1.2 Objective

The main objective of the research is to gain an overview of variations in follow-up strategies in cancer currently employed in routine clinical practice in the UK and the role of clinical guidelines. An initial focus on four key cancers (bladder, breast, colorectal, prostate) was agreed with colleagues from DH.

A secondary objective is to determine if economic evaluations of alternative follow-up strategies are required and feasible based on current evidence. Additional aims include:

- Identify relevant clinical guidelines relevant to UK practice
- identify any unpublished relevant research due for imminent publication (either clinical or economic)
- identify any areas of uncertainty for future economic modelling projects (such as lack of robust or detailed clinical evidence)
- identify any feasible and justifiable research questions relating to the cost-effectiveness of alternative follow-up strategies (such as sub-group populations stratified by cancer stage at the point of diagnosis)

2. METHODS

A series of semi-structured telephone interviews with leading clinicians (two / three per clinical area) was conducted.

The interviews consisted of open-ended questions relating to:

- Details of follow-up strategies used in routine clinical practice (sub-grouped by patient characteristics, risk factors, disease severity, stage etc. if applicable)
- Any known local or regional variation in follow-up strategies
- Ongoing unpublished local or national clinical / observational studies relating to alternative follow-up strategies
- Unpublished studies relating to alternative follow-up strategies
- Known uncertainty associated with existing evidence (and what this implies for NHS decisions regarding follow-up practice and additional research area priorities)
- The characteristics of high-value additional research relating to cost-effectiveness of alternative follow-up strategies including:
    - If this is feasible given current evidence
    - What evidence is may be lacking
    - Potential sources of evidence (e.g. local studies, registries)
- Knowledge of national guidance on follow-up strategies (sub-grouped by patient characteristics, risk factors, disease severity, stage etc. if applicable)
- Clinician's own opinion on current clinical practice and/or national clinical guidelines on follow-up strategies
- Any other comments relating to the project

A copy of the interview questionnaire is provided in the Appendix.

The interviews were not recorded, but two academics were present at each interview and responses were fully documented by one and checked by the second. The report was shared with all interviewees (this draft report does not include any minor amendments or comments received from clinicians). It should be noted that the detail covered in the interviews, and summarized here, varies between clinical experts due to time availability.

3. RESULTS

The following sections describe the collated responses received from the clinicians by clinical area.

3.1 Results for bladder cancer

3.1.1 Geographical area and patient mix

One consultant is based at University College London Hospital (UCLH). This covers a catchment area of around 4.5 million and has a diverse population. The other is based at 2 hospitals in Manchester (University Hospital South Manchester and The Christie). This covers the geographical area of South Manchester for bladder cancer, and the whole of the North West for some rarer cancers (such as penile cancer). This also has a diverse population with an annual number of about 100 bladder cancer cases.

3.1.2 Hospital follow-up strategy for Bladder cancer

At UCLH, follow up is dependent on risk status. This is characterized as high, medium or low based on the work of Max Palmer in 1990s. Cytology is the preferred method of follow up and has a very high sensitivity. Biomarkers are promising and continue to be researched. Recent systematic reviews of their performance have been conducted and although NICE guidance suggests that biomarkers should be used in follow up, this tends not to be done as there would be so many false positives (where the cytology was negative).

In Manchester, the follow up is also based on assessing risk and follows NICE guidance.

3.1.3 Knowledge of national clinical guidelines

Several guidelines are available including NICE, European Association of Urologists (EAU), Japanese guidelines and US guideline from the National Institute for Health. Only NICE and EAU guidance are followed. Both clinicians were very aware of the variety of guidelines and the implications for patient follow-up.

Box 1: NICE guidance for follow up in bladder cancer(1)

Follow-up after treatment for non-muscle-invasive bladder cancer

1.4.1 Refer people urgently to urological services if they have haematuria or other urinary symptoms and a history of non- muscle invasive bladder cancer.

1.4.2 See recommendation 1.2.1 on the use of urinary biomarkers for follow up after treatment for bladder cancer.

Low-risk non-muscle-invasive bladder cancer

1.4.3 Offer people with low-risk non muscle invasive bladder cancer cystoscopic follow up 3 months and 12 months after diagnosis.

1.4.4 Do not use urinary biomarkers or cytology in addition to cystoscopy for follow up after treatment for low risk bladder cancer.

1.4.5 Discharge to primary care people who have had low risk non muscle invasive bladder cancer and who have no recurrence of the bladder cancer within 12 months.

1.4.6 Do not offer routine urinary cytology or prolonged cystoscopic follow up after 12 months for people with low risk non muscle invasive bladder cancer.

Intermediate-risk non-muscle-invasive bladder cancer

1.4.7 Offer people with intermediate-risk non muscle invasive bladder cancer cystoscopic follow up at 3, 9 and 18 months, and once a year thereafter.

1.4.8 Consider discharging people who have had intermediate risk non muscle invasive bladder cancer to primary care after 5 years of disease free follow up.

High-risk non-muscle-invasive bladder cancer

1.4.9 Offer people with high-risk non muscle invasive bladder cancer cystoscopic follow up:

- every 3 months for the first 2 years then
- every 6 months for the next 2 years then
- once a year thereafter.

1.4.10 For people who have had radical cystectomy for high risk non muscle invasive bladder cancer, see recommendations 1.6.1 and 1.6.2 of NICE guidance.(1)

3.1.4 Local, regional or national variation in follow-up strategies for bladder cancer

In the UK, most centres follow either NICE or EAU guidelines and there is little variation from these. The two guidelines are very similar with the main difference being where patients are categorized as “low risk”, EAU guidance recommends discharge after 5 years follow up, whereas NICE recommend discharge to primary care after 12 months of no recurrence. The main variation, it was suggested, is

probably in these low risk patients, where some consultants are reluctant to discharge. Variation in high risk patients was much less and probably confined to differences in the timing of follow up.

3.1.5 Value of follow-up to identify recurrence

Patients are followed up and recurrence is an issue. At present there is no biomarker (or combination of biomarkers) with sufficient performance to allow testing in primary care and GP/patient interpretation of the results of the test.

3.1.6 Awareness of the evidence available

There is an ongoing trial in Spain comparing the effectiveness of cystoscopy plus biomarker versus cystoscopy alone. Several recent papers on the performance of biomarkers in bladder cancer, and a recent systematic review (ref of around 90 studies) comparing performance of single biomarkers and combinations (up to 150) of biomarkers.(2)

There is an ongoing trial (CALIBER) exploring management of low risk bladder cancer. Details can be found here: http://www.icr.ac.uk/our-research/our-research-centres/clinical-trials-and-statistics-unit/clinical-trials/caliber

3.1.7 Future research questions worthy of consideration and possible evidence sources

A multi arm adaptable RCT similar to STAMPEDE (REF) in prostate cancer would be most useful. A trial generating primary data that allowed arms to be created and dropped as and when necessary would be useful. This could include different biomarkers/sequences of biomarkers.(3)

3.2 Results for breast cancer

3.2.1 Geographical area and patient mix

The hospital catchment areas are in close geographical proximity (Doncaster and Bassetlaw, Chesterfield and North Derbyshire) and have population catchments of 300,000 and 400,000 (Table 1). The number of new patients diagnosed annually with breast cancer range from around 345 to 400-450 with virtually all patients receiving surgery and being followed.

The hospitals cover slightly more deprived populations than the UK population norm, and are predominantly white with a very small proportion of ethnic minorities.

Table 1: Hospital case mix for breast cancer

	Doncaster and *Bassetlaw Hospitals* NHS FT	*Chesterfield Royal Hospital NHS FT*
Hospital information		
Area covered	Doncaster, Bassetlaw, Worksop, Retford up to Newark/Mansfield Also take referrals from North Lincolnshire, Pontefract, Rotherham, Barnsley, Chesterfield, Mansfield.	Chesterfield and North Derbyshire Screening catchment area is larger (up to high peak and Manchester) – largest screening catchment area in UK
Approximate size of population within hospital catchment area	Approx. 420,000 people	Approx. 300,000 people
Number of patients referred for BC symptoms	Approx. 6,000 people	Approx. 8,500 referred by GP
Number of patients diagnosed with BC	Approx. 400-450 people	Approx. 345 (1/3 from screening and 2/3 from GP referral) people
Number of patients who have surgery & are followed up	Majority (375-400) of the 400-450 have surgery (this includes local anaesthetic)	Virtually all 345 (90%) have surgery (the balance (5-10%) are very elderly, very frail, have primary endocrine – these patients have much more intensive FU)
Patient mix		
Is population covered broadly representative of whole of UK?	Considered to be reasonably representative	Considered not to be representative
Ethnicity	Predominantly white (very few non-whites) population, High rates of obesity and DM	Smallest proportion of ethnic minorities of any Trust in England
Deprivation	Considered to be a deprived area - not a wealthy area	

BC = Breast cancer

NHS FT = National Health Service Foundation Trust

GP = General Practitioner

FU = Follow-up

DM – Diabetes Mellitus

3.2.2 Hospital follow-up strategy for breast cancer

Both hospitals have the same approach to follow-up which involves mammograms and clinical visits. In particular, follow-up is standardized in both hospitals and based on the follow-up protocol develop by the North Trent Cancer Network.

In the Chesterfield hospital, patients who receive chemotherapy stay within the oncology unit team for follow-up, while patients who receive surgery, hormonal treatment or radiotherapy are followed-up by the surgical unit. It is unclear whether the same approach is used in Doncaster and Bassetlaw as this was not covered during the interviews. In both hospitals follow-up strategy is primarily nurse-led, but a combination of nurse and clinicians is used when appropriate with direct access to clinicians if necessary.

Clinicians suggested that follow-up strategies did not vary according to disease severity in people with invasive cancer. However, one clinician indicated that high risk patients are more likely to have had chemotherapy and followed by the oncology team and receive an annual review.

In both hospitals, follow-up is determined according to patient needs (in particular whether patients are able to self-manage or not or for physiological/emotional reasons) or whether the cancer is invasive or non-invasive (DCIS). A holistic approach is used where the patient's needs is assessed on completion of treatment (nurse-led clinic but with combination nurse/clinicians). Patients who are considered to have special needs (due to learning difficulties, anxiety, treatment received etc) are then followed-up more intensively. In particular the follow-up strategy is:

- **In people deemed to be able to self-manage/no additional need – most people (around 80%-90%)**
    - Annual mammogram up to 5 year – in young women annual mammogram until general population screening age for breast cancer is reached
    - Two clinic visits (Nurse-led): 2-3 & 5 years
        - In one hospital, all patients have open access to return without going through GP for referral
        - More intensive follow-up if recurrence (annually) or axillary surgery - only mentioned by one hospital
        - If on anti-estrogen treatment, bone marrow density scan at baseline & 2 years - only mentioned by one hospital

- **In people with additional needs (i.e. those who cannot self-manage) – this is a minority of patients**
    - Annual mammogram up to 5 year – in young women annual mammogram until general population screening age for breast cancer is reached

- Clinical visit (Nurse-led) 6 monthly up to 2 years, then annually up to 5 years
    - In one hospital, all patients have open access to return without going through GP for referral

- **In people with DCIS (non-invasive cancer)**
    - Annual mammogram up to 5 year – if young, women continue annual mammogram until reaching screening age for breast cancer
    - No clinical visits

It was suggested that stratification is difficult in breast cancer as follow-up needs will vary by individual factors and will be difficult to predict. Risk factors also change over time, and they are variable and complex. Consequently the same follow-up is provided for everyone.

3.2.3 Knowledge of national clinical guidelines

Recommendations for follow-up from the NICE clinical guideline are reproduced in Box 2.

Box 2: Follow-up breast cancer National Clinical Guidelines(4)

Follow-up imaging

1.14.1 Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHSBSP/BTWSP. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years.

1.14.2 On reaching the NHSBSP/BTWSP screening age or after 5 years of annual mammography follow-up we recommend the NHSBSP/BTWSP stratify screening frequency in line with patient risk category.

1.14.3 Do not offer mammography of the ipsilateral soft tissues after mastectomy.

1.14.4 Do not offer ultrasound or MRI for routine post-treatment surveillance in patients who have been treated for early invasive breast cancer or DCIS.

Clinical follow-up

1.14.5 After completion of adjuvant treatment (including chemotherapy, and/or radiotherapy where indicated) for early breast cancer, discuss with patients where they would like follow-up to be undertaken. They may choose to receive follow-up care in primary, secondary, or shared care.

1.14.6 Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:

- designated named healthcare professionals
- dates for review of any adjuvant therapy
- details of surveillance mammography
- signs and symptoms to look for and seek advice on
- contact details for immediate referral to specialist care, and
- contact details for support services, for example support for patients with lymphoedema.

Two out of three clinicians were aware of the NICE clinical guideline and considered that the guideline was relatively poor, vague and outdated. However, clinicians acknowledged that the guideline reflects the evidence available and that the evidence used in the guideline is very heterogeneous and therefore difficult to interpret. Clinicians also recalled that there are no variations in follow-up strategies according to patient's characteristics.

All the clinicians were aware of the regional guideline (North Trent) from which their protocol for follow-up has been adapted from.

3.2.4 Local regional or national variation in follow-up strategies for breast cancer

Clinicians were asked if they were aware of any local, regional or national variations in follow-up strategies for breast cancer. Clinicians agreed that there was little variation at the regional level with few differences, mostly on who will see the patients.

Clinicians understood that there were some variations in follow-up strategies at the national level, in particular:

- Follow-up may be undertaken by GP following discharge in West Yorkshire, Liverpool and Oxford
- Follow-up may be undertaken by trainees in other areas of the country

However, it should be noted that their responses were based on their perception or interpretation of variations and were informed by discussions with external colleagues during networking at conferences, or through anecdotal evidence. It is unlikely that the suggested variations can be characterized accurately without expanding this research to cover additional geographical areas.

3.2.5 Value of follow-up to identify recurrence

Clinicians were in agreement that follow-up visits were unlikely to pick up recurrences and that the majority of recurrences are identified by self-referral or by mammograms. Clinicians considered that recurrences are typically picked up between visits. However, one clinician suggested that about 40% of recurrences could be picked up through follow-up.

The clinicians did not think there was a great deal of clinical benefit in terms of picking up recurrence from increasing follow-up. However, they were in agreement that follow-up is important psychologically for the patient and they were not in favour of reduced follow-up from a patient point of view. One clinician also suggested that whilst there is a focus on recurrence, managing morbidity is equally or more important and that the emphasis of follow-up may need to shift to reflect this.

3.2.6 Awareness of the evidence available

Two out of three clinicians had knowledge of the evidence available. They felt that the evidence is in favor for reduced follow-up (as currently undertaken in the hospitals – before follow-up used to be more intensive). However, one clinician mentioned that there is not a huge volume of evidence saying which the best strategy is.

In particular clinicians were aware of the following published work:

- using telephone contact in Australia (for geographically remote location)
- work around the frequency of mammogram, notably benefits around 3-yearly mammogram, unless young or women at high risk.

The clinicians suggested that evidence of follow-up strategies on survival is lacking. Furthermore, two clinicians suggested that that is evidence/research on side effects of treatment and identifying these. However, one clinician suggested that the evidence regarding the impact of follow-up on morbidities and managing these (side effects of hormonal treatment, surgery, long-term sequelea etc.) is not available. In particular it was suggested that patients can have lots of complications from treatment and that historically, the priority has been the cure (with an acceptance of side effects) but that there is a move toward emphasis on quality of life (QoL) experience, as patients live for many years and most are cured but left with diminished QoL.

Knowledge of unpublished research in this area

Only one clinician was aware of unpublished/ongoing research. This is an ongoing project funded by the NIHR (mammo50) that examines: annual mammogram for 3 years followed by 2 yearly mammograms, verses 3 yearly or 2 yearly mammograms with patients randomised (1:1) using a 9 year follow-up period.

3.2.7 Future research questions worthy of consideration and possible evidence sources

Clinicians considered the evidence available is generally sufficient regarding the intensity of follow-up but noted that more research could be undertaken.

The following research questions were mentioned as potential areas for future research:

Qualitative study on patients and staff experience of follow-up

- Examining patients and staff (clinician/nurse) satisfaction/experience
- What is the best way/approach to provide reassurance to patients?
- What clinicians/nurses can do to make a difference to patients?

Examining the benefit of Follow-up

- Do alternative follow-up strategies improve survival? – although it was acknowledge this would be difficult to conduct and would require a long study (10-15 years)
- What is the value of increased follow-up following breast conservation? – notably given the low risk of recurrence
- How effective is follow-up in identifying morbidities/side effect of treatments?

How follow-up should be undertaken

- Who should see the patients, and what the interaction should consist of
- Should the role of breast cancer nurses expanded? In particular, patients are most comfortable with nurses and could play an important role.
- Should follow-up be within hospital setting? Should it be a rigid structure or available as and when required? Should patients be managed by GPs?
- Is it possible to personalized follow-up? While more intensive follow-up may not be needed clinically for most patients, some patients would benefit from intensive follow-up for psychological benefits, or given complications following surgery, side effects, operative defects or reconstruction issues.
- Audit of the different strategies used nationally – to identify variation and what works or not.

Quality of life

- Appropriateness of the EQ-5D to capture the psychological benefits associated with intensive follow-up.
- How to capture holistic benefits of follow-up such as reassurance

Costs/Cost-effectiveness

- Does it cost more to follow-up less intensively given that patients self-refer or are referred by GP? Notably when followed-up, patients are typically seen by nurses but if referred by GP (new referral) or self-referred, they are typically seen by a consultant (therefore more expensive). Furthermore new referral (through GPs) is more expensive than self-referral (existing patient) – about 50% more expensive.
- Is the reduction in anxiety worth the cost of the mammogram?

3.3 Results for colorectal cancer

3.3.1 Geographical area and patient mix

Although predominantly North and Midlands, the hospital catchments cover a substantial geographical area (Bradford, Leicester and Sheffield) and population sizes range from around 400,000 to 1,000,000 (Table 2). The number of new patients seen annually range from around 200 to 500, and surgical resection rates range from 140 to almost 340.

Two of the hospitals cover slightly more deprived populations than the UK population norm, and two have higher than average proportions of South East Asian patients. The severity of colorectal cancer is covered across all hospitals (classified using Dukes Stage).

Table 2: Hospital case mix for colorectal cancer

	Bradford City Teaching Hospital	University Hospitals Leicester City	Sheffield Teaching Hospital
Hospital information			
Approximate size of population within hospital catchment area (,000)	380-420	985 (Leicestershire) 300 (Leicester City)	Sheffield area (plus tertiary hospitals in region)
Number of new patients seen annually	200	508	340
Number of patients who have surgery & are followed up	140	268	Most of the above
Patient mix			
Ethnicity	1/3 Asian, otherwise representative of general population – majority of those are young	High proportion of SE Asians (relative to UK average), otherwise representative of UK population.	Representative.
Deprivation	Slightly more deprived than average in UK	Not mentioned	A little more socially deprived than UK norm, and possibly a little older than the norm.
Severity of cancer	Majority are Dukes stage A-B with some stage C		The majority are Dukes stage B-C (50-60%)

3.3.2 Hospital follow-up strategy for colorectal cancer

Follow-up for patients with colorectal cancer post resection generally involves CT scans, CE assay (CEA) and colonoscopies (Table 3). These are provided as standard to the vast majority of patients

within each hospital although there are some variations depending on the hospital attended. Any described variation in follow-up strategies is small and generally relates to the frequency of the tests and procedures which is driven by the hospital or regional guidelines. The largest variation in practice is the length of follow-up with one hospital ceasing follow-up at three years post-op and the other two continuing follow-up to five years. Outpatient appointments are conducted in specialist nurse led clinics with immediate access to consultants/registrars if required.

Variations by patient characteristics:

All three consultants indicated there was a small proportion of patients (5-10%) who do not receive (or received very limited) follow-up that involved tests or procedures. These patients were described as elderly and frail who had received non-curative surgery, were considered to be unfit for additional surgery with curative intent on recurrence, and were likely to be receiving palliative care.

While one hospital stratified patients by stage of cancer (Dukes stage) and risk (e.g. multimodal), the other two did not. In the former, the schedule of CT scans for high risk patients was increased and lengthened to accommodate a third scan. One clinician indicated there may be an increase in regularity of follow-up if there is a history of polyps, or if the patient is symptomatic or in need of more frequent reassurance.

One hospital based their follow-up strategy on the NICE CG while the second was governed by the minimum agreed follow-up for the geographical region. The third used a strategy that had been revised over time but was originally informed by guidelines developed by the Yorkshire Cancer Network (1990).

Table 3: Summary of follow-up strategiesBradford City Teaching Hospital	University Hospitals Leicester City	Sheffield Teaching Hospitals
Follow-up strategy		
Vary according to Stage of cancer Patients stratified into low risk (Duke A or B) or high risk (Duke C, vascular invasion, nodal inclusion)	Standardised FU protocol as agreed by East Midlands group – same protocol for all patients (no variation by stage etc) FU post resection is decided at a MDT meeting either: a) Treat on symptoms only b) Active surveillance	Strict FU - No stratification of FU by stage of disease
Low Risk (vast majority): • CT scan at 18 & 30 months • CE assay at 6 month intervals (up to 3 years) • Colonoscopy at 3 years **Standard Risk** • CT scan at 12, 24 & 36 months • CE assay at 6 month intervals (up to 3 years) • Colonoscopy at 3 years	**Symptoms only**: Typically elderly/frail patients with comorbidities who have long hospital recovery & required nursing support post discharge. 7-10 days post surgery will discuss options with family: either phone monitoring of symptoms or 3m appointments with specialist cancer nurse. Treatment will be symptomatic relief only and no scans etc. **Active surveillance**: • Colonoscopy within 1 year of surgery (if pre-surgical tests were not able to image beyond tumor, this will be within the first 3-4 months to investigate beyond the resection point; otherwise will be towards the end of the first year) & repeated at 5 yearly intervals. • CT scan at 12, 24 & 36 months, final scan at 5 years. • CE Assay pre-op, post-op, immediately before discharge, then at 6, 12, 18, 24, 30, 36, 48 and 60 months	Most seen every 3 months for 2 years – then discharged to GP • Every 3 months for the first 2 years and 6 months thereafter for a further 3 years • CT Scan at 9 month and 2 years • If pre-op colonoscopy, again at 3 & 5 years. If no pre-op colonoscopy, at 1 year, 3, 5 year
Variations in follow-up strategy within the hospital		
5-10% are very frail patients who have non-curative	Described above	Patients who have chemoRT after

surgery (e.g. to relieve a blockage) and do not receive standard FU		surgery are followed-up by Western Park hospital for the first 6m post end of treatment, then transferred back to STH and follow same FU policy as surgical patients.
		A small proportion (20%) are FU every 6m (e.g. if patient needs reassurance and is not keen on discharge, or if patient is symptomatic (function)). If prone to polys FU is more regular than standard.
Out-patient appointments		
Clinical nurse led clinics	Not mentioned	FU is nurse led – but see consultant, registrar if any issue
Source of current hospital follow-up strategy		
Hospital strategy has been revised over time but was initially adapted from guidelines developed by Yorkshire Cancer Network (approx. 1990) and the Coloproctology Society	Informed by the agreed minimum FU in East Midlands Group and consistent across East Midlands Some clinicians request more frequent CE Assay, some do not do CE Assay at 30 mths	Informed by regional guideline which is based on NICE CG

3.3.3 Knowledge of national clinical guidelines

Recommendations for follow-up from the NICE clinical guideline are reproduced in Box 3.

Box 3: Follow-up colorectal cancer National Clinical Guidelines(5)

Follow-up after apparently curative resection

Offer follow-up to all patients with primary colorectal cancer undergoing treatment with curative intent. Start follow-up at a clinic visit 4–6 weeks after potentially curative treatment. Offer patients regular surveillance with:

- a minimum of two CTs of the chest, abdomen, and pelvis in the first 3 years and
- regular serum carcinoembryonic antigen tests (at least every 6 months in the first 3 years).

Offer a surveillance colonoscopy at 1 year after initial treatment. If this investigation is normal consider further colonoscopic follow-up after 5 years, and thereafter as determined by cancer networks. The timing of surveillance for patients with subsequent adenomas should be determined by the risk status of the adenoma.

Start reinvestigation if there is any clinical, radiological or biochemical suspicion of recurrent disease.

Stop regular follow-up:

- when the patient and the healthcare professional have discussed and agreed that the likely benefits no longer outweigh the risks of further tests or
- when the patient cannot tolerate further treatments.

Two of the clinicians were familiar with the latest NICE CG(5), and considered that while the guidelines for follow-up were vague, they reflected the huge uncertainty in the evidence base on the benefits of alternative follow-up strategies appropriately.

One hospital based their follow-up strategy on these guidelines while the second was governed by the minimum agreed follow-up for the geographical region. The third used a strategy that had been revised over time but was originally informed by guidelines developed by the Yorkshire Cancer Network (1990).

3.3.4 Local regional or national variation in follow-up strategies for colorectal cancer

Clinicians were asked if they were aware of any local, regional or national variations in follow-up strategies for colorectal cancer. All clinicians agreed that follow-up could differ substantially depending on where the patient was seen. However, while one understood that patients in the South West of England did not receive follow-up, a second view was that patients in the South of England received a more intensive follow-up approach (additional exemplars are provided in Box 3). The clinicians stated their responses were based on their perception or interpretation of variations and were informed by discussions with external colleagues during networking at conferences, or through anecdotal evidence. It is unlikely that the suggested variations can be characterized accurately without expanding this research to cover additional geographical areas.

Box 4: Suggested variations in follow-up across the UK

- Bath & south-west of England do not FU
- Some areas do less intensive FU (less is good)
- Some areas do FU for a maximum of 1 or 2 years
- Some advocate an annual CT scan up to 10 years post resection (no evidence to support this)
- Some areas do 2 CT scans (e.g. East Yorkshire give CT scans at 18 and 36 months)
- South of England have a more intensive approach and perform CT scans at 6m intervals up to and including 8 years after resection (no evidence to support this)
- York are less enthusiastic about providing FU for low risk patients
- Some more aggressive FU (CEA), some do not do CEA at 30 months

One clinician suggested that it may be possible to standardize follow-up strategies by using audit data (e.g. NUOCA) to identify the strategies covered by the larger units.

3.3.5 Value of follow-up to identify recurrence

The clinicians agreed that the vast majority of recurrences were currently identified through the follow up strategies in place with very few patients presenting symptomatically between visits. It was suggested that over 85% of recurrences occurred within three years of surgery and recurrence in more advanced stages tended to occur earlier.

3.3.6 Evidence comparing alternative follow-up strategies in colorectal cancer

There was a consensus that the current evidence on the benefits of alternative follow up strategies was inconclusive, particularly in terms of any survival benefit. However, it was suggested that there may be unmeasured benefits associated with more intensive follow-up strategies such as a decrease in patients' anxiety and an increase in satisfaction.

The large FACS study was discussed and the clinicians identified issues such as potential sample bias and lack of generalizability caused by the difficulties with recruitment and the sparsity of patients in advanced stages (Duke Stage C) respectively.(6) The evidence from the US was not considered appropriate for UK guidelines due to the small sample sizes and the frequency of tests and procedures used which were driven by financial incentives rather than potential benefits to the patient. The results from a recent NHS England funded study that recruited in Solford, Bath and Guys, suggested that it may be possible to replace face to face follow-up strategies with virtual follow up without any loss in ability to identify recurrence.(7)

Knowledge of unpublished research in this area

The clinicians were able to provide information on a several large pieces of relevant research. One study (2002-2009), followed 1,000 patients recruited from York, Bradford, and Huddersfield. The objective was to examine how recurrence was identified (endoscopy, scan or bloods) with a view to risk stratification for follow up intensity variation. Of the 1000 recruited, 300 died during the five year follow up period. Of the remaining 700 there were between 250-300 resectable with intent to cure recurrences. As a result of this research, patients are now stratified by Duke Stage to receive either standard or higher level of follow up (see section 3.3.2). Although the research is as yet unpublished, and there is no formal report, the results can be presented in more detail if required.

Leicester are currently collecting evidence on their strategy for consistent follow up for all patients. The data will be analysed at three years to determine if there is a benefit to patients or if the tests

are unnecessary (e.g. colonoscopy invasive so need to see a benefit). Depending on the results, patients may be split into low and high risk for follow up strategies.

An additional piece of research is currently being written up for publication. This study (again conducted by researchers based in Leicester), explored the feasibility of using luminal CT scan to inform decisions to perform colonoscopy i.e. only perform colonoscopy if the scan identifies an abnormality. While this is a feasibility study, and additional evidence is required, if successful this could provide both cost savings and benefits to patients who do not like the intrusive standard procedures.

3.3.7 Future research questions worthy of consideration and possible evidence sources

It was agreed that the existing evidence does not conclusively support an optimal follow up strategy and there is a need for additional research before follow up is standardised across the UK particularly as follow up incurs a substantial expense with limited proven benefit to the patient. For example it is unclear if an intensive strategy provides a survival benefit (in addition to an increase in curative intent surgical rates).

The following research questions were mentioned as potential areas for future research:

Patient characteristics

- What follow-up strategy should be employed after liver resection following metastices. Currently scan at 3 monthly intervals.
- Group of patients (Chemo Radiotherapy) likely to have late recurrence and extending FU for these patients may be beneficial
- If recurrent polyps, then FU should be more intensive

Type of follow-up / procedures

- Remote FU vs non-remote FU
- Is there a better test than CEA
- The feasibility of virtual FU
- The feasibility of luminal colonoscopy

Patient quality of life

- Evidence on post-operative quality of life is extremely poor. Quality of life is generally low post surgery and decreases over time since surgery in many patients.

- Is the improvement in QoL associated with increased FU worth paying for (irrespective of increase in survival)
- Individual decision making: are patients happy with the invasive FU procedures given the possible benefits and risks

It may be possible to answer some of these research questions using existing evidence. Many centres have large (Wessex is the oldest and largest) longitudinal (Leicester have evidence from 1999) registries that could potentially provide evidence on resection and recurrence rates. These regional registers are likely to have more detailed evidence than the compulsory audit on diagnosis (incidence) which does not include a field for recurrence

Using evidence from Leicester

Stratification: can patients be identified who are suitable for additional surgery and therefore would benefit from intensive FU.

Cost–effectiveness

It was considered that while costing studies would currently favour a less intensive follow up strategy, more robust clinical evidence on long term survival benefits and associated health related quality of life was required before a robust formal economic evaluation could be considered.

3.4 Results for prostate cancer

3.4.1 Geographical area and patient mix

The hospital catchment areas are in large urban areas (Queen Elizabeth Hospital (QEH), Birmingham and University College Hospital (UCH), London). The areas have large catchment areas; QEH sees over 500,000 patients per year while UCH London sees 1 million outpatient and A&E attendances per year. Both hospitals have diverse ethnic populations and cover a range of sociodemographic classifications. QEH sees approximately 200-250 surgical procedures per annum, while UCH has almost 1000 radical procedures in the same period.

3.4.2 Hospital follow-up strategy for prostate cancer

There was no official policy/strategy in either centre. In QEH, the follow-up is largely dictated by the wishes of the patient. Patients have their PSA test done and submit their results. If it is within a certain threshold, then patients don't need to see a consultant (and usually don't). The majority of follow-up visits for surgical patients are for adverse events associated with prostate surgery,

primarily impotence and incontinence. Typically follow-up is conducted by a specialist nurse rather than a consultant.

At UCH, the follow-up procedure again doesn't follow any specific guidance. As with QEH, patient preference plays a large part in determining the follow up strategy. Often patients are discharged to their GP but this depends on local capacity.

The timing of follow-up is also variable at both centres, though it tends to be based on consultant habits and there is therefore a tendency to stick with 6 months as that is how it has been done before.

3.4.3 Knowledge of national clinical guidelines

Both clinicians interviewed were aware of existing guidelines produced by NICE and also other guidance by European Association of Urology (below)

Box 5. Follow up in prostate cancer

Summary of NICE Follow-up guidance

Discuss the purpose, duration, frequency and location of follow-up with each man with localised prostate cancer, and if he wishes, his partner or carers.(8)

Clearly advise men with prostate cancer about potential longer-term adverse effects of treatment and when and how to report them.

Men with prostate cancer who have chosen a watchful waiting regimen with no curative intent should normally be followed up in primary care in accordance with protocols agreed by the local urological cancer MDT and the relevant primary care organisation(s). Their PSA should be measured at least once a year.

Check PSA levels for all men with prostate cancer who are having radical treatment at the earliest 6 weeks following treatment, at least every 6 months for the first 2 years and then at least once a year thereafter.

Do not routinely offer DRE to men with localised prostate cancer while the PSA remains at baseline levels.

After at least 2 years, offer follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications to men with a stable PSA who have had no significant treatment complications, unless they are taking part in a clinical trial that requires formal clinic-based follow-up. Direct access to the urological cancer MDT should be offered and explained.

Box 6. **EAU Guidelines for follow-up during hormonal treatment**

Recommendation	**GR**
Evaluate patients at 3 - 6 months after the initiation of treatment.	A
As a minimum, tests should include serum PSA measurement, DRE, serum testosterone, and careful evaluation of symptoms in order to assess the treatment response and side effects.	A
In patients undergoing intermittent androgen deprivation, monitor PSA and testosterone at fixed intervals during the treatment pause (monthly or at three month intervals).	A
Adapt follow-up to the individual patient, according to stage of disease, prior symptoms, prognostic factors and the treatment given.	A
In patients with stage M0 disease with a good treatment response, schedule follow-up every 6 months. As a minimum requirement, include a disease-specific history, DRE and serum PSA determination in the diagnostic work-up.	A
In patients with stage M1 disease with a good treatment response, schedule follow-up every 3 to 6 months. As a minimum requirement, include a disease-specific history, DRE, serum PSA, haemoglobin, serum creatinine and alkaline phosphatase measurements in the diagnostic work-up. The testosterone level should be checked, especially during the first year.	A
Counsel patients (especially with M1b status) about the clinical signs suggestive of spinal cord compression.	A
When disease progression occurs, or if the patient does not respond to treatment, adapt/individualise follow up.	A
In patients with suspected progression, assess the testosterone level. By definition, CRPC requires a testosterone level < 50 ng/mL (< 1 mL/L).	B
Do not offer routine imaging to otherwise stable patients.	B

CRPC=castrate-resistant PCa; DRE=digital rectal examination; PSA=prostate-specific antigen.

Ref: http://uroweb.org/guideline/prostate-cancer/#7

3.4.4 Local regional or national variation in follow-up strategies for bladder cancer

As described above, local follow-up strategies did not follow either guidance, nor did they have a specific follow up protocol. Instead, follow-up was based on patient preferences and local capabilities.

3.4.5 Value of follow-up to identify recurrence

Both clinicians questioned the rationale for follow up. Patients might say that it is to identify recurrence, but the PSa test is very good at this and does not require consultant interpretation. The value of follow-up was often to deal with the consequences of radical procedures (such as incontinence or impotence).

3.4.6 Future research questions worthy of consideration and possible evidence sources

Potential research questions were identified. These included the possibility of doing some modelling around the different models of follow-up; though there would be a need to see what current practice looked like in other centres. Also, there could be a trial of whether the current strategy which is focused on patient testing, interpreting and then self care versus consultant follow up. A feeling was expressed that the management of prostate cancer was now more like Chronic Disease Management and could therefore use the same strategies.

APPENDIX

Copy of interview questionnaire

Semi-structured interviews

Introduction

Good morning/afternoon, Thank you for agreeing to be part in this research.

The Department of Health and NHS England is seeking to gain an overview of follow-up strategies in cancer currently employed in routine clinical practice in the UK, and indication of where there is variation in practice and where there is uncertainty about the most appropriate approach to follow-up.

We have been approached by the DH to conduct a series of semi-structured interview with experts in four main cancer area, including Breast, Prostate, Bladder and Colorectal. Interviews are expected to last no longer than an hour.

We approached you as an expert in XX cancer to understand current follow-up strategies in people with XX cancer, ongoing research and identify further areas of research.

Our discussion will be summarised in a report to DH which will compile responses from yourself and other experts in cancer. This report will be used by DH to identify research priorities.

The report send to DH will be shared with you.

Before commencing the interview, could you please confirm that you are happy to be named in the report. If you prefer not to be named, please let us know. Furthermore, the interviews won't be tape, but we will be taking notes.

The interview will be semi-structured, and therefore the same questions will be asked in the same order to each clinical expert, but you will be given the opportunity at the end to discuss any other aspect you feel is relevant. The interviews will be structured as follow; general questions about yourself and your hospital, questions regarding how follow-up is undertaken within your hospital, questions regarding current guidelines on follow-up and finally questions about the evidence available and relevance of alternative follow-up strategies.

Background clinician, hospital and target population

First we are going to ask you a series of questions about yourself and your hospital. These will be used to describe the mix of patients you are seeing and your hospital.

1) Could you please describe yourself, in particular, your title (e.g consultant..etc), relevant experience, and whether you are involved in guidelines or sitting in commitee etc
2) Could you please describe the mix of patients seen within your hospital, notably,
    a. What geographical area is covered by your hospital?
    b. Are patient characteristics in terms of age, ethnic background seen within your practice representative of the whole of the UK?
    c. Roughly, how many patients do you (and your hospital) see annually?
    d. Roughly, how many patients receive surgery and are followed annually (yourself and your hospital)?

Follow-up strategies currently used in routine clinical practice

We are now going to ask you some questions regarding the follow-up strategy used within your hospital and whether you are aware of local/regional variations in follow-up strategies

3) Please describe follow-up strategies in XX cancer used within your clinical practice.
    a. Do follow-strategies vary according to patient characteristics such as age, comorbidities, risk factors or disease severity (stage…)?
4) Are you aware of any local, regional or national variation in follow-up strategies for XX cancer?
    b. If applicable, please describe these variations.

National / local clinical guidelines

We are now going to discuss current national/local clinical guidelines relevant to UK practice for the follow-up of XX cancer

5) Are you aware of any local, regional or national clinical guidelines for follow-up strategies in XX cancer?
    c. If applicable, please describe how follow-up strategies for XX cancer in your practice vary compared with these guidelines (prompt if different why?)
    d. Do follow-up strategies defined in these guidelines vary according to patient characteristics?
    e. Do you consider current clinical guidelines to be appropriate and reflect the current state of the evidence available?

Evidence on benefits of alternative follow-up strategies

We would like have your view on current published evidence on alternative follow-up strategies and to identify whether there are unpublished relevant research due for imminent publication in terms of clinical effectiveness and cost-effectiveness of alternative follow-up strategies

6) Are you familiar with any published evidence on alternative follow-up strategies in XX cancer?
    f. If applicable, what are key strengths and uncertainty in this evidence-base?
    g. Do you consider that the current evidence on alternative follow-up strategies is sufficient/robust to inform NHS' decisions regarding follow-up practice and additional research area priorities
7) Are you aware of any unpublished research or ongoing research relating to alternative follow-up strategies in XX cancer?
    h. If applicable, could you please describe the ongoing research and when results may be available? If complete, can results be shared to inform DH policies?

Feasibility of conducting an economic evaluation

We would like to identify any areas of uncertainty for future economic modelling projects, such as lack of robust or detailed clinical evidence

8) Do you consider that current evidence on alternative follow-up strategies in XX cancer is sufficiently robust to conduct an economic evaluation?
    i. What alternative follow-up strategies do you consider relevant/appropriate to evaluate?
    j. Which sources do you consider appropriate to use (e.g. local studies, registries)
    k. What do you consider to be the main weaknesses to in the current evidence and evidence that is lacking

Area of future research

We would like to identify any feasible and justifiable research questions relating to the cost-effectiveness of alternative follow-up strategies (such as sub-group populations stratified by cancer stage at the point of diagnosis).

9) Do you consider that additional research is required to understand/determine the value of alternative follow-up strategies?
    I. If so, please describe the type of research you consider relevant to undertake to answer the question of alternative follow-up strategies

Other questions

10) Do you have any other comments relating to current strategies for follow-up in XX cancer or alternative strategies for follow-up.

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