



The Royal College of **Pathologists**  
Pathology: the science behind the cure

**Review of cellular pathology governance,  
breast reporting and immunohistochemistry at  
Sherwood Forest Hospitals NHS Foundation Trust**

**A report prepared for the Care Quality Commission  
in respect of diagnostic and screening procedure**

**20 February 2013**

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## **Foreword**

The Care Quality Commission has commissioned The Royal College of Pathologists to assist with the investigation into breast cancer reporting at King's Mill Hospital. This collaboration is a first for both organisations and is essential if we are to understand the nature of sophisticated pathology tests, how their quality can be assured and how they support patients' care.

This investigation has revealed both expected and unexpected important findings which have implications not just for the Sherwood Forest Hospitals NHS Foundation Trust but also for the organisation of pathology departments in general and the distribution of work between them. The findings also have implications for the management of quality assurance processes, including the need for better communication between disparate responsible organisations.

The expectation that there might be systematic issues about such quality assurance led to the Secretary of State's call for a full national review of the management of quality in pathology testing for the NHS. The findings of this investigation will inform that wider review which has now started with the assistance of The Royal College of Pathologists.

The aim of all this work must always be to provide the best possible service which can deliver the best possible outcomes for all patients whose care is dependent on reliable pathology results. National External Quality Assurance Schemes for UK pathology have a strong international reputation. This can only be enhanced by open scrutiny of their performance and results.

## Executive Summary

- 1) Sherwood Forest Hospitals NHS Foundation Trust concluded that an audit by the East Midlands Breast Screening Programme Quality Assurance Reference Centre of the work of King's Mill Hospital cellular pathology department showed under-reporting of oestrogen receptor (ER) positivity in breast cancer biopsies. This conclusion is not sound. King's Mill is a very small breast screening unit therefore greater care should have been taken in drawing conclusions from such a small sample.
- 2) National improvements in laboratory technology and increased sensitivity of antibodies have improved the testing of ER status of cancers in breast biopsies. Short term decision-making by managers at Sherwood Forest Hospitals NHS Foundation Trust prevented cellular pathology keeping up with such technological advances. This contributed to the impression of under-reporting of ER positivity by this department. The consultants at King's Mill identified problems with immunohistochemistry and mitigated them as far as they could.
- 3) The ER antibody (6F11), used by an external agency to retest archived tissue in a second and separate audit, has been shown by the EQA scheme to give false positive results, i.e. it is too sensitive. This also compounded the impression of under-reporting of ER positivity at King's Mill.
- 4) The UK National External Quality Assessment Service (UK NEQAS) external quality assurance (EQA) scheme for monitoring the performance of pathology departments which do ER tests on breast biopsies was operating independently of these audits. Re-analysis of the EQA scheme data in this current investigation does not support the findings of these two audits. The King's Mill Hospital cellular pathology department was not and has not been a significant outlier in EQA exercises. The problems inherent in this EQA scheme are described in detail.
- 5) This report recommends how pathology quality assurance (QA) should be performed, how data are collected and interpreted and how performance should be reported back meaningfully to participants. These recommendations include minimum workload thresholds for effective quality assurance in histopathology.
- 6) Problems with inadequate laboratory staffing levels and their difficulty maintaining consultant and scientific oversight of this service together indicate that in-house ER testing should not be recommenced at King's Mill Hospital.
- 7) Uncertainty about the appropriate ER antibody positivity 'cut off' measure; the upward drift in ER positivity rates internationally; and the identification of false-positivity using an ER antibody are all well known in the field of breast cancer pathology. Complexity and lack of certainty are uncomfortable for patients, relatives and clinical teams. However it must be recognised that these problems make bench-marking and quality assurance a difficult task requiring high-level system strategic planning and adequate resources.

## **1. Background**

### **1.1 Background to this investigation**

- 1.1.1 Potential issues with oestrogen receptor (ER) testing were identified at Sherwood Forest Hospitals NHS Foundation Trust which led to the retesting of affected cases and the commissioning of an external review by the Trust. Acting on the findings of the external review, the hospital notified patients and briefed the media.
- 1.1.2 The findings of the external review prompted the Care Quality Commission to undertake an urgent investigation of cellular pathology at King's Mill Hospital, part of Sherwood Forest Hospitals NHS Foundation Trust.
- 1.1.3 Sherwood Forest Hospitals NHS Foundation Trust is an acute hospitals Trust providing healthcare services for people in and around Mansfield, Ashfield, Newark, Sherwood and parts of Derbyshire and Lincolnshire. There are two hospitals in this Trust: King's Mill Hospital and Newark Hospital. This report refers to the single cellular pathology service for the Trust which is based at King's Mill Hospital.
- 1.1.4 In order to get to the root of the problem, investigate the complex ER issues, the role of external quality assessment and the possible implications for other pathology services, a collaborative approach to the investigation was agreed. An investigation team led by The Royal College of Pathologists' Professional Standards Unit and including a representative of the Institute of Biomedical Science was set up to work on behalf of the Care Quality Commission.
- 1.1.5 The Care Quality Commission has completed a 'deep dive' according to their procedures and this preceded this investigation. Sections of the Care Quality Commission's 'deep dive' were deferred to this investigation, specifically diagnostic and screening procedures focussing on cellular pathology governance, breast reporting and immunohistochemistry. The team has been asked to investigate these issues at King's Mill Hospital, and related governance and oversight at the Trust and at regional and national levels.

### **1.2 Terms of reference and report structure**

- 1.2.1 The following terms of reference were agreed:
- i. the user perception of the problem identified and its impact on patient care
  - ii. undertake an objective analysis of evidence about the quality of the service at King's Mill Hospital
  - iii. evaluate the quality of breast pathology reporting at King's Mill Hospital
  - iv. evaluate of the quality of immunohistochemical laboratory processes at King's Mill Hospital
  - v. evaluate the quality of histopathological evaluation of immunohistochemical investigations, particularly ER testing, at King's Mill Hospital
  - vi. evaluate the quality of internal quality control and clinical governance procedures with respect to this Trust
  - vii. evaluate the quality of external quality assurance processes and oversight with respect to this Trust
  - viii. evaluate the relationship with external quality assurance bodies and Clinical Pathology Accreditation (UK) Ltd with respect to this Trust.
  - ix. within these terms of reference, the investigation team is invited to offer general comments where appropriate.

- 1.2.2 To comply with the agreed terms of reference, the investigation team has investigated the issues and concerns by interviewing a wide range of people, performing a slide review and examining a number of documents.
- 1.2.3 The report describes events and considers the previous investigation. It also offers an analysis of laboratory scientific processes, including immunohistochemistry. It presents benchmarking information on ER status of King’s Mill patients as identified by regional and national audits and statistical analysis. The report provides a commentary on related governance processes and their strengths and weaknesses at a local, regional and national level. Finally, the report offers a judgment on whether histopathology processes and immunohistochemistry are now safe and ‘fit for purpose’ at King’s Mill Hospital, and a series of recommendations mapped to the investigation’s terms of reference.
- 1.2.4 In the investigation report, we raise the possibility of weaknesses in culture, quality assurance and the implementation of national guidance. Where this is the case, the report clearly identifies possible concerns and suggests proportionate responses. The investigation conclusions are based on what occurred at Sherwood Forest Hospitals NHS Foundation Trust and on the subsequent investigation. They are made in the light of the planned review of quality assurance in pathology. They do not represent the result of investigation of issues elsewhere.

### 1.3 The investigation team

- 1.3.1 The members of the investigation team were:

Dr Rachael Liebmann  
Breast Pathologist and Registrar, The Royal College of Pathologists.

Professor Tim Reynolds  
Chair, Joint Working Group on Quality Assurance, The Royal College of Pathologists.

Mr Paul Williams  
Biomedical Scientist, Institute of Biomedical Science.

Ms Stella Macaskill  
Head of Professional Standards, The Royal College of Pathologists.

### 1.4 How the issue came to light

- 1.4.1 A specific sequence of events led to the issue being raised and investigated, as shown in the table below.

28 June 2011	The East Midlands Breast Screening Programme published <i>East Midlands Regional Pathology Booklet: An audit of individual and departmental pathology performance 2004–2010</i> . <sup>1</sup> The booklet showed that the performance of the King’s Mill cellular pathology service with respect to ER testing was an outlier in comparison to other centres in the East Midlands.
June–September 2011	The issue was escalated within the Trust.
September 2011	Expert advice was sought on behalf of Sherwood Forest Hospitals NHS Foundation Trust by Dr Shafiq Gill, Consultant Histopathologist.
September 2011	Expert advice from Professor Ian Ellis was received. The advice recommended the retesting of all cases, to establish if there was a problem.

7 October 2011	Backlogs Ltd, a commercial pathology reporting service, was commissioned by Sherwood Forest Hospitals NHS Foundation Trust to deliver the retesting. A specialist in Cambridge was identified to interpret the retests.
24 October 2011	All cases between 2006 and 2010 were sent to a specialist in Cambridge for retesting.
12 January 2012	Retest reports on all cases between 2006 and 2010 were received by King's Mill Hospital.
9 February 2012	All cases from 2004 and 2006 were sent to a specialist in Cambridge for retesting.
9 February 2012	Sherwood Forest Hospitals NHS Foundation Trust began a case note (clinical record) review to establish the implications of the differences between original and retest results for each patient affected.
9 March 2012	Decision was taken by the Trust to convene an expert review panel.
9 July 2012	Expert review panel was convened.
1 October 2012	Expert review panel issued a draft report to the Trust.
3 October 2012	All affected patients were informed by telephone.
3–6 October 2012	Some affected patients were seen in specially convened breast clinics to discuss potential changes to treatment.
8 October 2012	Sherwood Forest Hospitals NHS Foundation Trust held a press briefing.
8 October 2012 onward	The remainder of affected patients was seen or offered appointments in specially convened breast clinics to discuss potential changes to treatment
9 October 2012	Expert review panel final report was issued.

## 1.5 Details of the investigation

The investigation process consisted of a site visit, interviews, slide review and review of all documentation.

- 1.5.1 Between 3 and 6 December 2012, the investigation team visited King's Mill Hospital at Sherwood Forest Hospitals NHS Foundation Trust. The team visited all pathology laboratories, including cellular pathology and the mortuary. The team interviewed Trust staff and relevant regional and national individuals with knowledge of the issue.
- 1.5.2 Most of the interviews were performed on site at King's Mill Hospital. Additional telephone interviews were conducted with those not available during the site visit (see Appendix 2: List of interviews)
- 1.5.3 During January 2013, two members of the investigation team, Dr Rachael Liebmann and Mr Paul Williams, reviewed all of the cases identified as ER negative from 2006 to 2010 by King's Mill Hospital that had been retested. Slides from the retests carried out at Cambridge were also reviewed.
- 1.5.4 Documents examined as part of the investigation are listed in Appendix 5.

## 1.6 Oestrogen receptor testing

- 1.6.1 Some cancers, including breast cancer, have receptors for the hormones oestrogen and progesterone. Hormones act as chemical messengers and influence how cells grow and what they do. Oestrogen receptors are commonly abbreviated to ER because the US spelling of 'oestrogen' is 'estrogen'.
- 1.6.2 If a patient has been diagnosed with breast cancer, a sample of the breast tissue will usually be tested to see if it has oestrogen receptors. It is one of several tests used by specialists to decide an appropriate treatment for patients with breast cancer. The cellular pathology laboratory will use a special process that makes the hormone receptors in the sample of breast cancer tissue visible to a pathologist using a microscope. The ER test can be called an immunohistochemical analysis, immunocytochemistry or immunohistochemistry.
- 1.6.3 Breast cancer with a significant number of oestrogen receptors is known as oestrogen-receptor positive or ER positive. If a breast cancer does not have oestrogen receptors, it is known as ER negative. ER receptor status is used as a prognostic marker. Patients with ER positive tumours tend to have a better prognosis than those with ER negative tumours.
- 1.6.4 ER is a predictive marker that drives clinical treatment decisions. If the result is not accurate, there are serious clinical implications for patients. In false-negative cases, the patient will not be offered treatment that has a high probability of tumour response. In false-positive cases, the patient may suffer side effects of treatment with a low probability of tumour response.
- 1.6.5 The lack of standardisation of reporting practice and resulting discrepancies in ER testing results are well known and have been documented. Digital scanned images can be analysed using special software packages however this image analysis has not been shown to improve accuracy when compared to expert pathology scoring.<sup>2</sup>
- 1.6.6 In Newfoundland, one third of ER tests performed in 1997–2005 and originally reported as negative were positive on repeat central testing<sup>3</sup> and the Breast Cancer Intergroup trial ECOG 2197 reclassified 11% of ER negative tests on central testing.<sup>4</sup>
- 1.6.8 During a clinical trial of breast cancer treatments changes from ER positive to negative and from ER negative to positive have been found on central testing.<sup>5</sup>
- 1.6.9 In addition variable results can be obtained with different reagents (ER antibodies)<sup>6</sup> and the effects of tissue fixation and laboratory treatments on ER results has also been well described.<sup>7</sup>
- 1.6.10 The threshold for reporting ER positivity is particularly problematic and no cut-off point is definitively recommended in the breast screening programme guidance.<sup>8</sup>
- 1.6.11 Most ER tests are either strongly positive or completely negative on scoring.<sup>9</sup> This is called a bimodal distribution. However a full range of therapeutic responses are shown by patients depending on the ER score<sup>10</sup> and this response to treatment is not bimodal. So the dilemma faced by histopathologists about reporting ER as positive or negative is encountered in a minority of cases, but has considerable impact on treatment decisions for patients.



## 2 Investigation findings

### 2.1 Apparent outlier status

The first issue we address is whether King's Mill Hospital was an outlier with respect to breast cancer ER test results.

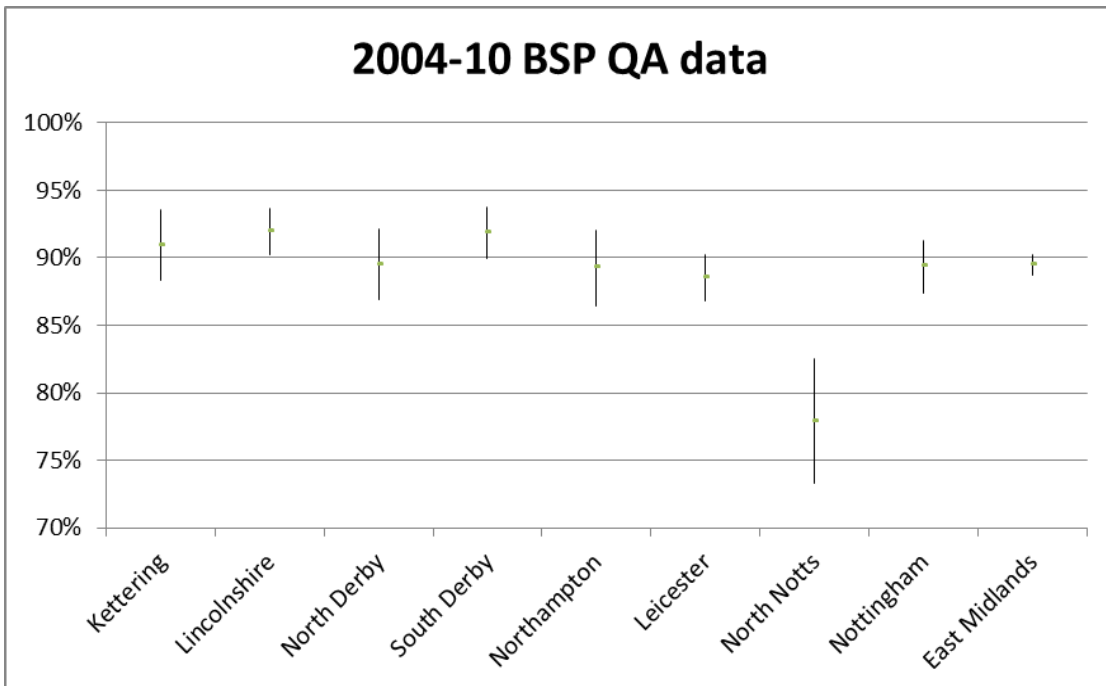
- 2.1.1 Two departmental clinical audits of ER positivity rates have been performed and were shared with the investigation team. These were performed in 2010 and 2011. No earlier information was available. No statistics were applied and there were no comparisons with the East Midlands' regional rates or national ER positivity rates. This is likely to be because this data was not available to the King's Mill histopathologists at the time.
- 2.1.2 An internal Trust investigation was performed called a Root Cause Analysis.<sup>11</sup> The report of this investigation indicated that the ER positivity rate was 77.9%, compared with a regional average of 89.5%.
- 2.1.3 In 2011 the East Midlands' Breast Screening Programme organisers published an audit of pathology reporting in the region. The numbers of cases reported in each unit in a year is relatively small. Therefore the audit team recognised the need to aggregate data to be able to draw statistical conclusions. This is why the *Regional Pathology Booklet*,<sup>1</sup> dealt with the period 2004–2010. It separates patients into geographical areas covered by a particular breast screening unit, which is not exactly the same as the catchment area of each East Midlands hospital.
- 2.1.4 The King's Mill Hospital Cellular Pathology laboratory is likely to be the main laboratory reporting breast cancer cases picked up by the North Nottinghamshire screening unit. The booklet shows that the North Nottinghamshire area has a lower ER positivity rate than other breast screening units. However, another small unit also has low positivity rates for part of the time under evaluation. In the booklet, there is a comment about the fact that North Nottinghamshire is statistically different but the significance of that difference was not further commented upon. It also shows that numbers of samples are low.
- 2.1.5 In this report the investigation team has demonstrated the data from the East Midlands Breast Screening Programme *Regional Pathology Booklet* in graphic form (see Figures 1–3), including vertical lines showing confidence intervals (CI). Confidence intervals are important to demonstrate how much significance should be applied to a particular result. A larger sample size normally will lead to a better estimate of the significance of the result. In this case the sample size is small as the North Nottinghamshire screening unit is small. A very wide confidence interval may indicate that more data should be collected before anything very definite can be said about the findings.\*
- 2.1.6 In the graphs it is clear that the confidence intervals for North Nottinghamshire (King's Mill) are always wider than for other units. Wide confidence intervals are not surprising since they relate to the number of screen-detected breast cancer cases at this unit. North Nottinghamshire is the smallest unit in the region and the third smallest in England. graphs show that King's Mill/North Nottinghamshire was a statistical outlier in the 6 year (2004–2010)

\* Footnote In all of the statistical figures in this section, the data is presented as a 95% confidence interval plot. The mean is marked by the central tick on the vertical bar representing the confidence range for each unit. The 95% confidence interval is the interval within which the true mean lies (with 95% confidence). This is because the central 'mean' drawn on the plots is the 'observed' mean that may not be correct because of statistical variation. Therefore, for example, the regional estimate in 2004–2010 was  $89.5 \pm 0.8\%$ , whereas for North Nottinghamshire (King's Mill), the estimate for 2004–2010 was  $77.9 \pm 4.61\%$ .

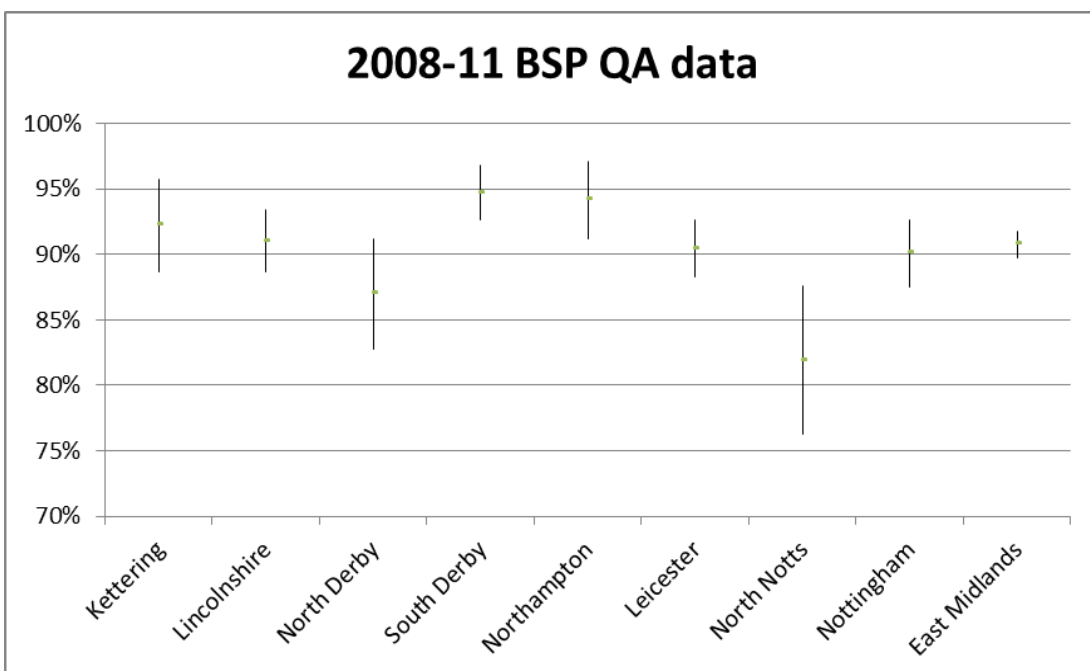
period. However when looked at separately it is not possible to identify King’s Mill/North Nottinghamshire as a definite outlier during the 2008–2011 and 2010–2011 periods because of overlap with other units in the region, or the East Midlands’ regional mean.

2.1.7 In the opinion of the investigation team, little confidence can be placed in reported ER positivity rates at King’s Mill compared to regional data. This is because the numbers of patients involved are small, and changes to just one, two or three patients may be sufficient to change the outcome. To demonstrate this the following graphs (Figures 4–6) have been produced by calculating the effect of changing the ER positive status by just one, two, three or four patients per year at King’s Mill/North Nottinghamshire.

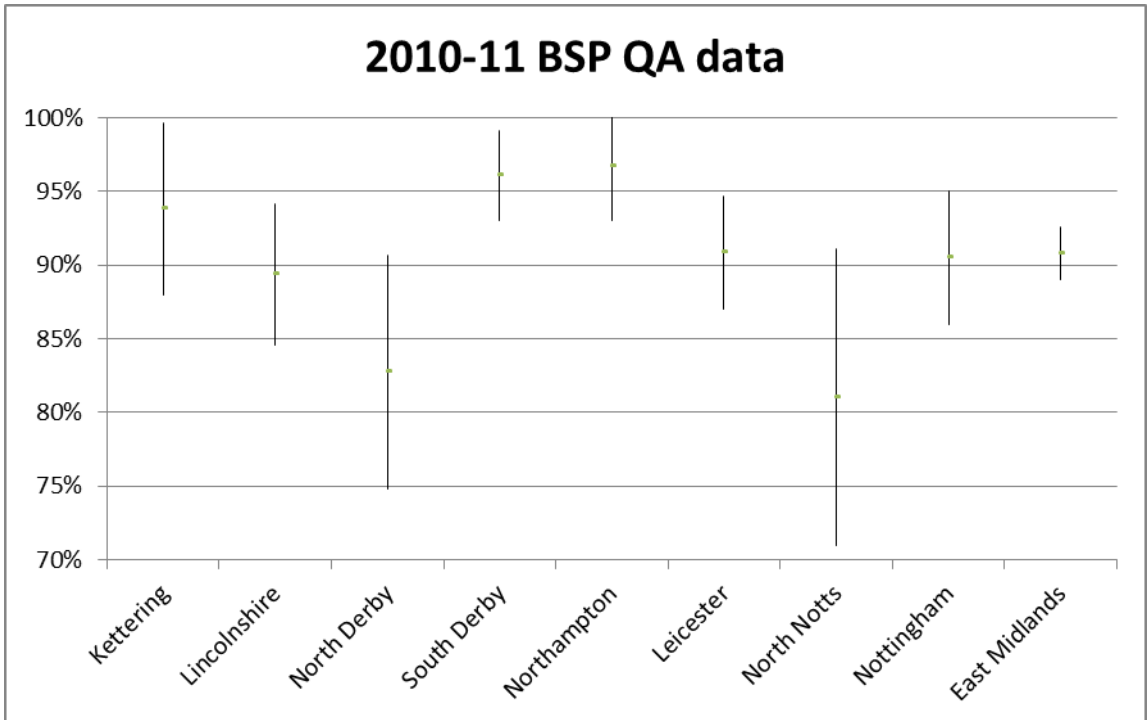
**Figure 1**



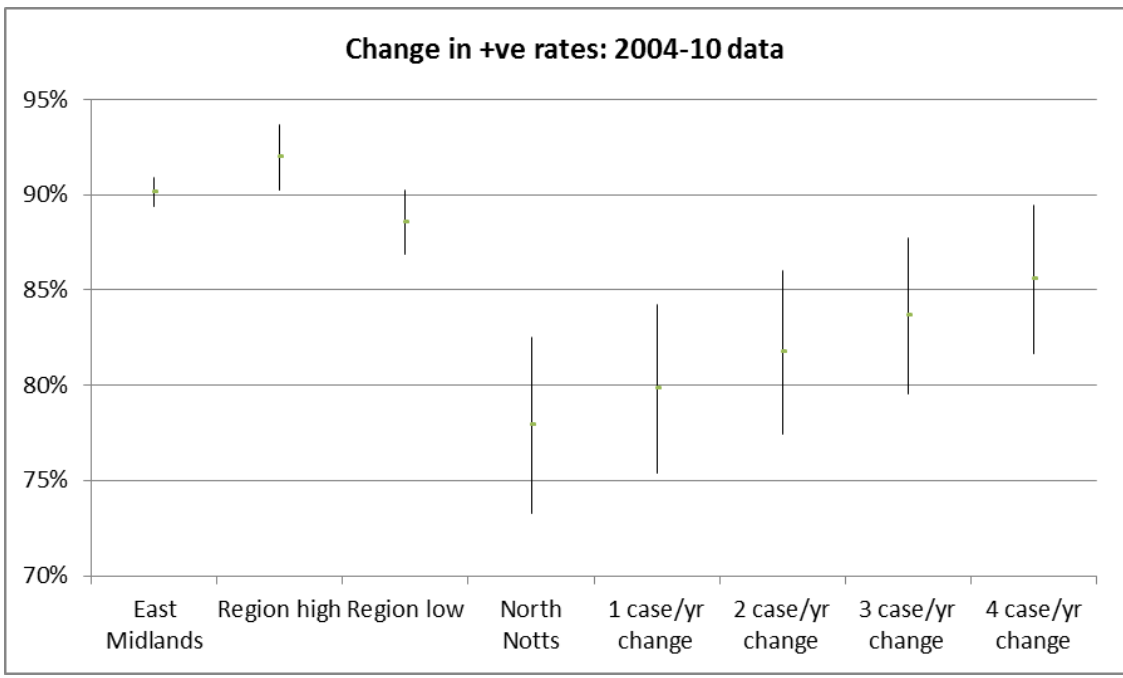
**Figure 2**



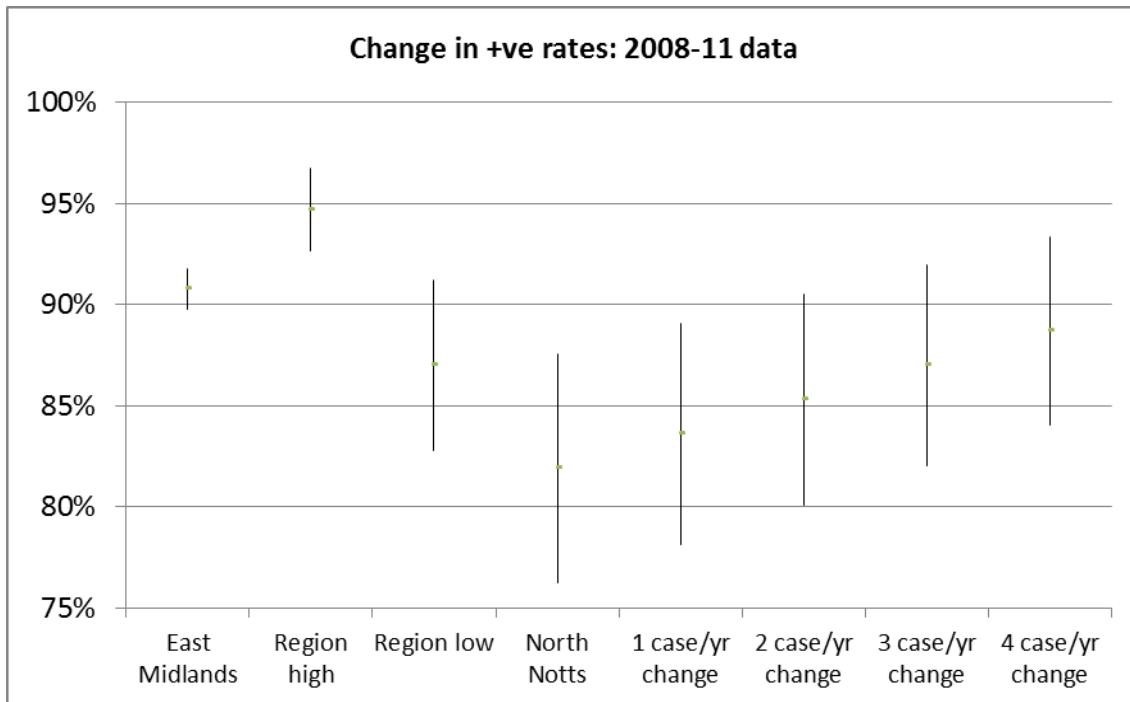
**Figure 3**



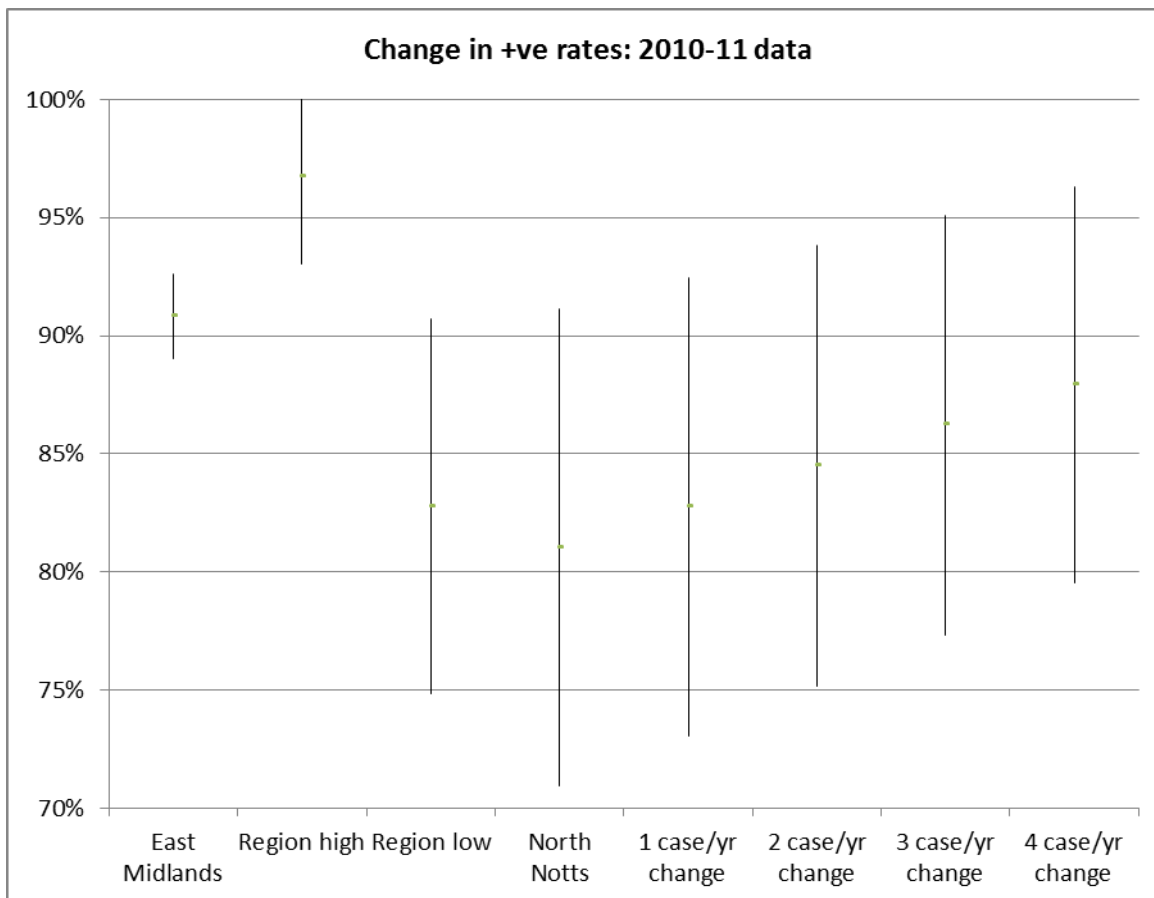
**Figure 4**



**Figure 5**

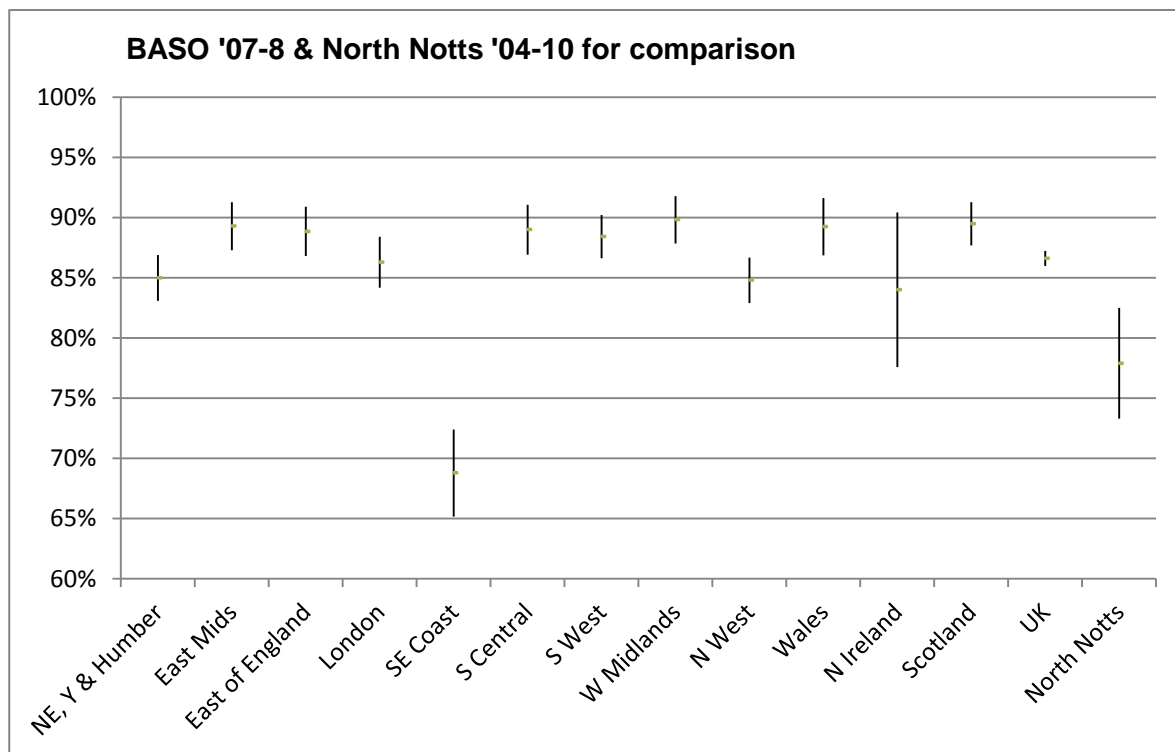


**Figure 6**

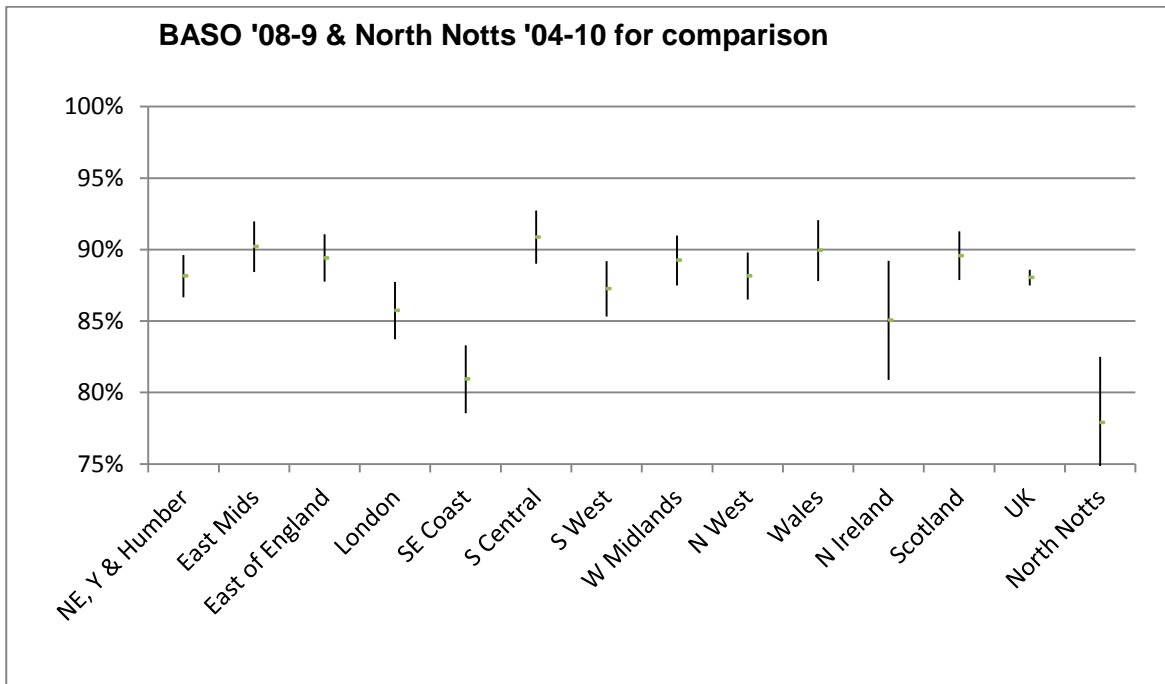


- 2.1.8 If just three cases per year in the period 2004–2010 were diagnosed as ER positive instead of ER negative, then the King’s Mill/North Nottinghamshire data would not be statistically different from the next lowest area in the region (Figure 4).
- 2.1.9 In the period 2008–2011, there was no statistical difference between the King’s Mill/ North Nottinghamshire rates and the next lowest unit. If just two cases per year in the period 2004–2011 were diagnosed as ER positive instead of ER negative, then the King’s Mill/North Nottinghamshire data would not be statistically different from the East Midlands regional mean (Figure 5).
- 2.1.10 In the most recent period included in the regional audit (2010–2011), there is no statistically significant difference between the King’s Mill/North Nottinghamshire data and the East Midlands regional mean (Figure 6).
- 2.1.11 In order to compare with a wider set of units we have also looked at national audit data. We have used the data supplied by the East Midlands regional Breast Screening Programme (Figures 7–9) and the national Breast Screening Programme and the Association of Breast Surgery.<sup>12</sup> This allows the ER positive rates at King’s Mill/North Nottinghamshire to be benchmarked against the English regions. The investigation team is grateful to Dr Jeremy Thomas from the Western General Hospital for providing data from the NHS Breast Screening Programme (BSP)/Association of Breast Surgery (BASO): *Breast Pathology QA: Review of ER status of screen-detected invasive cancer in Scotland 2008–2011*. Scottish data is not presented here.
- 2.1.12 It is clear that, in general, the East Midlands region has a higher ER positive rate than the UK mean in most years. However the confidence intervals do overlap with the UK mean. Comparison graphs of the aggregated King’s Mill/North Nottinghamshire data with the ABS (BASO) data are shown in Figures 7-9.

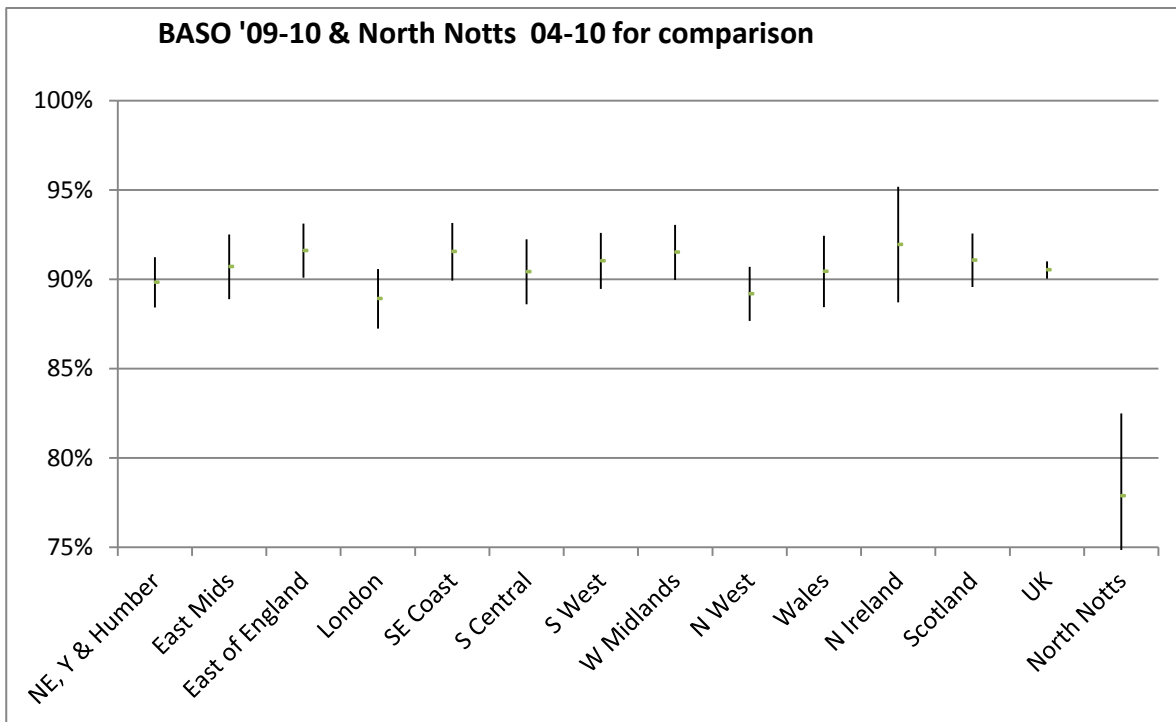
**Figure 7**



**Figure 8**



**Figure 9**



2.1.13 Figures 7–9 demonstrate that during the 2007–2008 and 2008–2009 periods King’s Mill/North Nottinghamshire was not an outlier in national terms. Northern Ireland and South East Coast region have ER positivity rates lower or very similar to King’s Mill. By 2009–2010, the national data had become similar across the board. This may relate to changes over time in laboratory technology, clinical interpretive practice or Breast Screening Programme data recording.

## **2.2 Apparent misreporting of oestrogen receptor in breast cancer cases**

The second issue we address is whether there was misreporting of ER status by King's Mill Hospital Cellular Pathology laboratory from 2004 to 2010.

- 2.2.1 When they became aware of the regional audit data apparently showing the King's Mill cellular pathology service to be an outlier, advice was sought from the national clinical pathology lead for the NHS Breast Screening Programme. The informal advice received that King's Mill should arrange an independent retest to identify whether there was really a problem with ER tests.
- 2.2.2 Having decided to undertake this retesting exercise, the Sherwood Forest Hospitals NHS Foundation Trust did not seek input from the Professional Standards Unit of The Royal College of Pathologists.
- 2.2.3 The retest exercise showed weak positivity in many cases of breast cancer previously reported as negative. The King's Mill Root Cause Analysis report<sup>12</sup> says that 120 women were incorrectly classified as negative over the six-year period 2004–2010. This is approximately 20 women per year. As many of the patients had already completed their breast cancer treatment this led to a considerable clinical dilemma.
- 2.2.4 In an attempt to consider the impact on individual patients of the apparently inaccurate King's Mill ER tests, external help was again sought by Sherwood Forest Hospitals NHS Foundation Trust. This external review did not involve a slide review of the retest slides and was predicated on the assumption that the retest results were correct and the King's Mill original results were inaccurate.
- 2.2.5 The King's Mill Root Cause Analysis report<sup>12</sup> says that 120 women were incorrectly classified as negative over the six-year period 2004–2010, i.e. approximately 20 women per year.

### **2.2.6 Slide review**

Using a conference microscope two members of the investigation team, Dr Liebmann and Mr Williams, together reviewed the slides from all of the cases identified by Sherwood Forest Hospitals NHS Foundation Trust as incorrectly classified as ER negative from 2006 to 2010.

- 2.2.7 At initial diagnosis between 2006 and 2010 many (52%) King's Mill breast cancer patients had the ER test repeated. These repeats were ordered by the King's Mill consultant histopathologists at the time, in order to clarify the ER status. During this time, a total of 162 repeat tests were performed, in some cases on the biopsy material and in others on the excision specimen.
- 2.2.8 Many of the ER negative cases (38%) had external control material tested at the same time and 68% of the cases had internal control material. The testing of external control material is good laboratory practice and this has developed over time at King's Mill Hospital as in other laboratories. External control material was included in all King's Mill Hospital 2010 cases included in the slide review. When it was present, the internal control material was predominantly intensely positive (Allred intensity score 3). The positivity of internal and external control material demonstrates that the technique had been applied and interpreted appropriately at the time. The testing of internal and external control tissue is helpful to assess whether the test has worked. However internal control is not in the control of the clinical team, pathologists or scientists. It is a random feature of some breast cancer biopsies that they contain some normal breast tissue as well as the cancer. The normal breast tissue can then act as the internal control.

- 2.2.9 As part of the slide review the investigation team also reviewed all of the slides from the retesting exercise commissioned by Sherwood Forest Hospitals NHS Foundation Trust. This retest was performed on King's Mill ER negative cases from 2006 to 2010 by Backlogs Limited at Addenbrooke's Hospital.
- 2.2.10 During the slide review, it was noted that a high proportion of the retested cases showed only weak/borderline positivity, giving an average Allred intensity score of 1.05. In comparison, the internal control material – where it was present in these cases – was very intensely positive, having an almost black microscopic nuclear appearance and an average Allred intensity score of 2.9.
- 2.2.11 All of the retest slides had been analysed using the ER antibody 6F11. This antibody has been identified by NEQAS as a common factor in recent poor performance due to false positivity. Advice has been given by NEQAS scheme to limit the false-positive findings in laboratories using this antibody.<sup>13</sup>

### **2.3 King's Mill laboratory problems with immunohistochemistry**

This report will next address whether there were problems with immunohistochemistry in King's Mill Hospital Cellular Pathology Department.

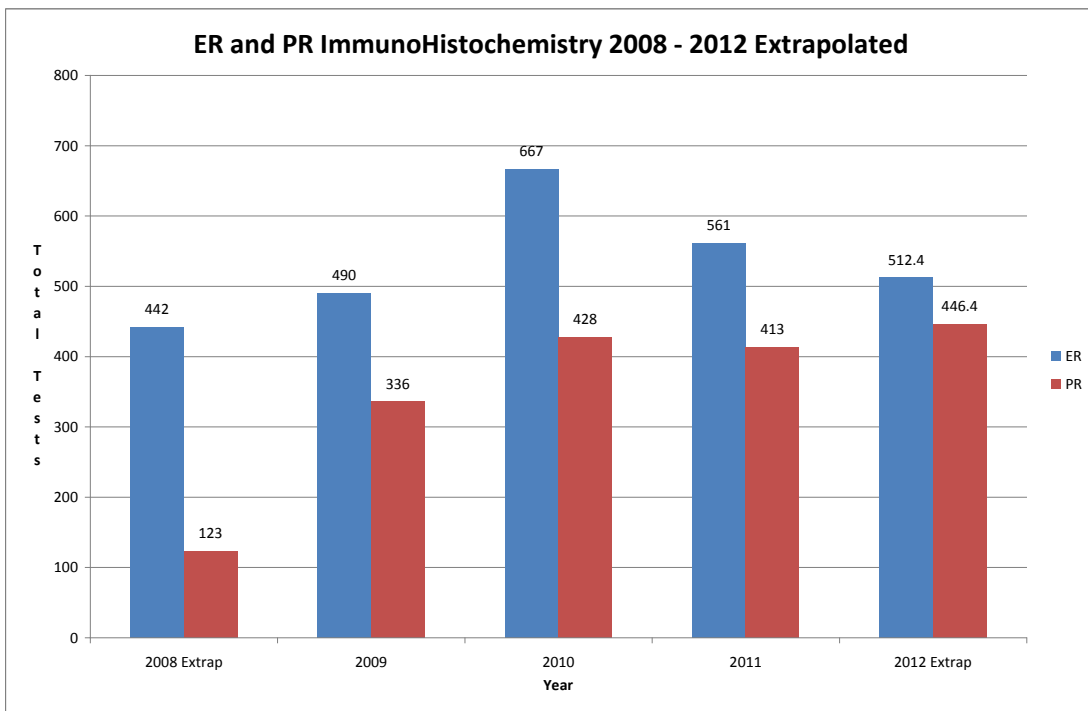
- 2.3.1 The slide review pointed to variable quality in some aspects of immunohistochemistry and other laboratory practices. In particular, artefacts were noted on the King's Mill immunohistochemistry slides, including frequent cytoplasmic positivity, making interpretation difficult.
- 2.3.2 Interviews with laboratory and consultant staff and documents received by the investigation team confirmed problems with immunohistochemistry at King's Mill Hospital.
- 2.3.3 These problems with immunohistochemistry led to an escalation of concerns to Trust management and action by the consultant histopathologists to mitigate the risk to patients.
- 2.3.4 Mitigating actions included the repeating of the ER testing on the same material or on the breast cancer excision specimen in many cases (see 2.2.6 above). Ultimately, in early 2011, the consultant histopathologists made the decision to suspend on-site ER immunohistochemistry testing.
- 2.3.5 During the site visit, an in-depth appraisal of scientific issues was performed. This can be read in full in Appendix 4. Findings of particular note that are relevant to historical and current ER and other immunohistochemistry performance are itemised below.
- 2.3.6 The slicing of breast excision specimens on receipt to aid formalin fixation was introduced by Dr Gill in 2007, but was not in place prior to this.
- 2.3.7 Routinely the fixative used for cellular pathology specimens is pH buffered 10% formalin. King's Mill Hospital use a formalin supplied by Genta Medical, but there is no checking of the pH of this solution.
- 2.3.8 In the enclosed and fully automated tissue processing equipment now in use at King's Mill Hospital, urgent biopsies have a processing time of four hours and 39 minutes, which includes a first station of 10% formalin for five minutes. The formalin is supplied as a concentrated buffered solution, which is diluted prior to use. Again the pH of the diluted buffered formalin used in this step is not checked.
- 2.3.9 Ideally external control material (see 2.2.8) should be taken at specimen dissection so that it is processed in a similar way to the specimen being tested. In the past at King's Mill



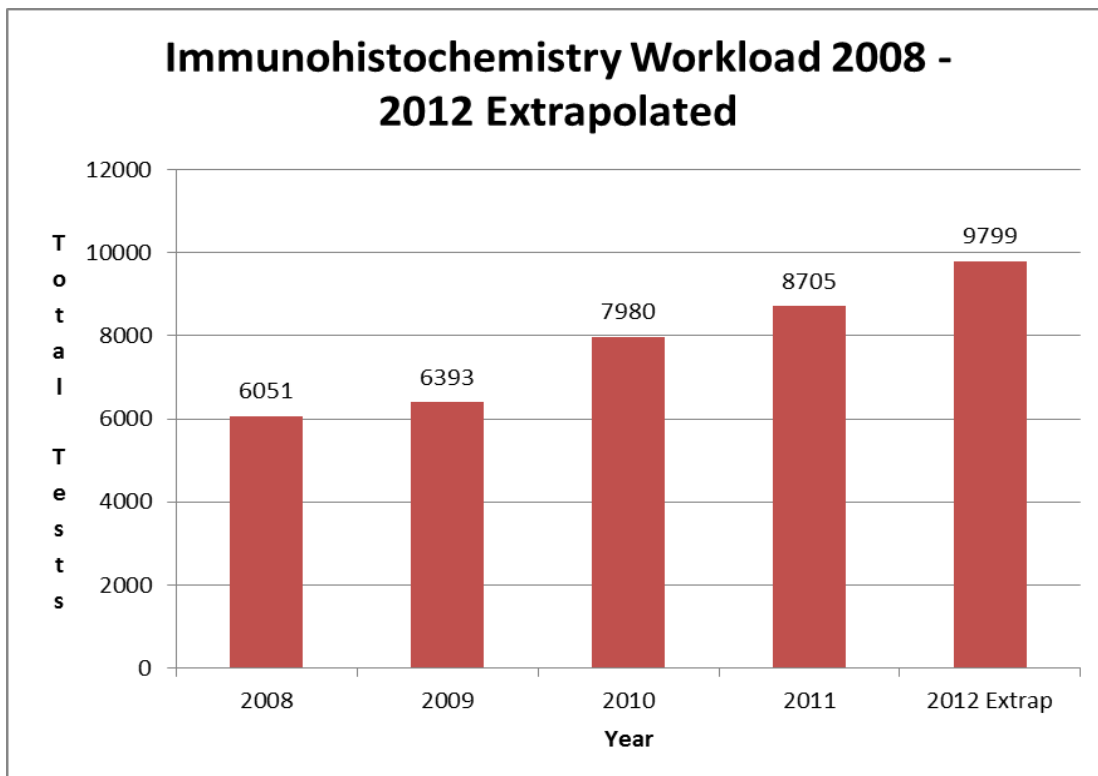
Hospital, breast external control material was taken from specimen discard cases, i.e. six weeks post authorisation. The King's Mill Hospital scientific staff told the investigation team that control material is now sourced at the time of specimen dissection.

- 2.3.10 From 2006 until the end of 2011, for immunohistochemistry, the King's Mill laboratory used the manual Shandon Sequenza with a domestic pressure cooker for antigen retrieval, or protease mediated retrieval as an alternative for some antigens. The use of varied manual methods can result in variable results.
- 2.3.11 From January 2012, the King's Mill Hospital Cellular Pathology laboratory has had the Intellipath (Menarini) installed, to replace the manual Sequenza. There was on-site training for four scientific staff and on-site validation provided by Menarini. The immunostainer has a warranty for 12 months from April 2012. For antigen retrieval, the laboratory has routinely used 'off board' methods including an antigen-retrieval pressure cooker with protease applied on a flatbed manual method. Now the laboratory is retrieving antigens on the Intellipath with protease. 'Off board' methods can result in variable results.
- 2.3.12 The Cellular Pathology laboratory made the decision to use bulk buffers supplied by Menarini to provide a robust method on the Menarini machine and avoid in-house induced variation. Commercial buffers are not checked for pH at King's Mill Hospital. Buffers with variable pH can influence the quality of immunohistochemistry results.
- 2.3.13 Despite immunohistochemistry testing being performed off site, in-house improvements in technique have continued and the laboratory has been comparing antibodies on the Menarini machine. Oestrogen and progesterone receptor labelling has not yet been tried on the new machine.
- 2.3.14 For most antibodies, the King's Mill cellular pathology scientists follow the suppliers' recommendations. The Intellipath is not a closed system and it offers the ability to 'tweak' protocols to ensure best results. The machine operates barcode-driven protocols but there is no laboratory information management system (LIMS) interface.
- 2.3.15 There is no air conditioning in the immunohistochemistry laboratory and therefore no adequate temperature control for immunohistochemistry processes. This will introduce variations in immunohistochemistry quality during temperature extremes, particularly during the summer. The investigation team noted how hot the laboratory's ambient temperature was during the visit.
- 2.3.16 All controls run on the Menarini machine so far were validated with the assistance of one of the consultants, Dr S Ibrahim. The intention is to run all remaining immunohistochemistry control material and validate over the next few months.
- 2.3.17 At Sherwood Forest Hospitals NHS Foundation Trust, the breast clinics occur on Tuesday, Thursday and Friday. The cellular pathology laboratory opening hours are Monday to Friday, 8am to 5pm (5.30pm on Friday). The length of time that breast biopsies spend in fixative therefore varies from a few hours (Tuesday and Thursday clinic cases) to over 48 hours (Friday clinic cases). Fixation times can influence the quality of immunohistochemistry.<sup>8,14</sup>
- 2.3.18 The King's Mill Cellular Pathology laboratory currently receives requests for five or six ER tests per week. This includes requests for non-breast cancer cases. Figure 10 shows the ER and PR workload for 2008–2012, and figure 11 shows total immunohistochemistry tests. This represents total slides processed including duplicates.

**Figure 10: Oestrogen (ER) and progesterone receptor (PR) workload 2008–2012 extrapolated**



**Figure 11: Total IHC workload for the last five years**



## 2.4 King's Mill pathology clinical governance and culture

The next issue we addressed is whether the processes and culture relating to quality and clinical governance at Sherwood Forest Hospitals NHS Foundation Trust were adequate.

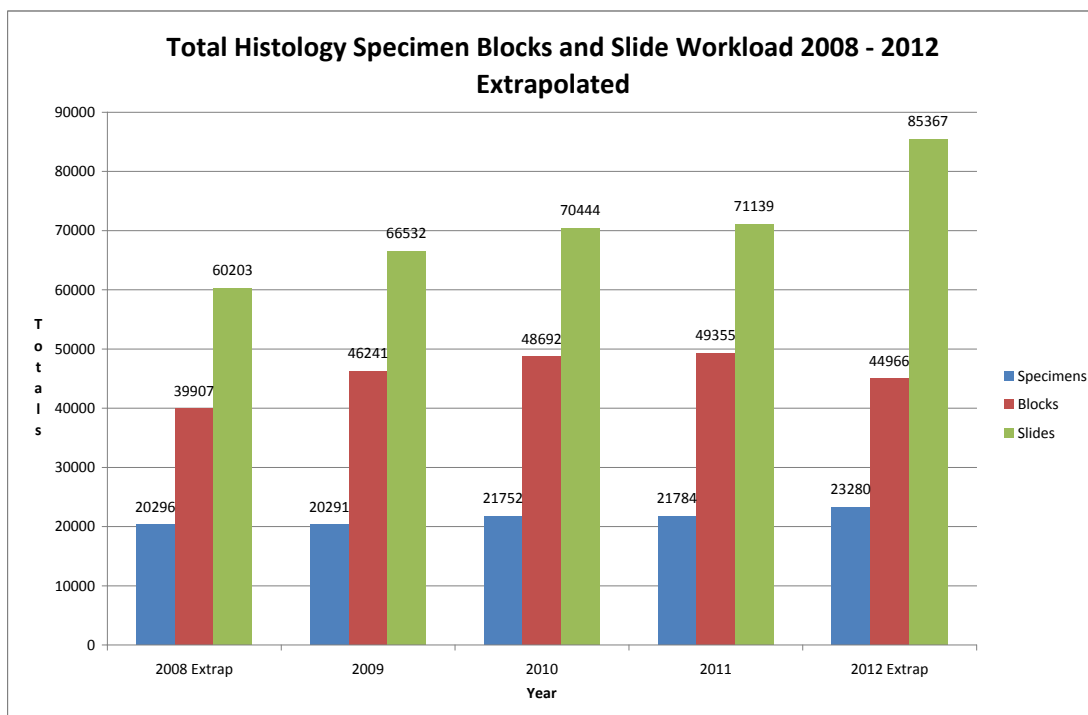
- 2.4.1 The Cellular Pathology laboratory at King's Mill Hospital is housed within a separate building from the rest of the pathology service. This is an ageing building but with sufficient space for the current service provision. The laboratory has been registered for training biomedical scientists since 2008 and fully CPA accredited by Clinical Pathology Accreditation (UK) Limited (CPA) since June 2012.
- 2.4.2 Ideally internal quality assurance and control is used to monitor all activities involved in the pathway of specimens through a laboratory, starting from reception and ending in the dispatch of a final report. Each laboratory will usually have a quality policy and standard operating procedures, describing the laboratory internal quality assurance and control processes. CPA process audits are distinct from clinical audits (see below) and are usually performed according to an audit schedule. The report on the Care Quality Commission deep-dive (see 1.1.5) comments on the absence of a CPA process audit schedule at King's Mill Hospital.
- 2.4.3 Clinical governance was originally defined by Scally and Donaldson as "a framework through which NHS organisations are accountable for continually improving the quality of their services and safeguarding high standards of care by creating an environment in which excellence in clinical care will flourish". Clinical governance should now be embedded in all pathology services.
- 2.4.4 An accepted definition of clinical audit is "a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and the implementation of change". Clinical audit is an integral part of clinical governance. It can be carried out by any practitioner involved in the treatment of patients. Clinical audit is principally the measurement of practice against agreed standards and implementing change to ensure that all patients receive care to the same standard. Cellular pathology at King's Mill Hospital sits within the Pathology Directorate. Management decisions are made on clinical governance, risk management, financial priorities and pathology strategic planning at directorate and divisional level.
- 2.4.5 The investigation team did not think that the official Sherwood Forest Hospitals NHS Foundation Trust reporting route for clinical governance was sufficiently direct. Ideally Consultants report clinically through their Clinical Lead and Clinical Director to the Medical Director. Nevertheless, the investigation was told that Dr Gill, the Cellular Pathology Clinical Lead, had made a direct report to Dr Ali, the Medical Director, about the NHS BSP regional audit and that action was taken promptly.
- 2.4.6 The Clinical Directorate team told the investigation that they were not sure that the correct process had been followed when the NHS BSP audit was shared with the Medical Director and when the decision was taken to cease in-house ER testing.
- 2.4.7 During the site visit, the investigation team observed that cellular pathology was in a separate building from the rest of pathology. The investigation team also noted relative under-resourcing of cellular pathology with respect to the other pathology disciplines.
- 2.4.8 Many people interviewed as part of the investigation recollected problems in cellular pathology at King's Mill dating back to 2000. At this time the consultant staffing levels fell to dangerously low levels. Only one consultant was in post. This consultant had serious health problems requiring lengthy periods of sickness absence. Recruitment was difficult and the service was provided by a series of locum consultants and visiting consultant staff from the neighbouring Nottingham City Hospital. Not surprisingly this resulted in an

absence of clinical leadership, difficulty achieving accreditation and a shift in the usual relationships between laboratory scientific and medical staff.

- 2.4.9 The appointment of the current consultant complement from 2007 onward was universally regarded to have resulted in a significant improvement in the quality of the clinical service. There was considerable support from clinical users for the histopathologists and understanding of the extremely difficult clinical circumstances they inherited. The clinical users and others also expressed appreciation for the efforts the histopathologists had made, over and above expectations, to improve cellular pathology clinical services.
- 2.4.10 A fifth consultant post has been proposed. The job description for this post has been reviewed and approved by The Royal College of Pathologists. However, the post is not yet funded by the Trust. The histopathology consultants have been advised to revisit the business case and update it. It is anticipated that this new post would enable all cellular pathology diagnostic work currently sent to the Nottingham City Hospital for reporting to be reported at King's Mill Hospital.
- 2.4.11 The investigation team heard from several interviewees about a Trust culture of short-term cost-cutting without the necessary strategic planning to ensure continuity of service. Specific examples given to us are outlined below.
- 2.4.12 The investigation team was told about considerable delays to procurement of the semi-automated immunohistochemistry platform on grounds of cost. A series of emails were seen that had been sent by the consultant histopathologists highlighting, over several years, the governance issues due to continued reliance on manual immunohistochemistry methods.
- 2.4.13 The relatively recent loss of four cellular pathology laboratory scientific staff as part of the Mutually Agreed Resignation Scheme (MARS) was a frequent topic raised by the cellular pathology team. They expressed dissatisfaction with the loss of permanent staff only for the vacated positions to be filled with agency locums. The cost of the MARS payments to the staff leaving the Trust and the greatly increased costs of locum staff, were considered to be difficult for Trust management to explain or justify. While the interviewees were grateful to have the posts filled by locums, there were feelings expressed that locums were not an adequate replacement for trained permanent scientists with respect to internal quality control and service development.
- 2.4.14 The investigation team heard about problems with approval for scientific staff to attend courses and find out about best practice elsewhere. Permission for release of staff from service work to attend specific courses was not given. This was also stated as the reason behind the failure to take up offers of help from the ER EQA scheme director. There is a dedicated training officer in each department and all courses requested by scientific staff have, to date, been funded. However, the investigation team was told of refusal by Directorate management to release staff to attend courses for continuing professional development (CPD).
- 2.4.15 During the interviews, it was mentioned that there had, in the past, been communication problems between histopathologists and the laboratory staff. This had resulted in issues being highlighted but not acted upon promptly or appropriately. There is now a shared drive system in place to report and identify problems for investigation.
- 2.4.16 The investigation team heard about regular governance, senior staff, technical and quality meetings and also about daily staff 'huddle' meetings attended by consultants and scientists. There is also a system of 'sticky notes' on the noticeboard, where staff can post suggestions and issues.

- 2.4.17 Minutes of these meetings were reviewed by the investigation team and showed a consultant-led, departmental commitment to quality and continual improvement.
- 2.4.18 In addition, the consultant histopathologists have each taken on clinical leadership for a specific area of the service. One histopathology consultant had been taking a particular interest in immunohistochemistry oversight and had been involved in procurement, validation of controls and monitoring of performance. She has recently stood down as Immunohistochemistry Lead after an altercation with the Clinical Director, perceived by the consultant histopathologist as undeserved criticism.
- 2.4.19 Scientific cover for an in-house immunohistochemistry service is also now problematic. The senior biomedical scientist has stepped down as Immunohistochemistry Lead recently and the number of senior scientists has been considerably reduced by the MARS programme. King's Mill Hospital staff felt it inappropriate to train locum staff in immunochemistry techniques in the circumstances.
- 2.4.20 Interviews with staff and the review of documents submitted to the investigation reveal a service struggling to cope with an increasing workload (see Figure 12).

**Figure 12 Demonstrates the specimen, blocks and slide workload for 2008 – 2012**



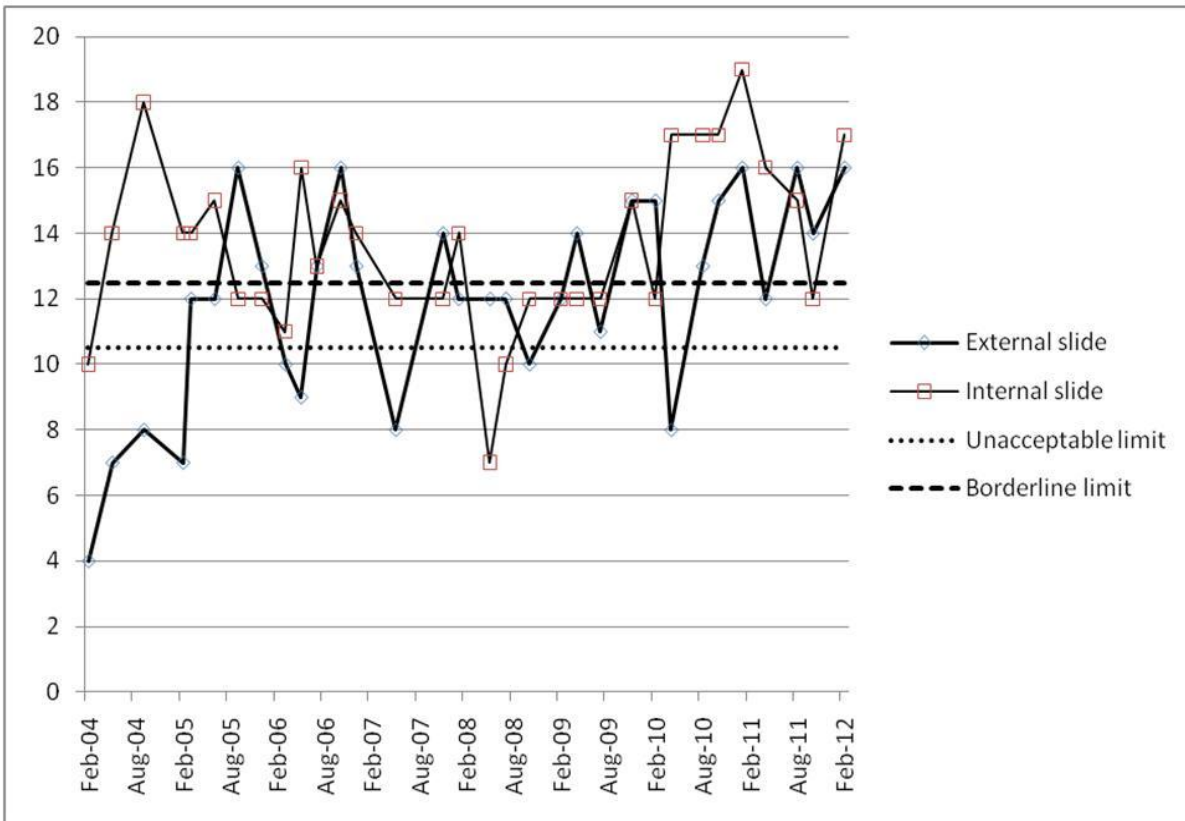
## 2.5 External quality assurance

The next issue addressed is whether the pathology external quality assurance systems were adequate.

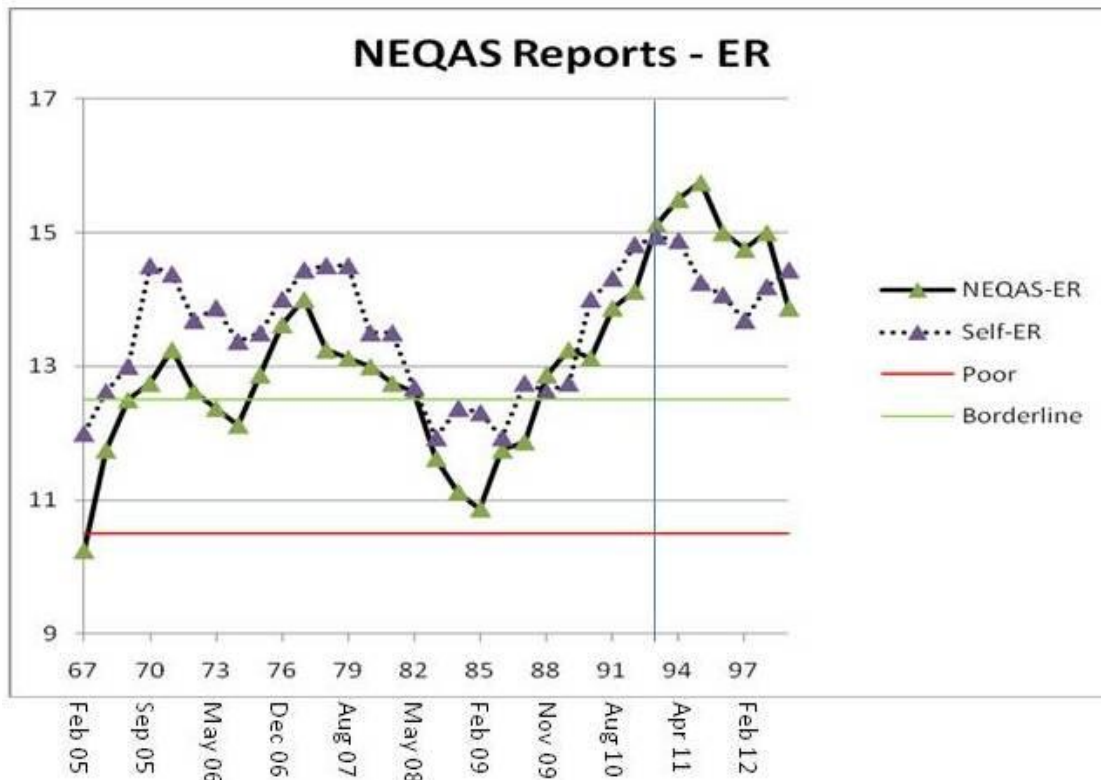
- 2.5.1 The term 'external quality assessment' (EQA) is used to describe a method that allows comparison of the testing performance in one laboratory to testing performance in others. EQA in cellular pathology is a system to check objectively the performance of a laboratory with regard to a particular test. Laboratory participation in any EQA scheme is voluntary, but regarded as best practice. There are several organisations providing EQA schemes.

- 2.5.2 EQA schemes may be accredited by CPA (UK) Ltd or another accrediting body. Currently not all cellular pathology EQA schemes are accredited.
- 2.5.3 The National Quality Assurance Advisory Panels (NQAAP) receive information on poor laboratory EQA performance. There are a total of six panels in the pathology disciplines and all report to the multidisciplinary Joint Working Group for Quality Assurance in Pathology (JWGQA). The JWGQA in turn reports to the Professional Performance Panel of The Royal College of Pathologists. The Department of Health has a representative on the JWGQA.
- 2.5.4 The EQA scheme for hormone receptors in breast cancer is module 2 of the UK NEQAS EQA for Immunocytochemistry and In Situ Hybridisation (ISH). Detailed information on the functioning of the scheme is described in the participants' manual, published on the UK NEQAS Immunocytochemistry website.<sup>15</sup>
- 2.5.5 On completion of each distribution (round) of the EQA scheme, each participating laboratory receives a written report on their performance. Scores and comments from the EQA assessors are compared to a self-assessment score from the participating laboratory.
- 2.5.6 Monitoring of long-term performance in all EQA schemes is initially carried out by the EQA provider according to a 'red, amber, green' (RAG) rating. Each EQA scheme sets and publishes the threshold for performance. Only laboratories falling below this threshold and receiving a red rating are referred to the NQAAP. Prior to reaching the threshold for receiving a red rating, a poorly performing laboratory will be sent a series of letters from the EQA provider. These letters will highlight the unsatisfactory performance and provide an offer of assistance to allow the participating laboratory to make improvements.
- 2.5.7 The role of the NQAAP is to manage poor performance within an appropriate timescale. If persistent poor performance remains unresolved, they will report the laboratory to the JWGQA. The JWGQA will work with failing laboratories to improve their performance and protect patients, but will also report persistent poor performance to the Care Quality Commission for investigation.
- 2.5.8 From 2004–2010, Cellular Pathology at King's Mill Hospital participated in the UK NEQAS EQA for Immunocytochemistry and In Situ Hybridisation, which covers ER testing. During this time, the laboratory received regular feedback on their performance from the scheme provider. This feedback has been shared with the investigation team. The feedback provided information that the laboratory at King's Mill could use to improve their ER testing results. The laboratory was not considered to be showing persistent poor performance and therefore did not trigger a red RAG rating.
- 2.5.9 Figures 13 and 14 show the distribution-specific results returned to the King's Mill laboratory by the EQA scheme. They also show the rolling average result over four distributions calculated by the review team. The EQA scheme supplies the laboratory with two slides for testing (labelled as external or NEQAS-ER) and also requires a sample to be tested which has been cut within the laboratory (labelled as internal or Self-ER).

**Figure 13 Distribution-specific results**



**Figure 14 Four-distribution rolling average**



- 2.5.10 Figures 13 and 14 show that although at times the King's Mill scores fell below the 'borderline' threshold, they did not fall below the 'poor' threshold. The data from King's Mill Hospital shows that the laboratory maintained a performance that was above the limit of acceptability. Distribution 93 (indicated by vertical blue line in figure 14) corresponds to January 2011 when ER samples started to be outsourced from King's Mill. It is also notable that the laboratory has continued to participate in EQA despite not running samples in house. King's Mill cellular pathology are doing this as part of their development/improvement process.
- 2.5.11 The EQA scheme did not provide data to allow King's Mill Hospital to review its performance against other laboratories, or against King's Mill performance in previous EQA rounds. Figures 13 and 14 to show this have been derived from the laboratory EQA data and prepared by the investigation team.

## **2.6 External monitoring, peer review, accreditation and quality assurance**

The next issue we addressed is whether the other external monitoring, peer review, accreditation and quality assurance mechanisms were adequate.

- 2.6.1 Analysis of the documentary evidence included the regional and national audits arising from NHS Breast Screening Programme (NHS BSP) data, along with minutes of national NHS BSP oversight meetings. Peer-review reports from the NHS BSP, Regional Cancer Network and Clinical Pathology Accreditation were also examined.
- 2.6.2 Breast screening is a method of detecting breast cancer at a very early stage. The first step involves an x-ray of each breast – a mammogram. The mammogram can detect small changes in breast tissue, which may indicate cancers that are too small to be felt either by the woman herself or by a doctor. The presence or absence of cancer is decided by a biopsy reported by a consultant histopathologist. The King's Mill Hospital histopathology consultants report the biopsies from patients screened in the North Nottinghamshire breast screening unit.
- 2.6.3 The NHS BSP covers the whole of the UK and has been in place since 1988. The programme offers women between the ages of 50 and 70 an opportunity to be screened for breast cancer every three years, at one of 82 units. An expanded age range of 47 to 73 is currently being phased in. In September 2000, research was published that demonstrated that the NHS BSP had lowered mortality rates from breast cancer in the 55–69 age group. In England, the BSP is now estimated to cost around £96 million per year.
- 2.6.4 There are 80 breast screening units across England, each inviting a defined population of eligible women (aged 50 to 70) through their GP practices. Women are invited to a specialised screening unit, which can be hospital based, mobile, or permanently based in another convenient location such as a shopping centre.
- 2.6.5 The NHS BSP is nationally coordinated. It sets national standards for radiology, pathology and surgery, which are monitored through a national quality assurance network. For England, there is a national coordinating office, based in Sheffield. An Advisory Committee oversees the programme and reports to government ministers.
- 2.6.6 *Consolidated Guidance on Standards for the NHS Breast Screening Programme* was published in 2005<sup>16</sup> and subsequent guidance documents are also available. There is guidance for the management of incidents identified by the BSP.<sup>17</sup>
- 2.6.7 During the period 2004 to 2010, the Cellular Pathology Department at King's Mill Hospital was subject to peer review visits as part of regular quality assurance and accreditation



processes by the East Midlands Cancer Network, the NHS BSP East Midlands Quality Assurance Reference Centre and Clinical Pathology Accreditation. All of these assurance processes are run by organisations which hold risk registers itemising, prioritising and addressing the risks faced by their organisation. However, risks to patient care which are encountered in the course of their quality assurance activity are not managed in this way.

## **2.7 Relationship with EQA bodies and CPA (UK) Ltd with respect to this Trust**

- 2.7.1 From document review and interviews with all parties, the investigation team found good attendance at regional meetings by the King's Mill consultant histopathologists. The consultants showed a keen interest in regional and national developments and in the adoption of best practice guidance.
- 2.7.2 All evidence given to the investigation team suggests that the King's Mill consultant histopathologists showed an appropriate level of concern when the NHS BSP regional audit was presented, apparently demonstrating their service to be a regional outlier. They communicated this concern through the Laboratory Director to the Trust's Medical Director.
- 2.7.2 Sherwood Forest Hospitals NHS Foundation Trust agreed to share all CPA reports with the investigation team representing the Care Quality Commission.
- 2.7.3 The Chair of the regional breast group of the regional cancer network was unaware of the issues at King's Mill with regard to ER until after the press release and media coverage.
- 2.7.4 No evidence was found of communication between the NHS BSP and regional cancer network breast team on the subject of the ER issues at King's Mill Hospital.
- 2.7.5 No evidence was found of communication between Sherwood Forest Hospitals NHS Foundation Trust and CPA when significant changes to the in-house immunohistochemistry repertoire were made.
- 2.7.6 No evidence was found of systematic feedback of the relevant results of the NHS BSP/Association of Breast Surgery (BASO) audit data to breast histopathologists.
- 2.7.7 National pathology reporting guidance produced by the national coordinating committee of the NHS BSP was considered by the investigation team to be of high quality, evidence-based and widely disseminated as part of The Royal College of Pathologists' cancer datasets.
- 2.7.8 Neither the ER tests reported at King's Mill nor the retests performed at Addenbrooke's Hospital were scored according to national breast screening programme guidance. National guidance mentions the H-score but recommends use of the Allred score. The reason for the substitution of the H-score by King's Mill and Addenbrooke's Hospitals is not apparent to the investigation team.
- 2.7.9 From a review of histopathology reports for the affected patients in 2006–2010, the investigation team considers that all other aspects of the NHS BSP's national pathology guidance appeared to have been implemented by the King's Mill consultant histopathologists.
- 2.7.10 No evidence was found of systematic monitoring of histopathologists attendance at regional and national NHS BSP pathology meetings or regional or local compliance with national pathology guidance.

- 2.7.11 The investigation team could find no evidence of systematic reporting of regional issues to the national pathology coordinating committee. Issues identified from regional statistical analysis, audit or peer review are included under Any Other Business.
- 2.7.12 The audit performed by the East Midlands regional breast screening programme was an attempt to demonstrate regional compliance. There was no evidence of national consideration of the East Midlands NHS BSP audit data. The East Midlands regional breast screening leads offered to host a national NHS BSP monitoring programme at minimal cost. The investigation team could find no evidence that an alternative monitoring system was planned.

### **3 Commentary and conclusions**

#### **3.1 User perception of the problem identified and impact on patient care**

- 3.1.1 The Sherwood Forest Hospitals NHS Foundation Trust breast care nurses had been running extra clinics to advise and support the affected patients for only two days before the Trust issued a press release. As a result, they had not had the opportunity to see all patients who had been invited as part of the disclosure process prior to the media storm. Outpatient clinic appointments for further affected patients were scheduled for the coming days and weeks after the press release.
- 3.1.2 The multidisciplinary team reported that levels of anxiety increased amongst patients after the press briefing. The patients who attended clinics before the press release showed a different response from those who attended after the press briefing. The latter were more anxious and angry and felt they had been misdiagnosed.
- 3.1.3 Breast multidisciplinary team members had input into the press release but rather than the correct phrases, e.g. 'immunohistochemistry' and 'adjuvant therapy,' words such as 'misdiagnosis' and 'treatment' were used by the media.

Examples were :

- ITV, 9 October 2012: [www.itv.com/news/central/2012-10-09/mp-calls-for-kingss-mill-hospital-board-to-step-down-after-faulty-breast-cancer-tests/](http://www.itv.com/news/central/2012-10-09/mp-calls-for-kingss-mill-hospital-board-to-step-down-after-faulty-breast-cancer-tests/)
- article in *Mansfield People*, 8 October 2012: [www.mansfieldpeople.co.uk/Kingsmill-Hospital-apologises-breast-cancer/story-17051603-detail/story.html](http://www.mansfieldpeople.co.uk/Kingsmill-Hospital-apologises-breast-cancer/story-17051603-detail/story.html)

- 3.1.4 Cancer survivors said this was dragging up the emotions they felt when their cancer was first diagnosed. They mentioned the opening of old wounds.

#### **3.2 Analysis of evidence about the quality of the service at King's Mill Hospital**

- 3.2.1 It became apparent during the visit, interviews and document review that decision making was finance driven, with too little attention given to clinical considerations.

The NHS is run for the benefit of patients, but takes cost into account. However, in Sherwood Forest Hospitals NHS Foundation Trust, finance appeared to take priority.

- 3.2.2 The investigation team was told about a management decision to change one of the immunohistochemistry antibodies (not ER) to another antibody, which was found not to work. This decision was based on price alone, saving a paltry sum. The consultant histopathologists were not informed of this substitution and only realised when the new antibody repeatedly failed to perform.

- 3.2.3 As a result of the review of documentary evidence, slide review and interviews with King's Mill staff and others, the investigation team considers that the consultant histopathologists were aware of problems with the ER immunohistochemistry. They made proportionate, professional and persistent recommendations to management to improve the ER service. This included the considerable time and effort involved in the clinical and technical oversight of the service by one of the consultants and the eventual decision to withdraw local provision of the service.
- 3.2.4 The investigation team observed evidence of continued management reluctance, even at the time of the visit, to accept the clinical imperative for the increased costs of the outsourced ER service.
- 3.2.5 As part of the immunohistochemistry quality improvement programme, invitations had been extended to members of King's Mill Hospital cellular pathology laboratory staff to visit centres of excellence. These invitations were designed to improve in-house performance, allow King's Mill Hospital staff to learn new techniques and investigate the most appropriate and effective technologies. This would be usual practice where a laboratory service is struggling. The investigation team was informed that King's Mill Hospital staff had not been allowed by their line management to take up such opportunities, as routine work took precedence. The investigation team regards this as short-sighted decision-making, not in keeping with a quality clinical service.
- 3.2.6 The investigation team was shown equipment, purchased two years previously to improve processing, which had not been put into routine use. This equipment, and its underlying technology, is in use in only a small number of cellular pathology laboratories and the investigation team was not clear why this equipment had been purchased.
- 3.2.7 In the view of the investigation team, improved networking with a wider range of external contacts by the consultant histopathologists and senior scientific staff would have helped to benchmark and support the service. Looking forward, the need for networking remains valid as it will help to develop services for patients in the locality.
- 3.2.8 In spite of pressure on the substantive laboratory staff, continuing professional competence and development (CPD) must be maintained for King's Mill consultant histopathologists and cellular pathology staff.
- 3.2.9 Inspection of the pathology laboratories at King's Mill Hospital revealed a spacious, new and well-equipped blood sciences laboratory in a modern building. Pride in this new laboratory was made clear to the Care Quality Commission (CQC) deep dive investigation. However, cellular pathology services are not provided in the new laboratory. Indeed, comparable investment in developing and maintaining cellular pathology did not appear to have taken place. Potential plans for future cellular pathology development appeared to be inappropriately biased to public mortuary services.
- 3.2.10 Sherwood Forest Hospitals NHS Foundation Trust had implemented the MARS with respect to four cellular pathology scientists and replaced those members of staff with locums. As a proportion of the total staff complement, the investigation team considers this loss excessive and that a full skill-mix review should have preceded these decisions.
- 3.2.11 A full review of staffing needs to be carried out to identify the necessary staffing structure for ongoing cellular pathology services. It should extend to the exploration of use of an extended working day and seven-day working, as well as the use of more support-grade staff and the balance between the laboratory and mortuary establishment.
- 3.2.12 In the middle of the last decade (2004–2008) the manual immunohistochemistry techniques in use at King's Mill Hospital were not significantly different from other units in the UK. However, with time, technological advances improved the performance of other

units while King's Mill Hospital was left behind. By continuing to rely on manual techniques, King's Mill Hospital became less aligned with the regional and national average in 2009–2010.

### **3.3 Evaluation of the quality of breast pathology reporting at King's Mill Hospital**

- 3.3.1 There was no evidence of deficiencies in clinical practice at King's Mill Hospital, based on:
- a. Analysis of the statistical evidence,
  - b. Interviews with breast screening regional quality assurance team, the cancer network breast regional chair, Clinical Pathology Accreditation staff, Trust management, a consultant histopathologist from a neighbouring Trust and clinical users of the service, as well as a slide review and the review of histopathology reports relating to the affected patients, showed no evidence of deficiencies in clinical practice at King's Mill Hospital.

### **3.4 Evaluation of the quality of immunohistochemical laboratory processes at King's Mill Hospital**

- 3.4.1 The investigation team observed a new immunohistochemistry machine had been installed. The Intellipath (Menarini) is an 'open' platform that requires multiple user interventions and manual processing steps, each of which has the potential to introduce error. These open systems allow the use of reagents sourced from a variety of suppliers, whereas 'closed' systems are constrained to using pre-packaged reagents from a single source.
- 3.4.2 When purchasing immunohistochemistry equipment a high-throughput machine was considered essential. This was due to the need to accommodate a large number of tests in two runs. The number of cases was high partly due to the need to repeat so many sub-optimal immunohistochemistry tests. The number of runs was limited to two due to restrictive working practices limiting the length of the working day. With an extended working day three runs could be performed each day. As a result, cost and volume considerations led to the choice of this system over others. While the immunohistochemistry machine represented an improvement for King's Mill Hospital immunohistochemistry, it was put in place in the laboratory two years after the funding was initially approved due to a stop-start series of management decisions. This implementation was too slow to take advantage of the pace of advances in technology.
- 3.4.3 At the time of the visit, this machine was not in routine use as the service had been outsourced. Menarini reagents were being used to validate antibodies in the hope of repatriating the currently outsourced immunohistochemistry work.
- 3.4.4 In the opinion of the investigation team, full walk-away automation should be considered as first choice, above cost considerations, to ensure minimal reliance upon human intervention. This would reduce manual errors and inter-operator variation. This has the added benefit of releasing staff resource and potentially allowing staff of lower skill and payscale to operate the technology reliably and safely.
- 3.4.5 The immunohistochemistry workload at King's Mill Hospital was small and the capacity of a fully automated machine would easily cope if the working practices included an extended laboratory working day and week.
- 3.4.6 Historically, the cellular pathology laboratory at King's Mill Hospital has used, for ER and other immunohistochemistry controls, breast material from cases about to be discarded. As part of the ongoing quality improvement programme, this practice has been discontinued. NEQAS best practice<sup>18</sup> recommends collection of control tissue from specimens recently received in the laboratory.

- 3.4.7 The small sample size of the data from King's Mill means it has not been identified as an outlier. However, the apparent outlier status has caused concern. Therefore the investigation team believes that it is essential to define minimum sample size rules to allow effective monitoring in future. Given that current monitoring of ER outcomes in cellular pathology is through the NHS BSP, the investigation team recommend a minimum number of 300 ER tests in this screening group.
- 3.4.8 A similar monitoring system should be introduced for non-screening cases (see recommendation 4.7.23). Assuming an exact split between symptomatic and screening cases of 50:50 this would require a departmental new breast cancer biopsy workload of 600 cases per annum. However since a 50:50 split is unlikely the workload in practice will of necessity be higher as the smaller biopsy workload must achieve the minimum workload threshold. The method used for calculation of suitable sample sizes is included as Appendix 3.
- 3.4.9 National guidance says that individual histopathologists involved in breast screening should report a minimum number of 50 breast cancer excision cases per annum.<sup>19</sup> Given that the NHS BSP depends on accurate biopsy outcomes it would be more logical to set a minimum number of breast screening biopsy cases per histopathologist.
- 3.4.10 Robust statistical monitoring of individual performance would require a minimum of 300 cases per histopathologist per year (see Appendix 3). To assure the quality of the service, Public Health England (or the equivalent in the devolved administrations), should consider monitoring outcomes through the NHS BSP for histopathology in a manner similar to that used for screening radiologists and for cervical screening in the NHS Cervical Screening Programme. The implementation of a minimum number of breast cancer screening biopsies to be reported by each individual pathologist involved in the programme would be a starting point for this robust monitoring.
- 3.4.11 The investigation team is aware of the implications of minimum workload thresholds for cellular pathology reconfiguration and sub-specialisation, but considers the case for assurance of the quality of patient care to be compelling.
- 3.4.12 In the light of the following, it is recommended that in-house ER testing should not be recommenced at King's Mill Hospital.
- Minimum ER immunohistochemistry workload thresholds to ensure effective statistical monitoring are not met.
  - There are ongoing problems with cellular pathology laboratory staffing and skill mix.
  - There are ongoing problems with laboratory ambient temperature control.
  - Since October 2012 there is, at best, reluctant consultant and scientific oversight of the immunohistochemistry service.

### **3.5 Evaluate the quality of histopathological evaluation of immunohistochemical investigations, particularly ER testing, at King's Mill Hospital**

- 3.5.1 The investigation team analysed the statistical evidence and performed interviews with the consultant histopathologists, as well as performing a review of all histopathology reports and slides from cases from 2006 to 2010 relating to the affected patients. The investigation team found no evidence of deficiencies in histopathological evaluation of immunohistochemical investigations at King's Mill Hospital.
- 3.5.2 Indeed, the in-depth slide review performed as part of the investigation revealed considerable caution on the part of the King's Mill consultant histopathologists in the interpretation of sub-optimal technical preparations. This was shown by the finding that

ER testing had been repeated on the biopsy or subsequent excision specimen to confirm ER negative results.

- 3.5.3 ER scoring, both of King's Mill tests and of the Addenbrooke's retests was performed according to the H-score. The H-score is a recognised scoring method, and one of two mentioned in the current national NHS BSP guidance, but it is not the scoring system currently recommended for use in the NHS BSP.<sup>19</sup> The investigation team was not able to explain this finding, but was also unable to ascertain if this had a significant impact on the audit findings or their subsequent investigation by the Trust.

### **3.6 Evaluation of the quality of internal quality control and clinical governance procedures with respect to this Trust**

- 3.6.1 During the site visit, slide review and interviews with staff members, the investigation team found inadequate consideration of the end-to-end process particularly, but not limited to, attempts to deal with immunohistochemistry problems.

Examples include:

- widely variable fixation times for breast biopsies
- non pH-tested formalin
- variable processing protocols and platforms
- variable antigen retrieval
- lack of ambient temperature control
- wide variations in, and manual labelling of, histopathology slides
- lack of robust provision, back up, appropriate servicing and slow speed of repairs for equipment across the whole of the cellular pathology service
- EQA performance reports not shared with the clinical head of service/laboratory director.

- 3.6.2 Current cellular pathology meetings are mostly informal and this reduces the ability to raise issues with and influence the Directorate management. The establishment of more formal, minuted cellular pathology governance meetings would allow a formal report including risks and concerns to be submitted to the Directorate governance meeting.

- 3.6.3 Discussion of cellular pathology EQA performance reports and feedback should be an integral part of these meetings.

- 3.6.4 Establishment of these meetings would encourage leadership development of the King's Mill histopathology consultants and the Laboratory Manager.

- 3.6.5 Cellular pathology control of departmental risks and their mitigation would improve service quality and provision. From the document review and interviews, it was clear that attempts to raise immunohistochemistry risks at Directorate level met with limited success, having initially been ignored. A risk register should be managed at cellular pathology departmental level with input from the consultant histopathologists. This should feed directly into the Directorate risk register which would make accountability transparent.

- 3.6.6 In light of the past culture of short-term and cost-driven decision making, the investigation considers that future budgetary control and clinical responsibility need to be clearly aligned. In addition, the role of the laboratory director needs to be explicit, adequately resourced, underpinned by a job description and should include budgetary management and accountability.

- 3.6.7 The overall impression formed by the investigation team is of a department isolated physically from the rest of the pathology service, trying hard to put things right, and struggling to leave behind an outdated culture of 'make do'. It operates in a climate of severe financial constraints and is not necessarily getting the full support of the Trust in terms of funding and support for quality improvements, staffing and IT support.
- 3.6.8 With hindsight, given that there was no suggestion that any of the King's Mill consultant histopathologists had a performance problem, an internal review of the original slides would have been a more timely and effective intervention than the retesting exercise actually performed.
- 3.6.9 In the opinion of the investigation team, more formal external support and advice from a professional body would have been helpful to those tasked with responsibility for the Trust's clinical governance. In particular, The Royal College of Pathologists' Professional Standards Unit has considerable experience in drafting terms of reference for 'look back' exercises and understands the potential pitfalls in planning, implementing and interpreting 'look back' exercises and audits. It also understands the differences between a 'look back' exercise and a Duty of Care review.
- 3.6.10 The investigation team have concluded that the retest results did not provide an accurate indication of the tumour hormone receptor status for the affected patients. This was based on the findings of the slide review and the use of 6F11 for the external retest. The weak positivity in the retested cases represented false-positive results.

### **3.7 Evaluation of the quality of EQA processes and oversight with respect to this Trust**

- 3.7.1 External Quality Assurance is part of a structured management system that aims to identify poor performance and prevent this becoming persistent. During the course of the investigation, the Department of Health England announced a review of quality assurance in pathology. [www.dh.gov.uk/health/2013/01/pathology-qa-review-launch/](http://www.dh.gov.uk/health/2013/01/pathology-qa-review-launch/)

The findings and recommendations of the King's Mill investigation reported here should be considered at the outset of the Department of Health review.

- 3.7.2 EQA can mean either external quality assessment or external quality assurance. An EQA scheme provides an *assessment* service, which a laboratory uses for *assurance* of its quality.
- 3.7.3 Unless otherwise stated, this report refers to laboratory EQA schemes rather than interpretive individual EQA schemes.
- 3.7.4 EQA schemes have the following essential criteria but, as there may be deficiencies in current schemes, recommendations for review of scheme design are listed in the recommendations section.
- a. **Timeliness:** delay in identifying problems is unacceptable.
  - b. **Effectiveness (targeting of clinical decision points/samples in appropriate analytical range):** the purpose of EQA is to ensure that routine samples can be used to answer clinical questions. EQA schemes should not simply pursue technical accuracy for the sake of accuracy, but should focus on the clinical question being asked.
  - c. **Effectiveness (identification of persistent poor performance):** schemes should be designed with the purpose of ensuring patient safety as their primary aim. This means that poor performance should be identified rapidly and dealt with rapidly.

Also, failure of a participating laboratory to engage with the scheme organiser should be seen in the light of a risk to patient safety.

- d. **Effectiveness (consistency in identification of persistent poor performance):** a multiplicity of scheme providers should not make it possible to choose an 'easy' EQA scheme.
- e. **Effectiveness (benchmarking):** since the information is held by EQA scheme providers, laboratories should be provided with feedback allowing them to benchmark their performance against past performance and that of other participants.
- f. **Transparency:** the purpose of EQA schemes is to ensure results are correct and thereby ensure patient safety. In this era of publication of individual surgeons' outcomes results in 'league tables', there can be no justification for continued secrecy over pathology EQA scheme performance. Laboratory identity should not be hidden by a participant number.

- 3.7.5 In the UK, all EQA schemes are expected to report persistent poor performance by laboratories to the relevant discipline-specific National Quality Assurance Advisory Panel (NQAAP). Not all EQA schemes comply at present.
- 3.7.6 The NQAAP will review the laboratory response to poor performance reports and, if the problem is not resolved, will refer the laboratory to the Joint Working Group on Quality Assurance (JWGQA).
- 3.7.7 The JWGQA directly contacts the laboratory manager and head of department, the hospital's chief executive, CPA/United Kingdom Accreditation Service (UKAS) and the CQC. Where a quality problem is due to poorly functioning equipment or reagents, the NQAAPs or the JWGQA will report problems directly to the Medicines and Healthcare products Regulatory Agency (MHRA).
- 3.7.8 The regulation of persistent poor performance by the JWGQA has been tightened in recent years. King's Mill Hospital cellular pathology ER performance would not have been identified as persistent poor performance under either the old or the new criteria.
- 3.7.9 The major difficulty faced by the current NQAAP/JWGQA system is funding. Currently, all EQA scheme providers are asked annually to pay a sum of money, relative to their size, to finance the NQAAP and JWGQA meetings. This does not compensate employers for the time committee members spend out of their workplace. In the current economic climate, NHS Trusts are increasingly refusing to allow employees to take time out to attend meetings. The ability of the NQAAPs to set performance criteria and monitor poor performers is therefore compromised. Also, the limitation on finance to pay expenses for NQAAP and JWGQA meetings restricts the frequency of meetings and therefore the timeliness of response to poor performance.
- 3.7.10 Laboratory participation in EQA schemes is voluntary. The principal motivating factor to improve quality in a poorly performing laboratory is professional pride. Laboratory clinicians and scientists are embarrassed to receive poor performance letters from the NQAAP/JWGQA because it suggests they have allowed the quality of their clinical service to slide. This motivating factor is only effective in laboratories where the laboratory director and laboratory manager prioritise clinical standards. It will fail if financial considerations alone drive the management of the service.
- 3.7.11 The NQAAP/JWGQA system is based on professional peers who understand the system they are monitoring. However, there is no overarching set of core principles governing EQA schemes. A mechanism that will strengthen the system, while maintaining its links to



professional standards, would therefore be helpful. Patients must be assured that the quality of the service they receive is of an acceptable standard, whether provided by the NHS or by private providers.

- 3.7.12 EQA schemes looking at individual performance and interpretation have grown up out of 'slide clubs' and educational activities. As a result, these do not provide assurance of personal competence in a reliable manner.
- 3.7.13 These schemes also are subdivided into 'specialist' and 'general' in a way that no longer reflects modern histopathology practice. Mono-specialist practice remains relatively rare in histopathology. However, oligo-specialist practice is increasing and generalists are decreasing in number. The investigation team does not consider individual performance and interpretation schemes to be adequately developed to provide assurance of personal performance. Publication of these performance reports would therefore be unhelpful until the schemes are suitably modified.
- 3.7.14. The fundamental function of the breast cancer hormone receptor EQA scheme is to ensure that women requiring treatment for breast cancer get the correct treatment. Therefore the scheme needs to ensure that the entire process, from tissue sample through to report, is giving the correct outcome.
- 3.7.15 The current scheme only covers the first part of the process: producing the slide that needs to be interpreted and scored by a histopathologist. The interpretation and scoring are not assessed in the current scheme.
- 3.7.16 Therefore, the investigation team considers that the UK NEQAS for Immunocytochemistry and In-Situ Hybridisation (ICC and ISH) for ER would be improved if responses from the participating cellular pathology services included interpretation of the distributed slide by the consultant histopathologist, including the recommended (Allred) score. This will require a major change in the scheme, but would focus the scheme on the clinical question.
- 3.7.17 The UK NEQAS for ICC and ISH for ER supplies tissue to participating laboratories that must be analysed and returned for assessment by the scheme organisers. The slide provided by the EQA scheme contains three sections of breast tumours having low, medium and high expression of receptors, and two tissue culture spots having known positive and negative expression. Slides are distributed every three months and always have the same pattern of tissues. For one out four distributions, progesterone receptors are included instead of oestrogen receptors.
- 3.7.18 Basic principles of EQA suggest that the participant in the scheme should treat the EQA sample as if it were a routine clinical sample. Also the person performing the analysis should not generally be able to identify the sample as an EQA sample. The participant should not be able to work out in advance the likely result of the sample being analysed.
- 3.7.19 This EQA scheme routinely sends out a positive, negative and intermediate reacting sample in every distribution. Therefore, the participants can clearly identify that it is an EQA sample because the configuration of tissue on the slide is different from any normal block they would usually process. In addition, the participants know that there will be a positive, negative and intermediate sample on the slide. It is therefore possible for samples to be easily identified and processed with extra care. Furthermore, since the sample always contains the same set of outcomes, the expected appearance can be predicted with certainty.
- 3.7.20 This EQA scheme sends out both oestrogen and progesterone receptor samples. The scoring of the scheme is significantly undermined by this mixture. For example, a laboratory that has a poorly functioning progesterone antibody but a well-functioning

oestrogen receptor antibody will be given a poor performance report every time a progesterone sample is distributed, but will then improve on the next oestrogen distribution. The poorly performing progesterone assay will never be highlighted as persistently poor under the red, amber, green criteria. Effectively, by mixing the hormone receptors in one scheme, the clinical effectiveness of the scheme is diluted.

### **3.8 Evaluation of the relationship with external quality assurance bodies and CPA (UK) Ltd with respect to this Trust**

- 3.8.1 Interviews with NHS BSP regional and national leads, the cancer network breast regional chair, CPA (UK) Ltd regional and national staff and consultant histopathologists revealed a disjointed and overlapping system of data production and peer review visits.
- 3.8.2 Formal and informal communication between the peer review and accrediting bodies was found to be *ad hoc* and inadequate.
- 3.8.3 CPA is in a privileged position to review and assess the statistical reports from a variety of quality-assurance sources with regard to identifying any concerning trends. Depending on the relative timing of visits peer review reports from other quality assurance bodies, such as the cancer screening programmes and cancer networks, may currently be made available to CPA visitors. Analysis can only take place, however, if the reports and statistical data are disclosed to CPA visitors in advance of the visit. Also the value of the examination of these statistical reports is reduced if CPA reports do not provide a record of their contents.
- 3.8.4 It is not clear to the investigation team why the accreditation status of a laboratory service is publicly available, but the CPA report on which the accreditation decision is made is not. In light of the commitment to transparency, the reports that underpin the decision to accredit – or not – are of interest to clinical users, the public and commissioners.
- 3.8.5 The investigation team was concerned about the absence of a duty to disclose CPA findings to the Care Quality Commission, which regulates the healthcare sector. In the case of Sherwood Forest Hospitals NHS Foundation Trust, agreement was quickly gained to disclose all CPA documents and the absence of a memorandum of understanding did not impede this investigation.
- 3.8.6 Currently, not all EQA schemes have accreditation based on ISO (The International Organization for Standardization) standards, such as CPA.
- 3.8.7 CPA requires each pathology service to have a system to review and address EQA performance reports. However, EQA performance reports are not necessarily made available to the CPA visitors and therefore borderline or poor performance may not be identified by the accreditation visit and influence the accreditation decision.
- 3.8.8 The role of the laboratory director/clinical head of service has been the subject of considerable discussion in recent years. In order to ensure a clear line of responsibility for technical and interpretive quality in pathology services, the investigation team considers that this role must be clarified and strengthened.
- 3.8.9 EQA scheme organisers are in a privileged position, collecting information about the performance of technology and reagents. At an early stage they may identify technologies or reagents that are not fit for purpose. EQA scheme organisers and the MHRA need to liaise on a regular basis to ensure a timely, proportionate response.
- 3.8.10 The investigation team understands that, for much of its clinical input, the MHRA is also relying on professional advice from unpaid volunteers.

- 3.8.11 National pathology guidance produced by the NHS BSP is of high quality, widely respected and used for screening and non-screening breast cancer cases by most breast histopathologists. However, responsibility for regional implementation is disjointed and not currently monitored. Transfer of all NHS BSP functions to Public Health England brings these national and regional systems under a single oversight organisation in April 2013. This provides an opportunity to reconsider the operational issues involved in compliance and the lines of accountability.
- 3.8.12 National audit of breast pathology performance against national guidance is required to bring this in line with the surgical audit currently performed as part of the NHS BSP/Association of Breast Surgery (BASO) and the suggestions from the East Midlands NHS BSP team should be given careful consideration.
- 3.8.13 As there is currently no national guidance on the Allred score 'cut off' point to be used to define ER positivity or negativity, variations in the interpretation of borderline scores with respect to positivity have been found between pathology services and between individuals in the same pathology service (Dr Jeremy Thomas personal communication).
- 3.8.14 In the absence of an international consensus and with no UK guidance on a 'cut off' point, the continued collection of NHS BSP data on ER positivity is almost meaningless. The use of this data for quality assurance in the UK is currently impossible.
- 3.8.15 Regional geographic boundaries for CPA, the NHS BSP and cancer networks are not co-aligned and bear no relation to the new National Commissioning Board and Public Health England regional structures. This makes ongoing quality assurance and commissioning difficult to achieve in a meaningful way.

### **3.9 Within these terms of reference, the investigation team is invited to offer general comments where appropriate.**

- 3.9.1 It is a repeated finding of this investigation that quality assurance organisations collect performance, audit and outcome data, but do not provide participants with the results of their data analysis in a way that can inform quality improvement and commissioning. Anonymised data is often presented as part of a one-off workshop or may be published in a learned journal. This may provide interesting and useful CPD opportunities, but participants whose data has contributed to the information should not be expected to pay for a workshop or subscribe to a learned journal for feedback.
- 3.9.2 It is entirely reasonable for participants to expect to receive the analysis of performance, audit and outcome data collection exercises sent electronically to them as feedback. Along with clear laboratory identifiers and confidence intervals this information should enable benchmarking as well as analysis of performance over time. This would also allow challenge and clinical validation of the data submitted.
- 3.9.3 Those involved in regulation and inspection regimes in healthcare would argue that the regulation and inspection they organise has an impact on patient care. It is not appropriate for organisations that have access to information about the performance of healthcare providers to fail to record, prioritise and mitigate clinical risks. Traditionally this was accomplished by the compilation of a risk register. The investigation team considers that organisations collecting performance and outcome data should keep a register of significant clinical risks and the actions taken by the organisation to mitigate these.
- 3.9.4 When a significant clinical risk is identified, there may be wider implications than those immediately apparent and lessons may be learnt which will impact on apparently unrelated areas of clinical practice.

- 3.9.5 The remit of the MHRA in the licensing of laboratory equipment such as histopathology tissue processors should be strengthened in the light of patient-care issues. Use of the Alert system must also become a top priority where appropriate.
- 3.9.6 More than one interviewee pointed out to the investigation team that the end-to-end standards being developed for molecular tests by several different bodies in parallel require urgent coordination.
- 3.9.7 Any provider considering a 'look back' exercise, internal or external review or investigation to identify problems in clinical services should take advice on terms of reference from the Professional Standards Department of the appropriate medical royal college or equivalent.
- 3.9.8 Once a true problem has been established (see 3.9.7 above), any provider considering a duty-of-care review to optimise patient management should take advice on terms of reference from the Professional Standards Department of the appropriate medical royal college or equivalent.

## **4 Recommendations**

### **4.1 User perception of the problem identified and impact on patient care**

- 4.1.1. Clinical teams should be given appropriate time and resources to contact all patients under their care to offer one-to-one discussion of the issue, prior to releasing details to the press.
- 4.1.2. When issuing a press release, healthcare providers should always consider the impact of the press interest on patient wellbeing and the potential for the issues to be sensationalised, increasing distress to patients directly involved and other patients.

### **4.2 Analysis of evidence about the quality of the service at King's Mill Hospital**

- 4.2.1. A patient-safety, risk-management approach to clinical services issues should replace the cost-based approach.
- 4.2.2. The management's criticism of the consultant histopathologists' decision-making and management failure to react appropriately to clinical concerns should be addressed.
- 4.2.3. Wide-ranging external organisational and personal contacts should be established to aid internal clinical decision-making.
- 4.2.4. Releasing laboratory staff outside the Trust for continuing professional development and service development is essential to reduce clinical risk.
- 4.2.5. The relative under-investment in cellular pathology should be addressed.
- 4.2.6. Histopathology seven-day working and an extended working day at King's Mill Hospital should be introduced, to comply with BSP guideline on hormone receptor testing.<sup>20</sup>
- 4.2.7. There should be a full laboratory and mortuary staffing skill-mix review.

### **4.3 Evaluation of the quality of breast pathology reporting at King's Mill Hospital**

- 4.3.1 No recommendations needed for improvement. See section 3.

#### **4.4 Evaluation of the quality of immunohistochemical laboratory processes at King's Mill Hospital**

- 4.4.1 Immunohistochemistry controls should be taken from specimens at initial sampling.
- 4.4.2 Decisions on the immunohistochemistry service should not be based solely on cost. (see 4.2)
- 4.4.3 This Trust should consider whether it can implement state-of-the-art methodology using best practice identified from other laboratories and national publications such as those from UK NEQAS for ICC and ISH.
- 4.4.4 The laboratory at King's Mill Hospital should not perform immunohistochemical analysis until all the recommendations in this report are followed.

#### **4.5 Evaluation of the quality of histopathological evaluation of immunohistochemical investigations, particularly oestrogen receptor testing, at King's Mill Hospital**

- 4.5.1 There should be a minimum number of ER tests on primary breast cancers that should be performed by a laboratory.
- 4.5.2 In the absence of an alternative evidence base, and to enable meaningful quality assurance data analysis and feedback, a minimum number of ER tests per department per annum is recommended. A minimum of 300 screen-detected cases is recommended which may mean 600 breast cases in total if there is a 50/50 split between screening and symptomatic cases (see Appendix 3).
- 4.5.3 Robust statistical monitoring of individual performance would be beneficial for the NHS BSP. This would also require a minimum of 300 cases per histopathologist per year (see Appendix 3). Public Health England, or the equivalent in the devolved administrations, should consider monitoring outcomes through the NHS BSP for histopathology in a manner similar to that used in radiology and surgery. A minimum number of breast cancer screening biopsies to be reported by each individual pathologist involved in the programme should be introduced.

#### **4.6 Evaluation of the quality of internal quality control and clinical governance procedures with respect to this Trust**

- 4.6.1 End-to-end quality control, from sample collection to completed report in cellular pathology, should be introduced. This applies to this Trust and nationally.
- 4.6.2 A formal minuted cellular pathology (including mortuary) clinical governance meeting involving all staff should be introduced, in addition to the directorate governance meetings and informal 'huddles' currently held.
- 4.6.3 The cellular pathology clinical governance meeting should keep a departmental risk register and update this regularly.
- 4.6.4 This risk register should feed into the pathology directorate clinical governance meeting and risk register.
- 4.6.5 Decisions about removal or downgrading of risks should not be made without the explicit agreement of the appropriate laboratory director or lead consultant.

- 4.6.5 Budgetary control should be part of the role and remit of the laboratory director and made explicit in the job description.
- 4.7 Evaluation of the quality of EQA processes and oversight with respect to this Trust**
- 4.7.1 The Royal College of Pathologists' Joint Working Group on Quality Assurance should establish a clear set of core principles for all EQA schemes using lay input.
- 4.7.2 Participation in EQA schemes is not currently a mandatory requirement and this should be addressed by the national review of quality assurance in pathology, commissioned by the Department of Health in December 2012.
- 4.7.3 Professional oversight of performance in EQA scheme is currently provided by the JWGQA and discipline specific NQAAPs. There is no national funding for this service, which relies on unpaid volunteers. This should be addressed by the national review of quality assurance in pathology.
- 4.7.4 EQA scheme specialist advisory groups should have members from other pathology disciplines able to give advice that is independent from the specialty concerned.
- 4.7.5 The current regional geographic boundaries for QA schemes are no longer relevant to the new commissioning arrangements for reconfigured pathology services. The NHS Commissioning Board and Public Health England, and equivalent in devolved administrations, should address this issue.
- 4.7.6 All EQA schemes should be linked directly to a system of ISO-based accreditation.
- 4.7.7 All EQA schemes should be equally performance critical, i.e. there should be no 'easy' schemes. Mechanisms to ensure scheme consistency should be considered by the planned national review of quality assurance in NHS pathology services.
- 4.7.8 EQA scheme providers should be required to apply the core principles defined by the JWGQA (see 4.7.1).
- 4.7.9 Anonymity should be removed for all EQA scheme providers, all schemes and for all participating laboratories.
- 4.7.10 EQA schemes should publish laboratory reports on a public-access section of their websites, with understandable laboratory identifiers.
- 4.7.11 Current practice in some areas, for example in individual reporting in histopathology, does not have end-to-end schemes that provide appropriate confidence. Such schemes need to be developed.
- 4.7.12 The UK NEQAS for ICC and ISH for ER should be expanded to include the interpretative phase. We recommend that after EQA slides have been processed in participant laboratories and prior to their return to the organisers, the slides should be reported individually and separately by all of the histopathologists involved in breast tumour reporting. Reporting should be according to the eight-point Allred scale, as used clinically, and the histopathologist should also indicate whether they consider the sample to be positive or negative (as used clinically to advise the surgeons and oncologists on appropriate treatment).
- 4.7.13 Feedback of laboratory EQA results should be sent to the laboratory director and the quality manager.

- 4.7.14 Failure of a laboratory to engage with the scheme organiser in dealing with poor performance should become a criterion for immediate referral to the EQA oversight body.
- 4.7.15 EQA reports should include benchmarking of the laboratory against its previous performance and against the performance of other participants.
- 4.7.16 The purpose of EQA is to ensure quality of care and that problems are addressed in a timely manner. Principles to decide distribution frequency for each EQA scheme should be considered by the JWGQA.
- 4.7.17 EQA reports should include data aggregated appropriately from different test systems for the same analyte, to allow informed choice of testing system, e.g. choice of antibodies for immunohistochemistry.
- 4.7.18 Each analyte or test in an EQA scheme, e.g. ER and PR should be assessed separately.
- 4.7.19 Test material should be random and the participating laboratory should not know in advance whether the test material they have received is positive or negative.
- 4.7.20 For certain tests, new methods of EQA need to be developed, including control cell line cultures and digital image analysis. This has financial implications that should be considered by the national review of quality assurance in NHS pathology services.
- 4.7.21 To enable accurate data collection and benchmarking of hormone receptor scores and positivity rates, the NHS BSP should enforce and monitor compliance with the guidance<sup>22</sup> that recommends the use of the Allred score. Despite the difficulties obtaining international agreement, the NHS BSP guidance should define a hormone receptor 'cut off' point to be used in the UK. The implication of the clinical definition of 'cut off' points for other areas of practice must be recognised and consideration be given to national guidance.
- 4.7.22 Informal verbal advice on performance from the NHS BSP should be confirmed immediately in a formal letter to the laboratory director and quality manager.
- 4.7.23 Public Health England should extend statistical quality assurance monitoring to symptomatic breast cancer cases, in light of the aim of the NHS BSP to reduce morbidity and mortality from breast cancer.

#### **4.8 Evaluation of the relationship with EQA bodies and CPA with respect to this Trust**

- 4.8.1 Laboratory EQA reports should be reviewed during the laboratory accreditation visit. The accreditation assessment report should include a summary of EQA performance covering the whole laboratory repertoire and the whole time interval between CPA visits.
- 4.8.2. CPA should require the job descriptions for each laboratory director to be made available to CPA peer reviewers in advance of each visit. The laboratory director's job description should include clear responsibility for laboratory service performance against EQA schemes for all analytes and tests in the laboratory repertoire.
- 4.8.3 The Royal College of Pathologists should develop and regularly update a model job description for laboratory directors and publish it on the College website.
- 4.8.4. CPA should require all screening statistical data and peer-review reports for each laboratory service to be made available to CPA peer reviewers in advance of each visit. CPA assessment reports should make reference to both the screening statistical data and peer-review reports.

- 4.8.5. The CPA website should make available to clinical users, the public and commissioners the CPA assessment report and all supporting information provided by provider laboratory services.

#### **4.9 General comments**

- 4.9.1 Organisations collecting performance and outcome data should analyse this and distribute the analysis in an electronic form to healthcare providers, commissioners and all participants, to protect quality of care.
- 4.9.2 Organisations collecting performance and outcome data should keep a register of significant clinical risks and the actions taken to mitigate these.
- 4.9.3 No organisation should collect performance and outcome data from healthcare providers or contributors solely to support the continued existence of the organisation.
- 4.9.4 When a report identifies a significant clinical risk, the wider implications of the findings and its impact in other areas of clinical practice – including those that may seem unrelated – must be considered.
- 4.9.5 The remit of the MHRA in the licensing of laboratory equipment such as histopathology tissue processors should be strengthened in the light of patient-care issues.
- 4.9.6 The end-to-end standards being developed for molecular tests by several different bodies in parallel require urgent coordination.
- 4.9.7 Any provider considering a review or investigation to identify problems in clinical services should take advice on terms of reference from the Professional Standards Department of the appropriate medical royal college or equivalent.
- 4.9.8 Once a problem has been established, any provider considering a duty-of-care review to optimise patient management should take advice on terms of reference from the Professional Standards Department of the appropriate medical royal college or equivalent.

## **5 Acknowledgments**

The investigation team would like to acknowledge the openness and collaboration shown by all staff members who were involved in the investigation and recognise that this was a stressful process for all concerned. We thank all those who gave up their time, often at short notice, to meet with the investigation team.

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## 7 Appendices

### 7.1 Investigation team details



**Dr Rachael Liebmann**  
**Consultant Histopathologist**  
**Registrar, The Royal College of Pathologists**

Rachael Liebmann is Registrar of the Royal College of Pathologists, Clinical Director of the Kent and Medway Pathology Network and a specialist breast pathologist.

Having chaired the multidisciplinary Kent and Medway Cancer Network Breast Group for several years, Rachael was appointed Clinical Director of the Kent and Medway Pathology Network, with leadership of all pathology services for a population of 1.7 million. Through this, she became the clinical lead for a major regional service reconfiguration project and successful business case development for an £8 million project for a centralised department. Previously awarded Fellowship of the British Association of Medical Managers, she is now a member of the Founding Council of the Faculty of Medical Leadership and Management.

Having been an elected member of the College Regional Council, National Recruitment Lead in Histopathology and South East Regional National Pathology Week Co-ordinator, Rachael was elected to the position of College Assistant Registrar in 2009 and then Registrar in 2011. Interested in commissioning quality, regional pathology reconfiguration and clinical leadership, she provides the link between the College and the Department of Health on the financial challenges facing the NHS; co-ordination of production of key performance indicators for pathology to guide commissioning, and makes specific suggestions to improve pathology quality assurance and accreditation.

Rachael helped to establish RCPATH Consulting in 2011, which provides independent and authoritative advice on pathology service and commissioning issues nationally, and she is the independent secondary care member of a CCG (Clinical Commissioning Group) Board.



**Professor Tim Reynolds**  
**Consultant Chemical Pathologist**

After training at Leeds Medical School, Tim Reynolds trained in Birmingham and South Wales. Tim is currently Consultant Chemical Pathologist at Queen's Hospital Burton-on-Trent, and Director of Down's Screening for the Sheffield sub-Regional scheme based at the Department of Immunology, Northern General Hospital, Sheffield. He has a wide range of research interests and his primary topic has been risk screening, investigating many aspects of the quality of risks including Down's screening risks, and cardiovascular disease risk.

#### **Relevant appointments**

Chairman of Joint Working Group on Quality Assurance from June 2011

Deputy Chairman, JWQA, October 2008 to May 2011

Chairman, Clinical Chemistry NQAAP, January 2005 to December 2008

Member, Clinical Chemistry NQAAP, June 2002 to December 2004

UK NEQAS, Clinical Chemistry SAC, August 1995 to December 2004

UK NEQAS, Immunoassay SAC, July 2002 to December 2008

UK NEQAS Steering Committee January 2005 to December 2008

WEQAS, Clinical Chemistry SAC, July 2002 to August 2005

The Royal College of Pathologists SAC on Clinical Biochemistry, June 2002 to June 2005

The Royal College of Pathologists Academic Activities Committee, January 2003 to June 2005.



**Paul Williams**  
**Head Biomedical Scientist**  
**East Kent University Hospitals NHS Foundation Trust**

Paul originally trained as a medical laboratory technician in histology in Plymouth, Devon. He moved to East Kent as a senior biomedical scientist (BMS) in 1981 and developed reporting skills in gynae and non-gynae cytology. Paul established the immunohistochemistry section for the department, was promoted to Chief BMS and subsequently to his current position of Head BMS.

#### **Professional activities**

Member of the East Kent Hospitals Organ Retention team, investigating the Trust for all tissue holdings across East Kent.

Regional facilitator for gynae cytology technical EQA, 2005–2009.

Visiting lecturer at the University of Kent for the cellular pathology module of the BSc (Hons).

Biomedical science degree years two and three, 2005–2011.

Established the use of video conferencing technology for multidisciplinary team meetings for East Kent Hospitals, 2000.

National Business Innovations award for the application of digital voice recording and speech recognition technology in cellular pathology, 2010.

Active member of The Kent and Medway Pathology Network Cellular Pathology sub group.

Currently leading a LEAN management programme in histopathology and piloting specimen tracking in East Kent.



**Ms Stella Macaskill**  
**Head of Professional Standards**  
**The Royal College of Pathologists**

Stella has been the Head of Professional Standards at The Royal College of Pathologists since 2005. She is responsible for:

- professional performance work, including the delivery of College individual and service reviews
- the provision of pathology advice in respect of revalidation
- clinical effectiveness including clinical audit
- continuing professional development.

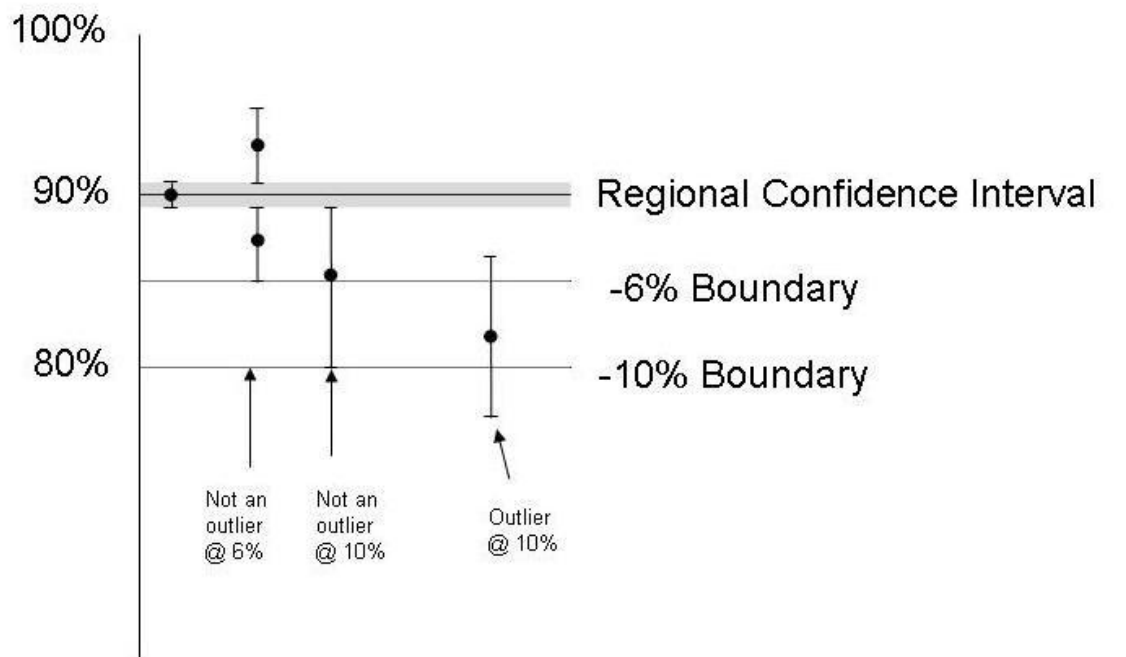
## 7.2 List of interviews conducted by review team (in chronological order)

Dr Samreen Ahmed	Chair of East Midlands Breast Committee, Regional Cancer Network (telephone)
Dr Melanie Griffiths	Clinical Director, King's Mill Hospital
Elaine Torr	Divisional Director, King's Mill Hospital
Clair Sloney	Histopathology Manager, King's Mill Hospital
Annette Davis Green	Pathology Service Manager, King's Mill Hospital
Susan Bowler	Director of Nursing and Quality, King's Mill Hospital
Carolyn White	Deputy Chief Executive, King's Mill Hospital
Mr Eric Morton	Interim Chief Executive, King's Mill Hospital
Dr Rahul Deb and Mrs Jacquie Jenkins	Regional Pathology QA Co-ordinator, BSP Deputy Regional QA for BSP (telephone)
Dr Shafiq Gill	Clinical Head of Service, Consultant Histopathologist
Dr Nabeel Ali	Medical Director, King's Mill Hospital
Dr Najamul Azad	Consultant Histopathologist
Dr Khorrum Abdulla	Consultant Histopathologist
Dr Samiya Ibrahim	Consultant Histopathologist
Mr Keith Miller	Director, UK NEQAS
Mrs R Boyer Blanchard and Dr Jane Beaumont	Regional Assessor CPA UK Ltd Director of Accreditation, UKAS
Mr M Jahan, Dr S Khan, G Clark, L Salmon, S Smith	King's Mill Hospital MDT – breast (non-pathology staff)
Professor Ian Ellis	Professor of Cancer Pathology, Nottingham University Hospitals (telephone)
Professor Julietta Patnick	Director NHS BSP (telephone)
Mr Neil Rothnie	Chair of NHS BSP and ABS audit group (telephone)

### 7.3 Calculation of minimum service size for effective monitoring

It is clear that very significant changes in the interpretation of the data can be caused by a very small change in the number of cases per year. Currently, the confidence interval (CI) for one year's data (2010–2011) for the East Midlands region is approximately  $\pm 1.8\%$ . The upper to lower CI range for all of the sub-regions for that data period extends from 70.95% to 100.4% due to small sample workloads of the various units. None of these results could be proven to be statistically different from the regional mean because the low workload results in extremely wide limits.

To allow better monitoring, it is therefore appropriate to choose a maximum CI boundary within which monitoring should be carried out. If it is assumed that the regional data boundary of  $\pm 1.8\%$  is a reasonable regional target, the question then becomes: 'What is a reasonable maximum confidence interval for sub-regional areas, such that outliers can be properly identified, without the target becoming unrealistically wide?'. This is important because when an acceptable bound is identified, the limits can be used to derive the minimum number of samples that need to be analysed by any individual laboratory. The figure shows the way that boundaries can be selected that would allow significant outliers to be identified.



Therefore, assuming a range of possible boundaries about a central 90% ER +ve rate, possible acceptable ranges for CIs that would allow a reasonable detection of low outliers are shown in Table 1. Only targets for low outliers are shown because the maximum possible receptor positivity rate is 100%, so calculating outliers above that limit is invalid.

**Table 1**

	<b>Low 95% CI</b>	<b>Mid band</b>	<b>Upper CI</b>	<b>CI allowed</b>
<b>Regional target = 90%</b>	88.20%	90.00%	91.80%	±1.8%
<b>Boundary target</b>				
<b>±5% band</b>	85.00%	86.60%	88.20%	±1.6%
<b>±6% band</b>	84.00%	86.10%	88.20%	±2.1%
<b>±7% band</b>	83.00%	85.60%	88.20%	±2.6%
<b>±7.5% band</b>	82.50%	85.35%	88.20%	±2.85%
<b>±8% band</b>	82.00%	85.10%	88.20%	±3.1%
<b>±9% band</b>	81.00%	84.60%	88.20%	±3.6%
<b>±10% band</b>	80.00%	84.10%	88.20%	±4.1%

To calculate band targets, the upper CI limit for any boundary will be 88.20% because this is the lower boundary of the regional confidence interval. Thus, with a 90% target and ±1.8% CI range for the regional summary data, it is clear that for a 90% ±5% band, the acceptable sub-regional maximum confidence interval would be less than the total regional band(±1.6% ), which would mean that a sub-region would need higher numbers than the entire region; and therefore a 5% band cannot be achievable. Considering ±6%, ±7.5%, and ±10% bands as acceptable options, the number of cases per year to allow a sub-regional unit to achieve relevant 86.10 ± 2.1%, 85.35 ± 2.85% or 84.1 ± 4.1% confidence intervals, the minimum number of cases can be estimated.

Since:

$CI = 1.96 * \text{SQRT}((p*(1-p))/N)$ , and given that p, and CI are known, this can be solved for N.

$$N = ((p*(1-p)) / ((CI/1.96)^2));$$

Therefore:

6% band: For 86.1 ± 2.1%; **N = 1043**

7.5% band: For 85.35 ± 2.85%; **N = 591**

10% band: For 84.1 ± 4.1%; **N = 306**

Thus, for the wider ±10% band, the minimum number of cases to achieve the target is approximately 300. If the narrower ± 7.5% band is required, the minimum number of cases would be approximately 600 per annum. If the narrowest practical limit for a band width of ± 6% is chosen, the minimum annual caseload per laboratory is approximately 1000.

This allows a simple method of calculating how many cases should be evaluated in any group. Logically, the number of potential sub-groups in a process should be evaluated. So, for example, for breast cancer ER testing, there could be two sub-groups: screening-derived cases and symptomatic cases. The laboratory workload for analysis therefore should be a minimum of 300 screening and 300 symptomatic cases. However, since there will never be an identical number of each type of case, the laboratory workload should be such that the smallest group size is 300. Another potentially useful analysis of sub-groups could be to review positivity rate by consultant. Thus, the minimum ER reporting numbers per consultant should be 300, assuming a 10% band is acceptable, or more if narrower bands are required.

## **7.4 Technical appraisal**

### **Sherwood Forest NHS Foundation Trust, King's Mill Hospital**

#### **Cellular Pathology Technical Appraisal**

**Conducted 3–6 December 2013**

The Cellular Pathology laboratory at King's Mill Hospital is housed within a separate building to the rest of pathology. While purpose built, this is now showing signs of ageing (estimated to be 30–40 years old). Space is sufficient for the current service provision, with the exception of storage facilities.

The unit is secured by 'fob' access and only authorised individuals are permitted access, with a sign-in procedure for visitors. Disposable white coats are provided for visitors. The laboratory has been registered for training biomedical scientists since 2008 and fully CPA accredited since June 2012.

#### **Specimen reception**

The Laboratory Information Management System (LIMS) is Webpath. Specimens are all assigned with barcoded labels. Urgent requests are identified with assigned pink dots on the request form.

#### **Specimen cut-up**

There is a single ventilated cut-up station adequate for the current workload of between 80 and 90 specimens per day. Cut-up sessions are timetabled around pathologists' availability. There is a BMS (Band 5 and 6) transfer cut up and the laboratory manager will cut up more complex specimens such as uterus, gall bladder, appendix and skin.

The cut-up is 'hands-free', employing Winscribe digital dictation. Unique identifiers used include name, specimen number and hospital number.

A cassette printer is normally in use, but was missing for repair during the course of this inspection.

The routine fixative is buffered 10% formalin, supplied by Genta Medical but pH not checked.

Breast control material was being derived from specimen discard cases in the past (six weeks post authorisation).

Slicing of mastectomy specimens to improve fixation was introduced by Dr S Gill in 2007.

#### **Tissue processing**

Enclosed fully automated tissue processing comprised of two Shandon Pathcentres for all tissues. These provide either a four-hour or routine 15.5-hour schedule. The Pathcentres operate a reagent management system, which through set threshold values for all reagents, ensure solutions and waxes are replenished at appropriate intervals. The tissue processors will not process if reagents require changing unless a manual override is applied. (This would only happen in rare situations such as late arrival of a very urgent sample.) All reagents are changed according to the reagent management system by support grade staff, who carry out the housekeeping and day-to-day maintenance. All programmes are PIN protected with full access accorded to super users only.

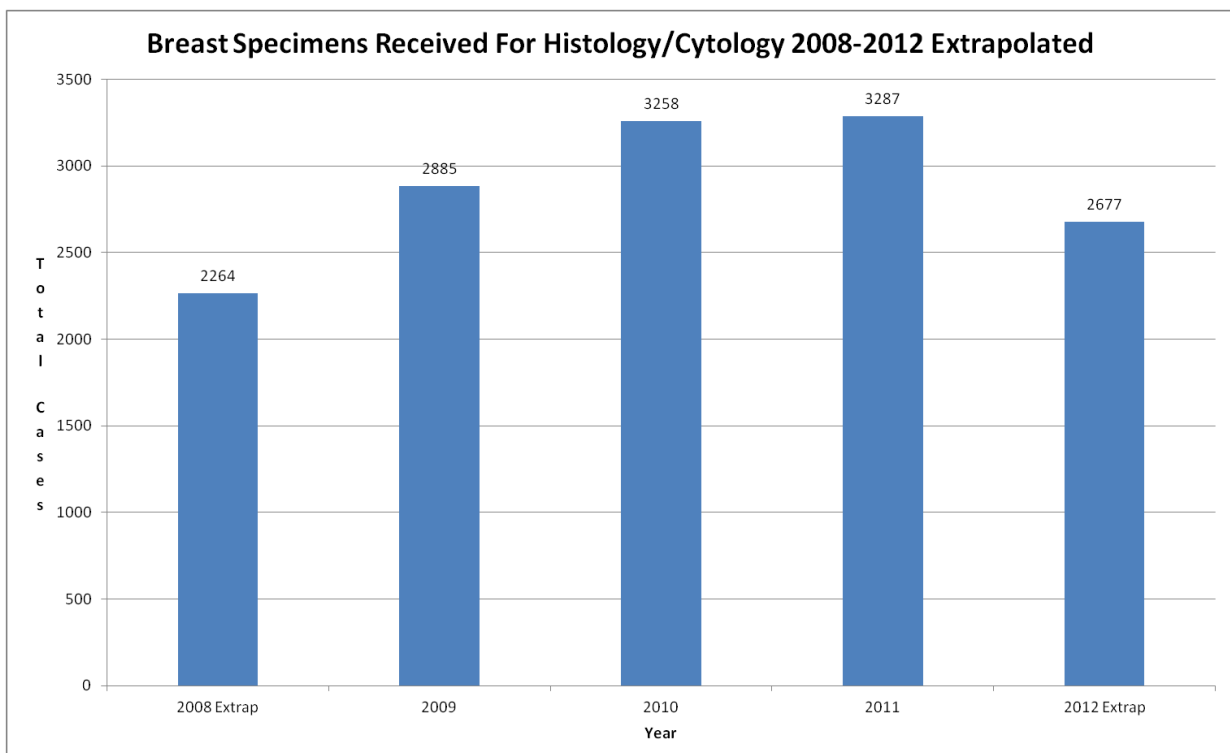
The routine overnight schedule of 15.5 hours has an on-board 10% formalin fixation step of five minutes, unless at the weekend where a delay of 48 hours in the formalin step would be employed.

Urgent biopsies (fixed tissue only) have a processing time of four hours 39 minutes, that includes a first station of 10% formalin for five minutes. The formalin is supplied as a concentrated buffered solution that is diluted prior to use. The diluted buffered formalin pH is not checked. All batch numbers of all reagents are logged.

Breast pathologist lead is Dr S Gill. Breast biopsy cut-up is by biomedical scientists (BMS). 75% of specimens are cut up by BMS.

The number of breast specimens received over the last five years is demonstrated in Figure 1. Table 1 illustrates the range of breast specimens for cellular pathology, including histology and cytology. *Please note data provided for 2008 and 2012 were incomplete therefore extrapolated for comparison.*

**Figure 1 Breast specimens received between 2008 and 2012**





**Table 1 Distribution of breast sample types for histopathological/cytological examination**

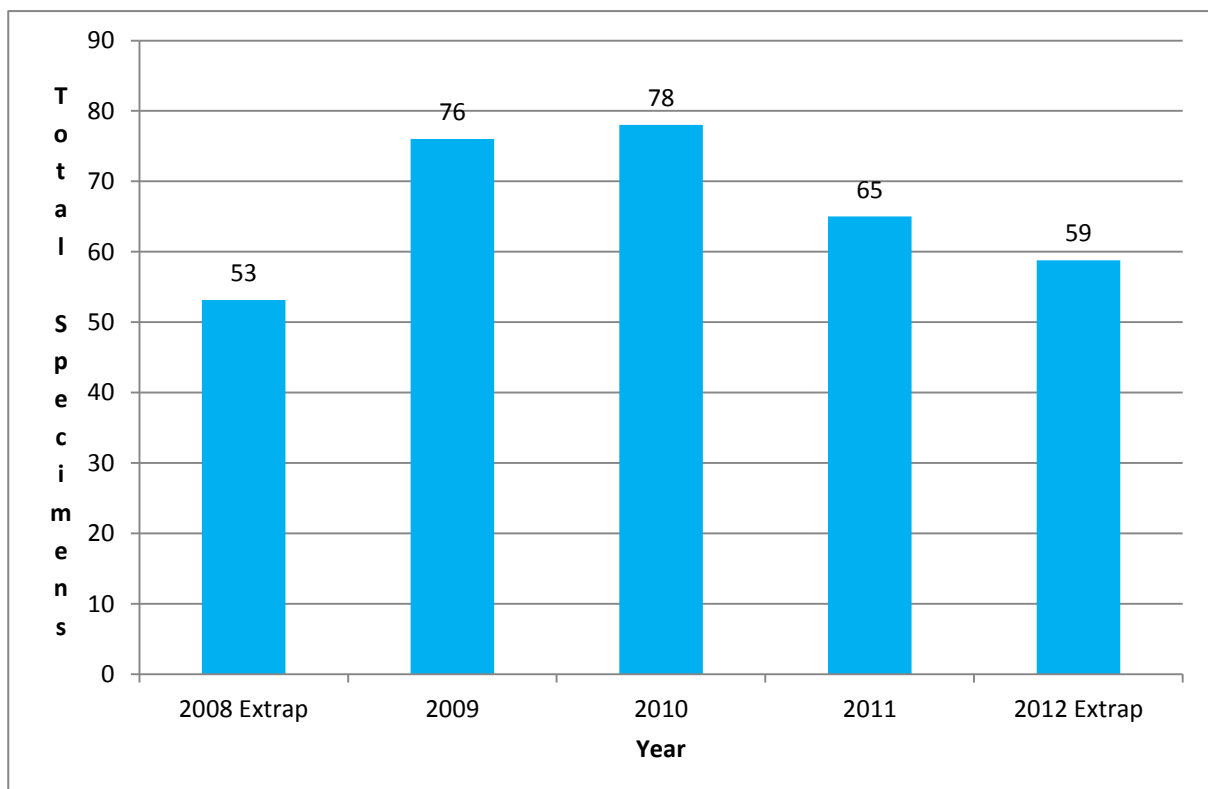
Specimen/qualifier	Year				
	2008 Extrap	2009	2010	2011	2012 Extrap
Axilla biopsy	10	14	31	29	46
Axillary lymph node sample	118	147	146	162	172
Breast	15	2	4	2	0
Breast mastectomy	129	132	142	126	112
Breast NC biopsy: urgent/x-ray	2				0
Breast needle core biopsy	960	827	1082	682	624
Breast open biopsy	0		1	1	1
Breast reduction	15	20	17	9	6
Breast re-excision	14	23	11	28	23
Breast tissue	79	99	153	161	187
Breast wide local excision	34	73	86	96	112
Lymph node clearance axilla	9	10	16	16	12
Breast – therapeutic marker	21	16	5	6	7.2
Breast diagnostic marker	46	14	22	14	19.2
Breast HER2 status	0			181	253
Breast hormone receptor	0		129	267	259
Breast FNA	29	31	40	31	46.8
<b>GRAND TOTAL</b>	<b>1481</b>	<b>1408</b>	<b>1885</b>	<b>1811</b>	<b>1879</b>

**Figure 2 Breast histology workload for 2008–2012**

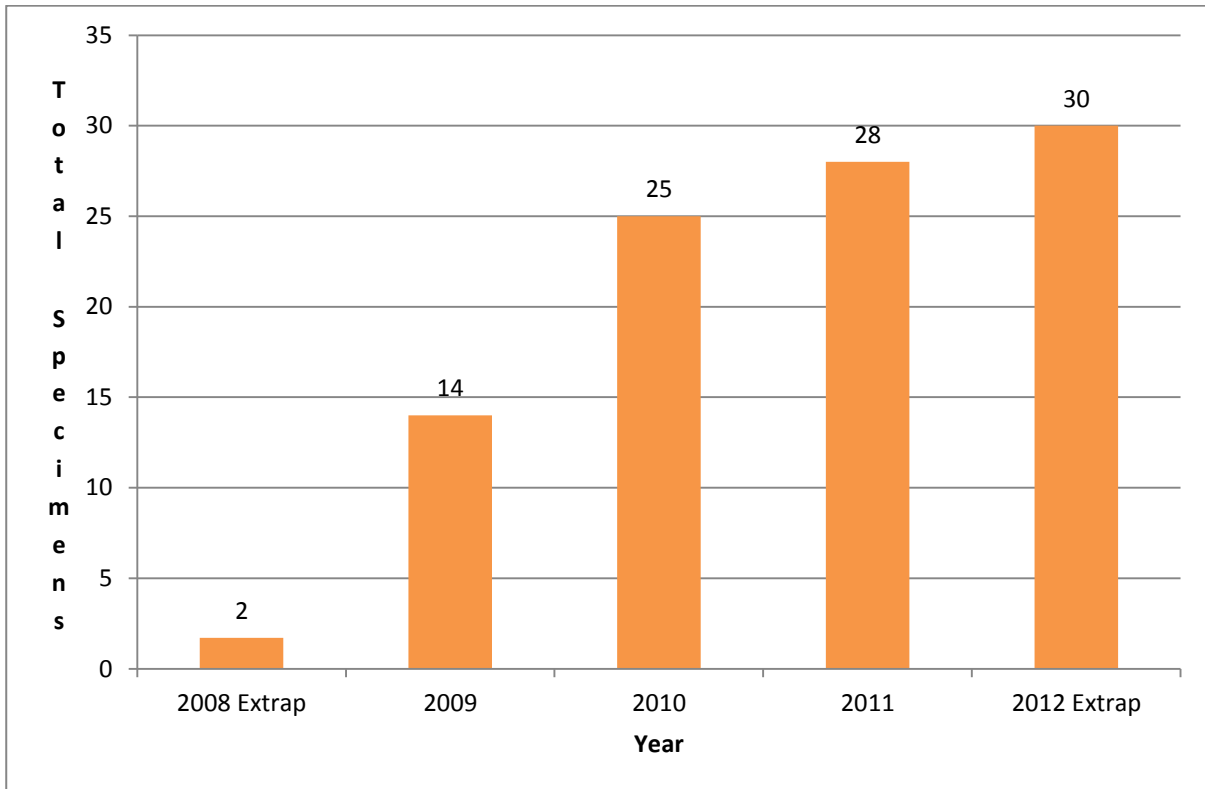


The diversity of samples received for histopathological assessment is typical of a small district general hospital, see Figures 3–15, including bone, breast, gynae, endocrine, head and neck, lower GI, lymphoreticular, miscellaneous (includes soft tissue), post mortem, skin, upper GI and urology.

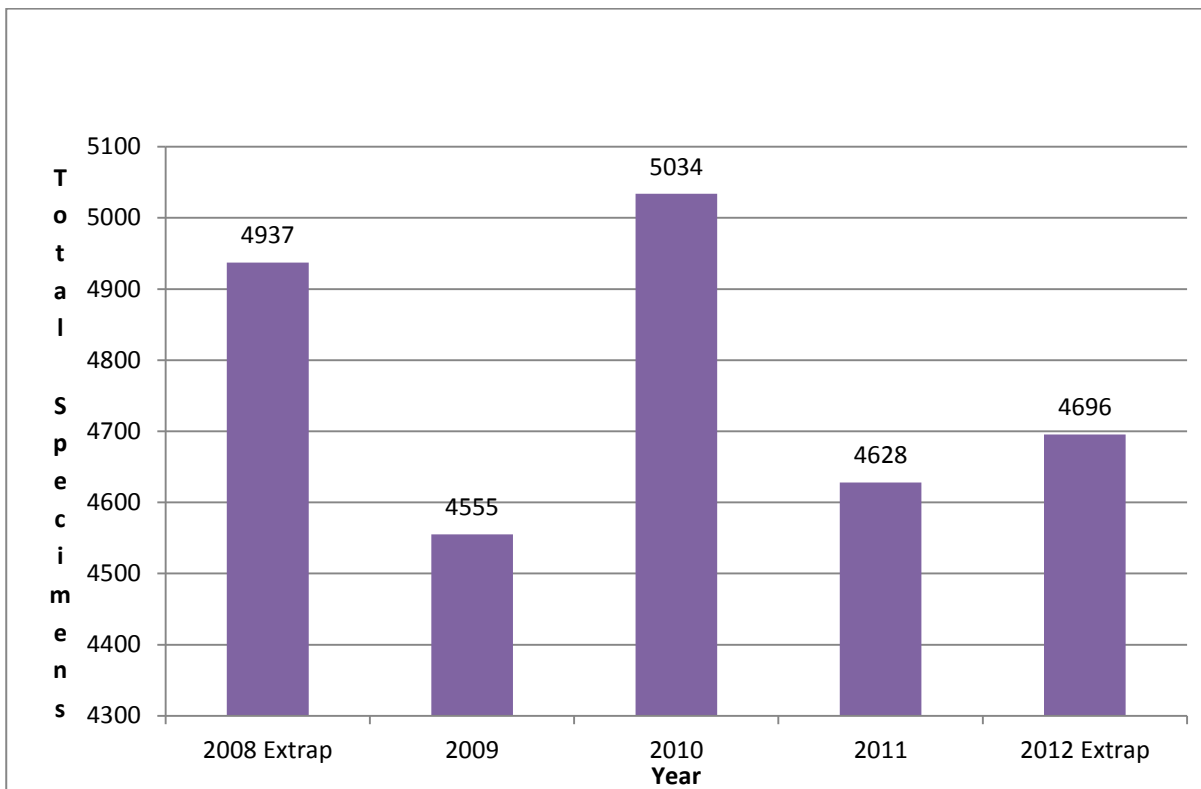
**Figure 3 Bone histopathology workload for 2008–2012**



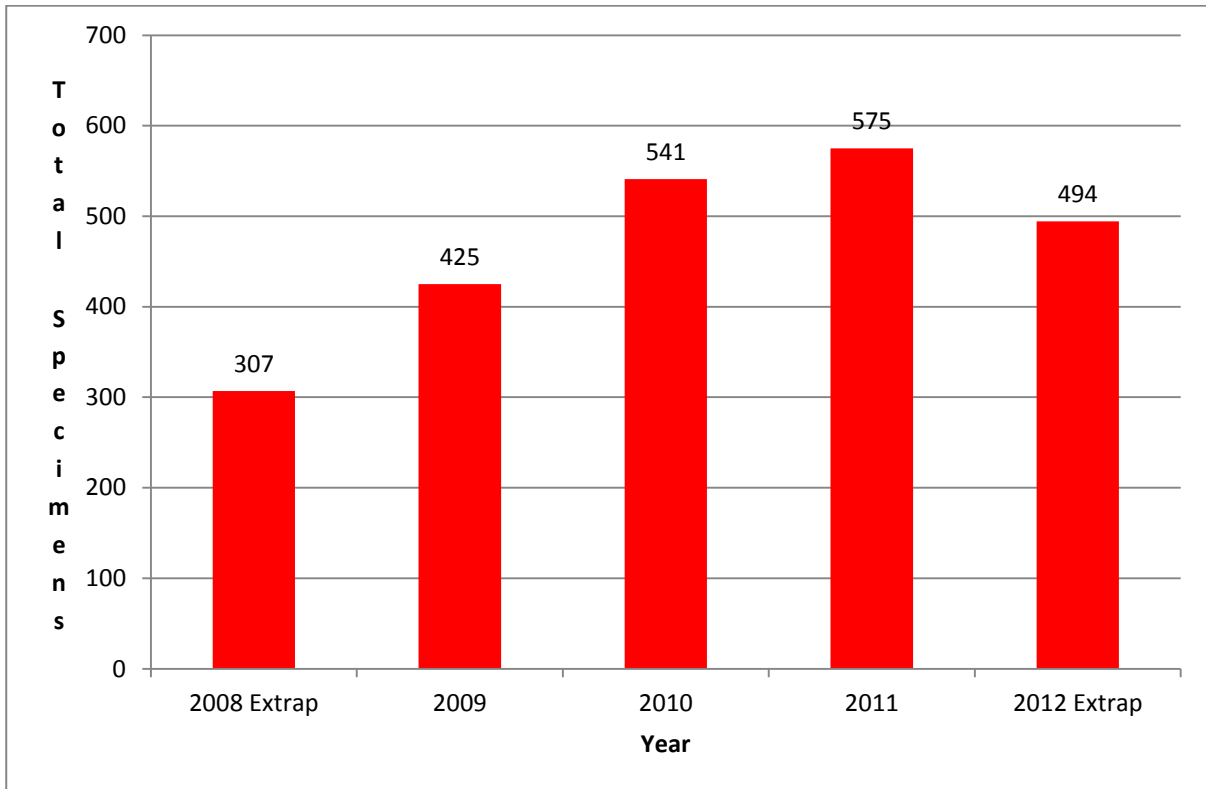
**Figure 4 Endocrine histopathology workload for 2008–2012**



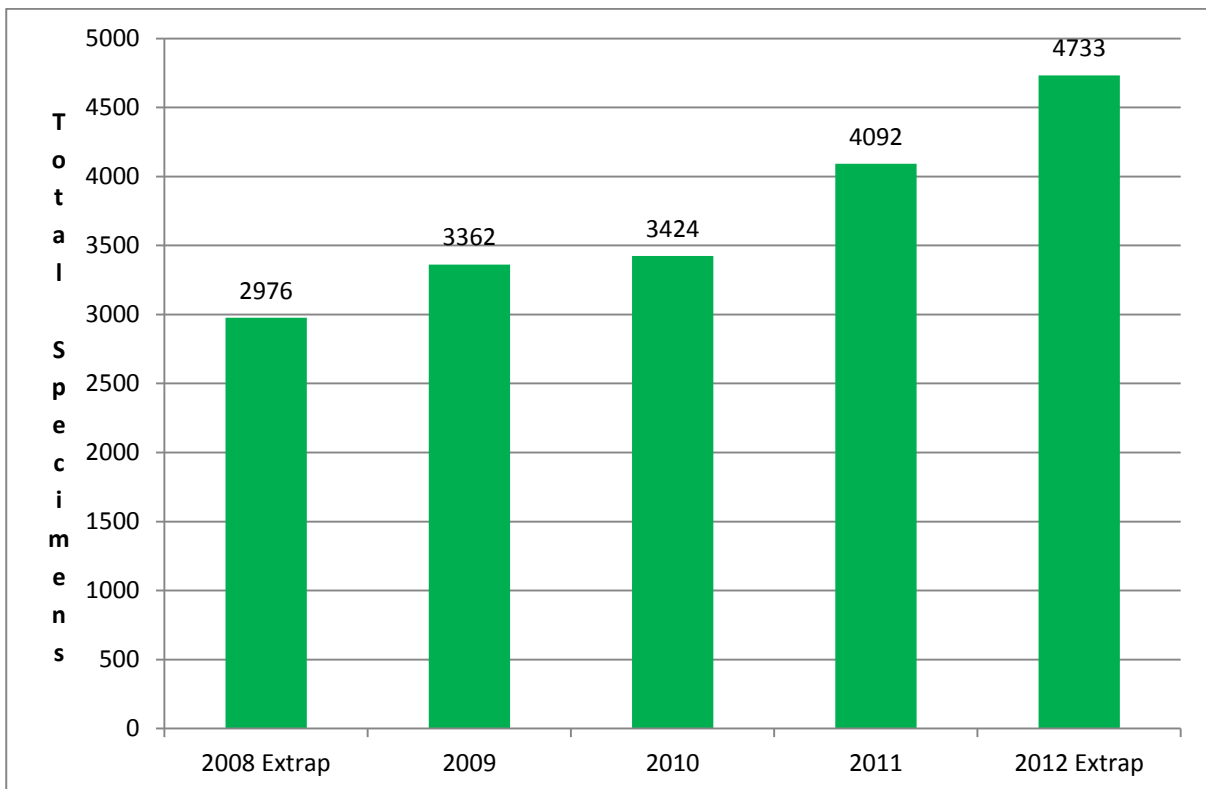
**Figure 5 Gynae histopathology workload for 2008–2012**



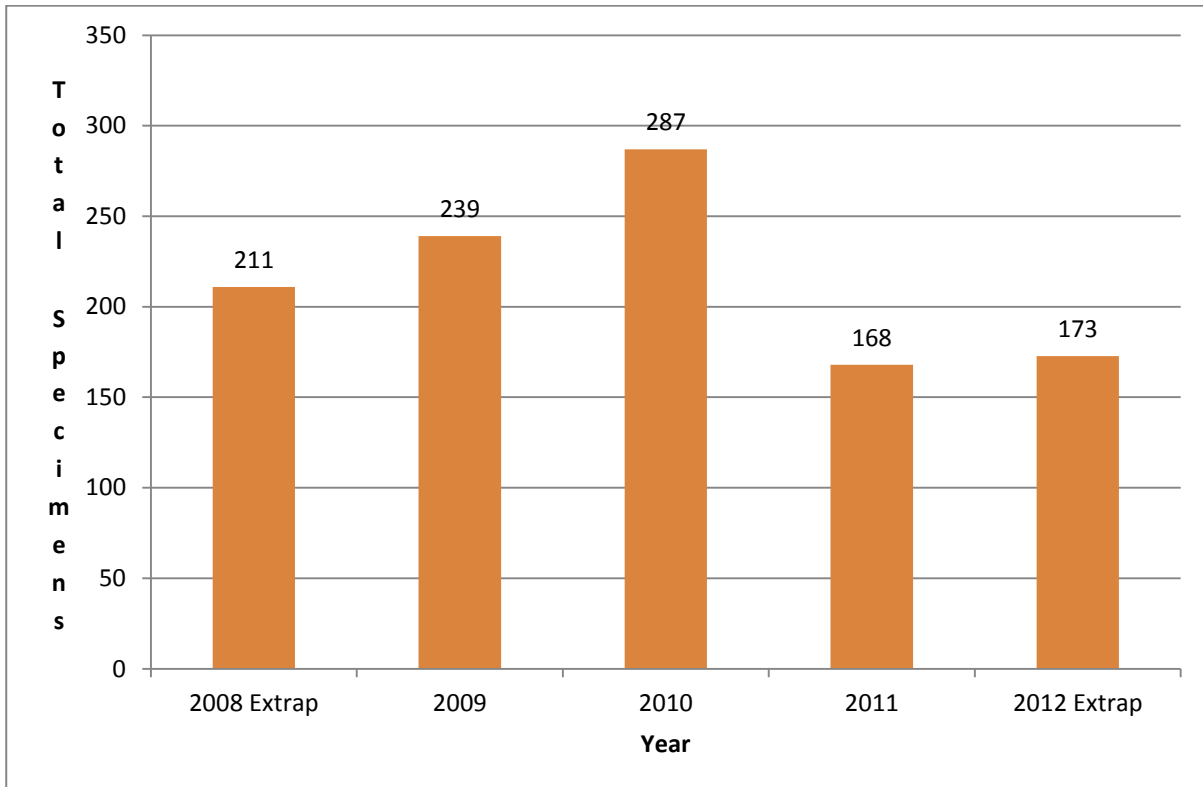
**Figure 6 Head and neck histopathology workload for 2008–2012**



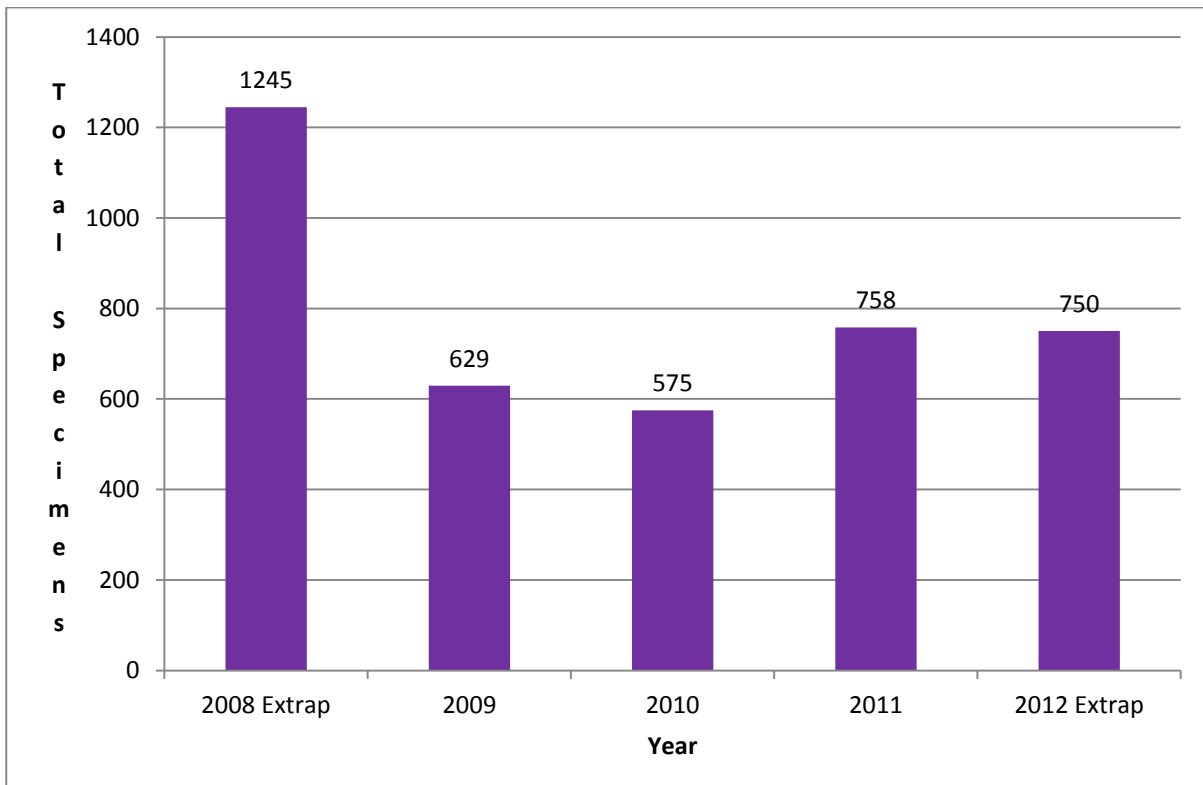
**Figure 7 Lower GI histopathology workload 2008–2012**



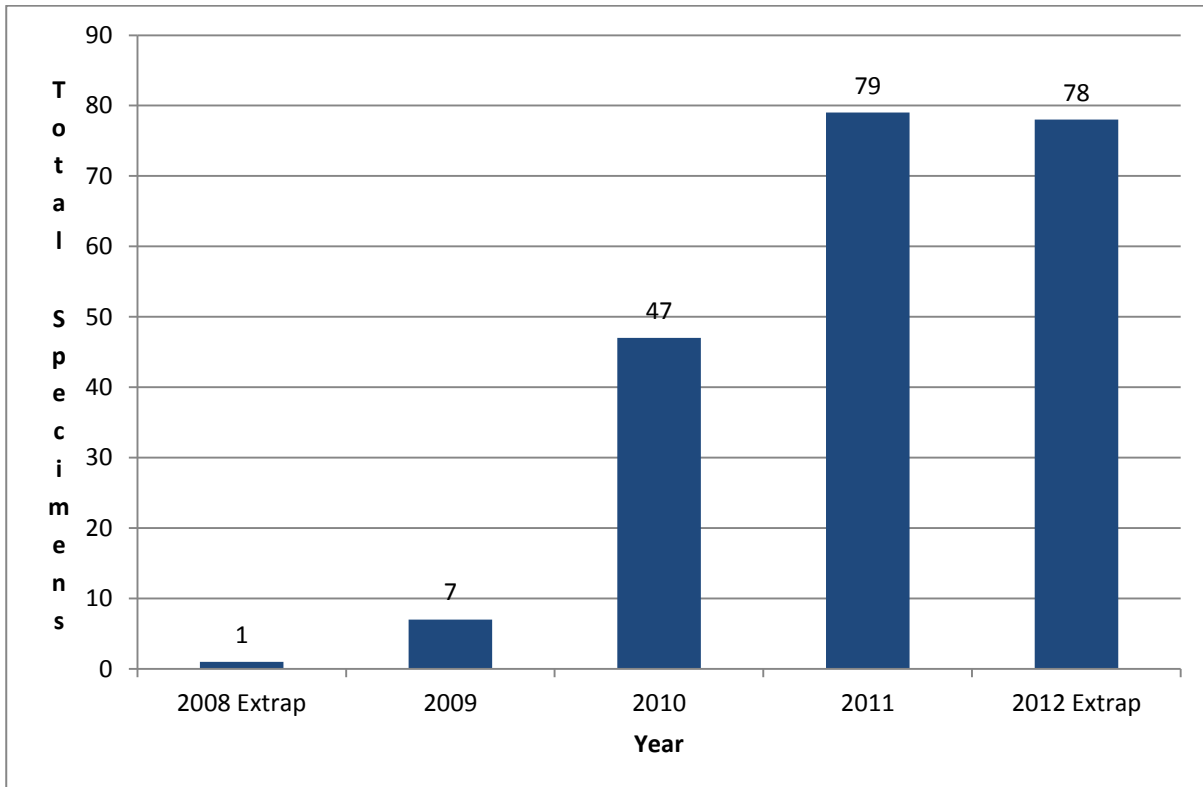
**Figure 8 Lymphoreticular histopathology workload for 2008–2012**



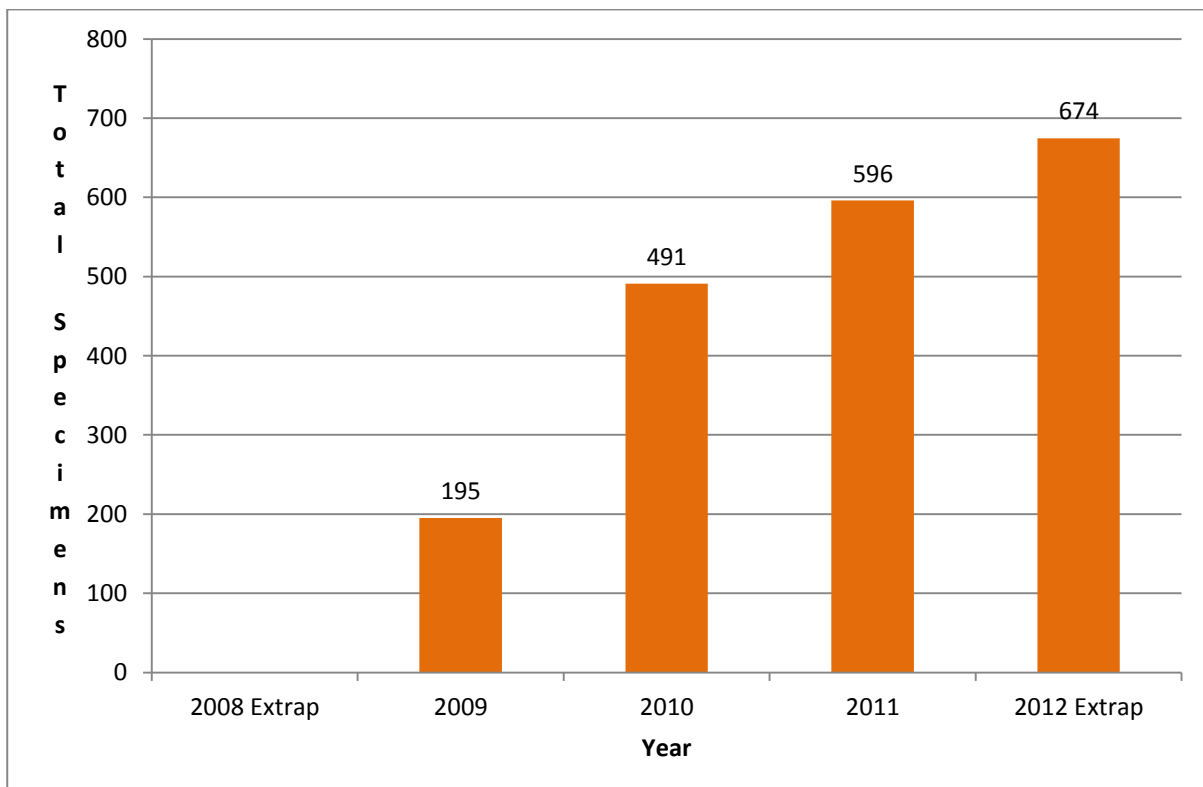
**Figure 9 Miscellaneous tissue workload that includes soft tissues for 2008–2012**



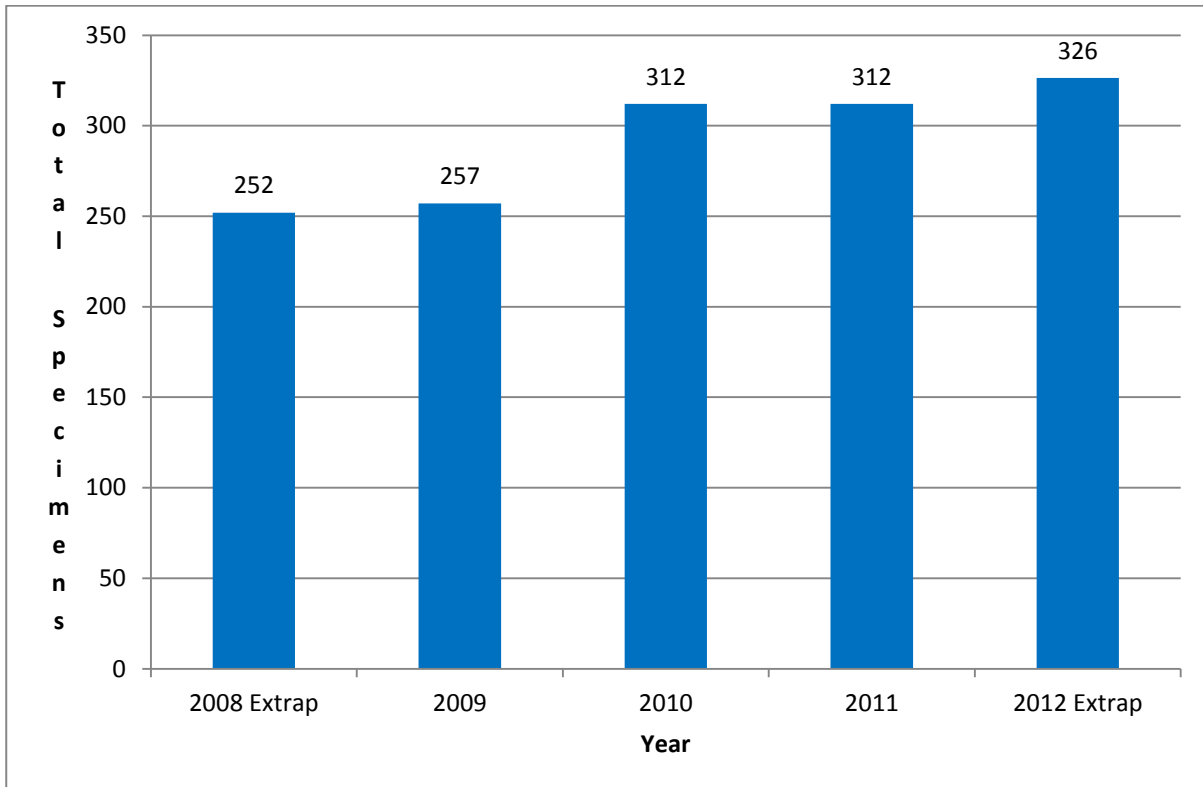
**Figure 10 Neuropathology workload for 2008–2012**



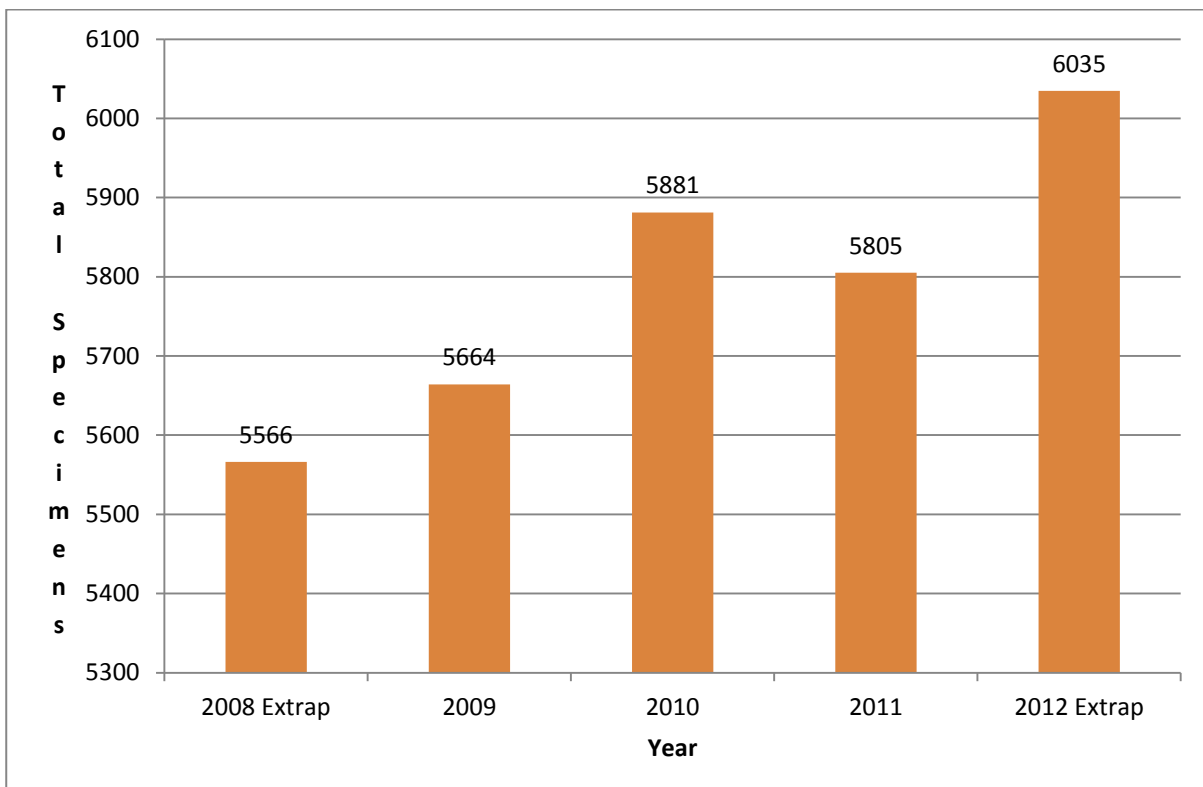
**Figure 11 Post-mortem histopathology workload for 2008–2012**



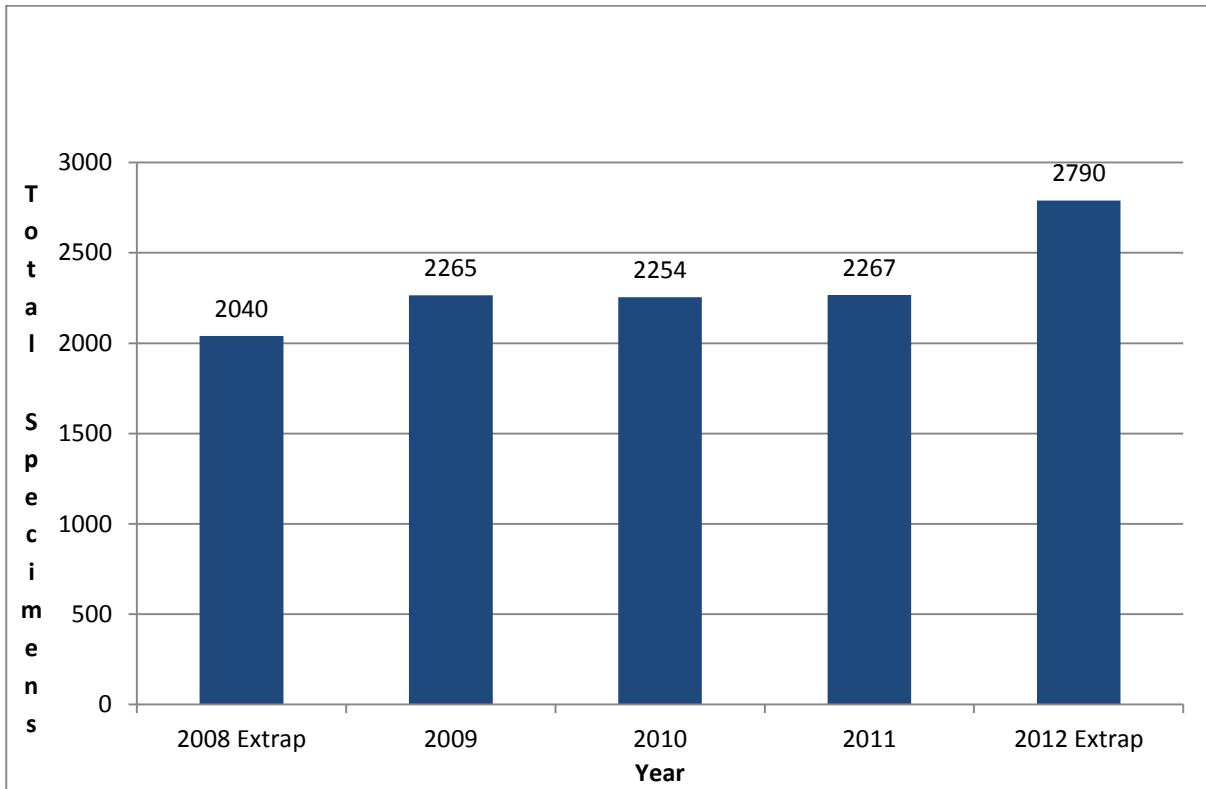
**Figure 12 Respiratory histopathology workload for 2008–2012**



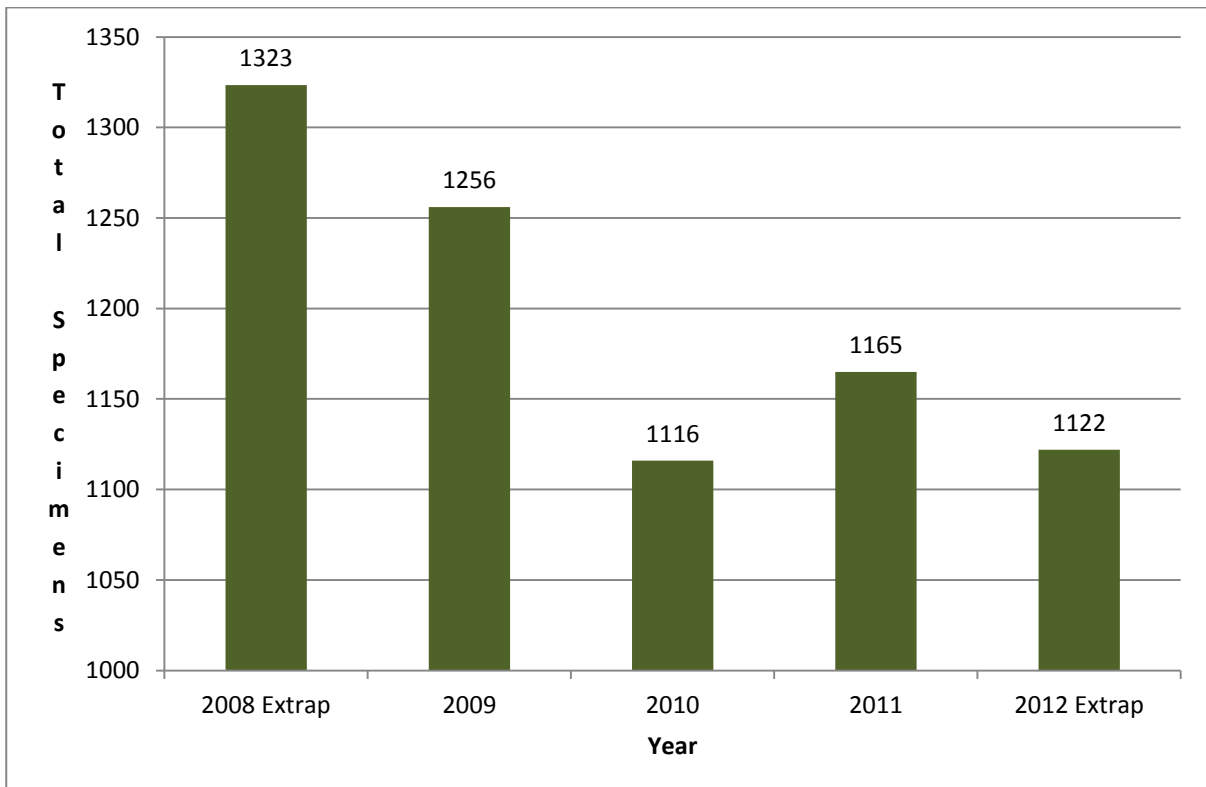
**Figure 13 Skin histopathology workload 2008–2012**



**Figure 14 Upper gastrointestinal (GI) workload 2008–2012**

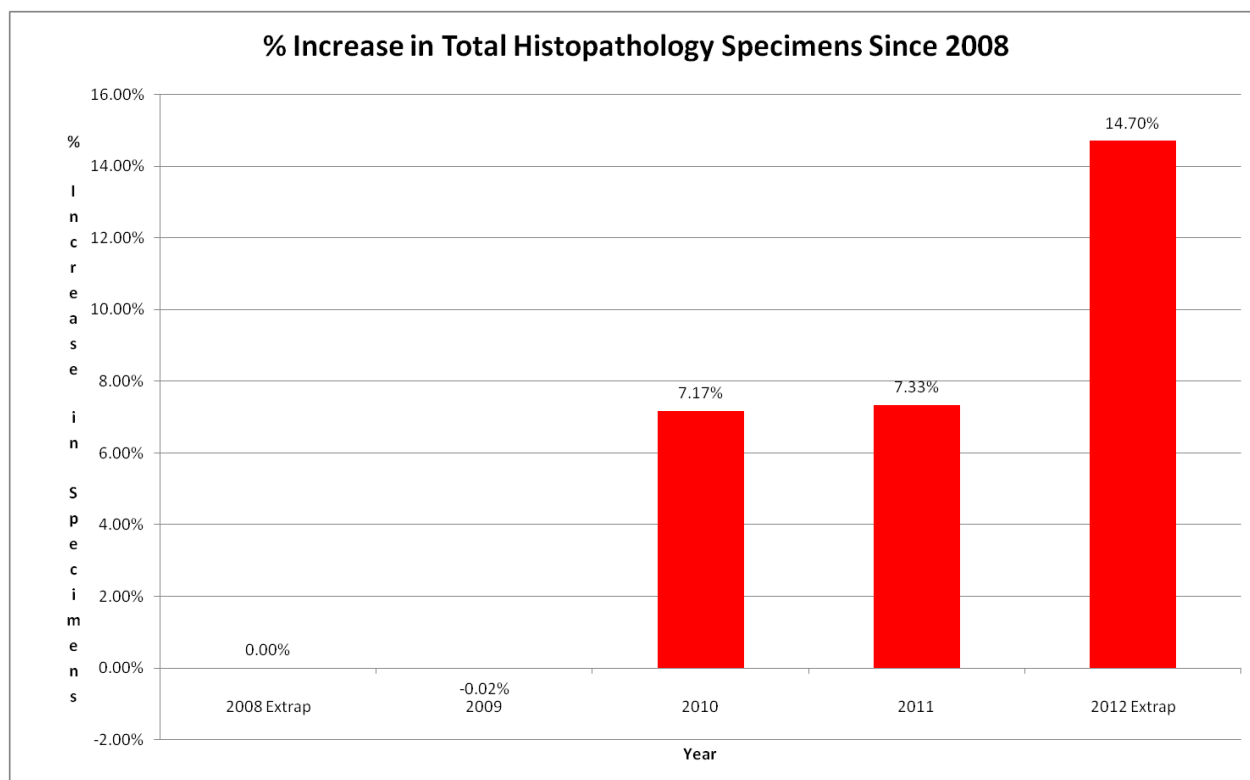


**Figure 15 Urology histopathology workload 2008–2012**





**Figure 16 Percentage increase in histopathology specimens since 2008**



There has been a 14.70% increase in histopathology specimens since 2008.

All specimens have a minimum of 24 hours fixation prior to processing. There is a problem with a delay in the prompt receipt of some specimens due to portering issues. At the end of each day the tissue processor is loaded at 4.30pm and processing ends at 8am. Routine embedding then starts at 8am the next day.

Fatty breast resections require extended processing of 23.5 hours after fixation.

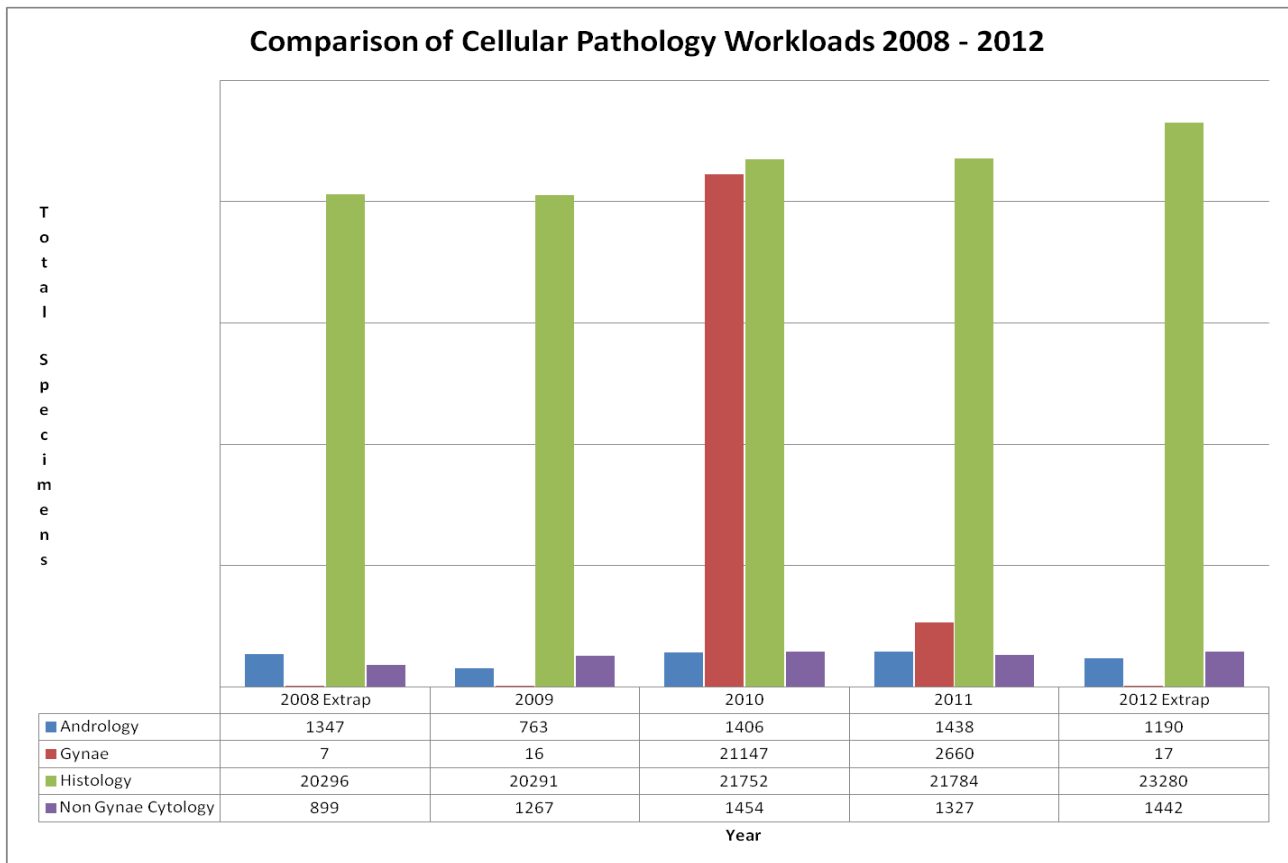
Each Pathcentre has a 250 block capacity. All tissues from cut-up in their cassettes are randomly placed in the processing basket to ensure good fluid exchange during processing. The tissue processor will apply both +ve and -ve pressure during each step of the processing cycle. Both of these tissue processors are 14 years old.

The department is currently validating the Trio (Medite) tissue processor that has the same capacity of 250 as the Pathcentre but no facility for positive or negative pressure. The 10% formalin is at an operating temperature of 30°C. Alcohol steps 40°C, Xylene 45°C, Wax 60°C. Routine processing is for 13 hours. All reagents are changed every five cycles. The Medite is capable of running three programmes simultaneously. The Medite is currently being validated to take all tissues.

All breast work has been processed on this machine and all other routine specimens since August 2012. All tissue processed on the Medite processor has produced better nuclear detail compared to the aging Pathcentre.

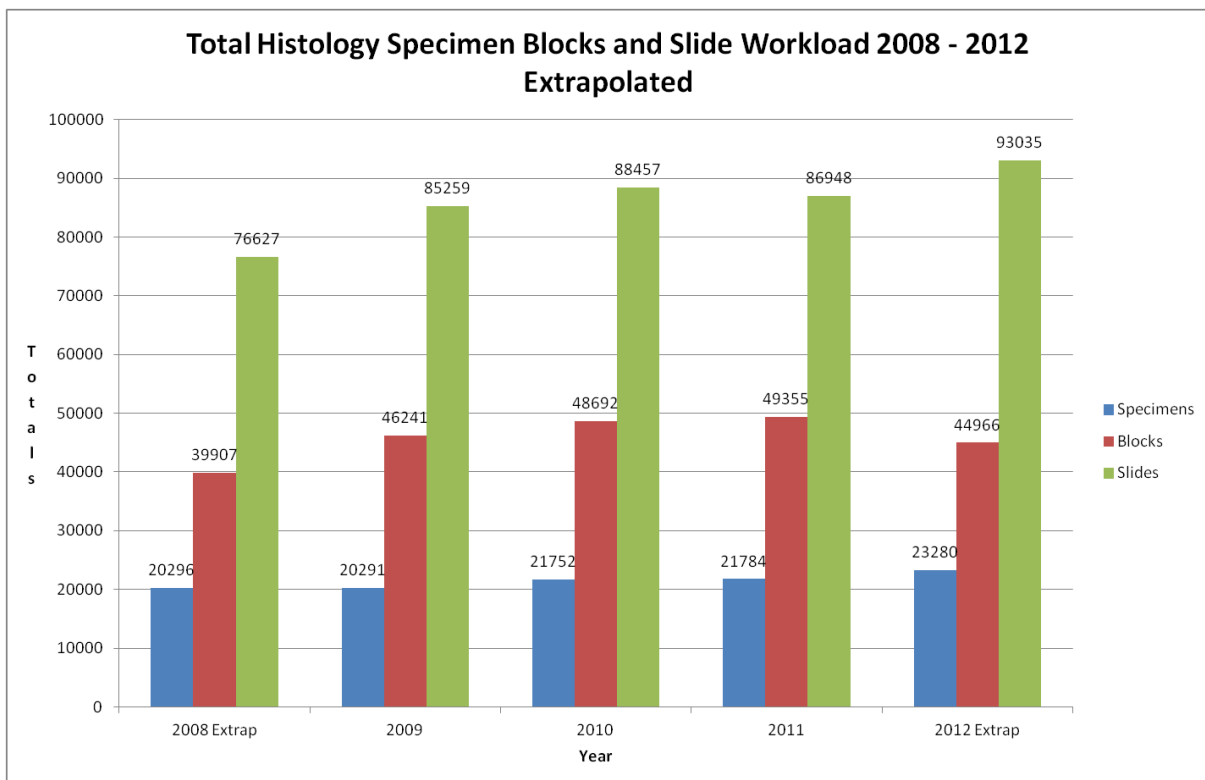
There is also an additional tissue processor – the Surgipath Pathos. This machine is not currently in use and has not been used for routine work in the two years the department has had it. The Pathos still requires validation. It was initially trialled with biopsies using 10% formalin as the routine fixative, followed by graded alcohols for dehydration. The Pathos has a reagent management system and uses Paraplast wax.

**Figure 17 Overall cellular pathology workload by sub sections of andrology, histology, gynae cytology and non-gynae cytology.**



Liquid based cytology (LBC) was transferred to the Royal Derby Hospital.

**Figure 18 Specimen, blocks and slide workload for 2008–2012**



Average blocks number 296 per day in 2008 to 461 at present (see Figure 18 for block workload between 2008 and 2012. Breast clinics Tuesday, Thursday, Friday. Laboratory opening hours Monday to Friday 8am to 5pm (5.30pm Friday).

### Embedding

There are two embedding stations. Band 3 non-critical orientation. BMSs embed everything else.

### Microtomy

There are four microtome stations. BMSs cut sections. Band 3 will cut anything other than biopsies. Batch approximately 20 cases at a time. Usually section cutting until 4pm.

Sections are drained and racked up. Immunohistochemistry sections are sent to Nottingham for immunohistochemistry together with dermatology and lower GI reporting. These send-away cases have turnarounds times of three–four days for reporting. Immunohistochemistry controls were originally cut in batches but now each week.

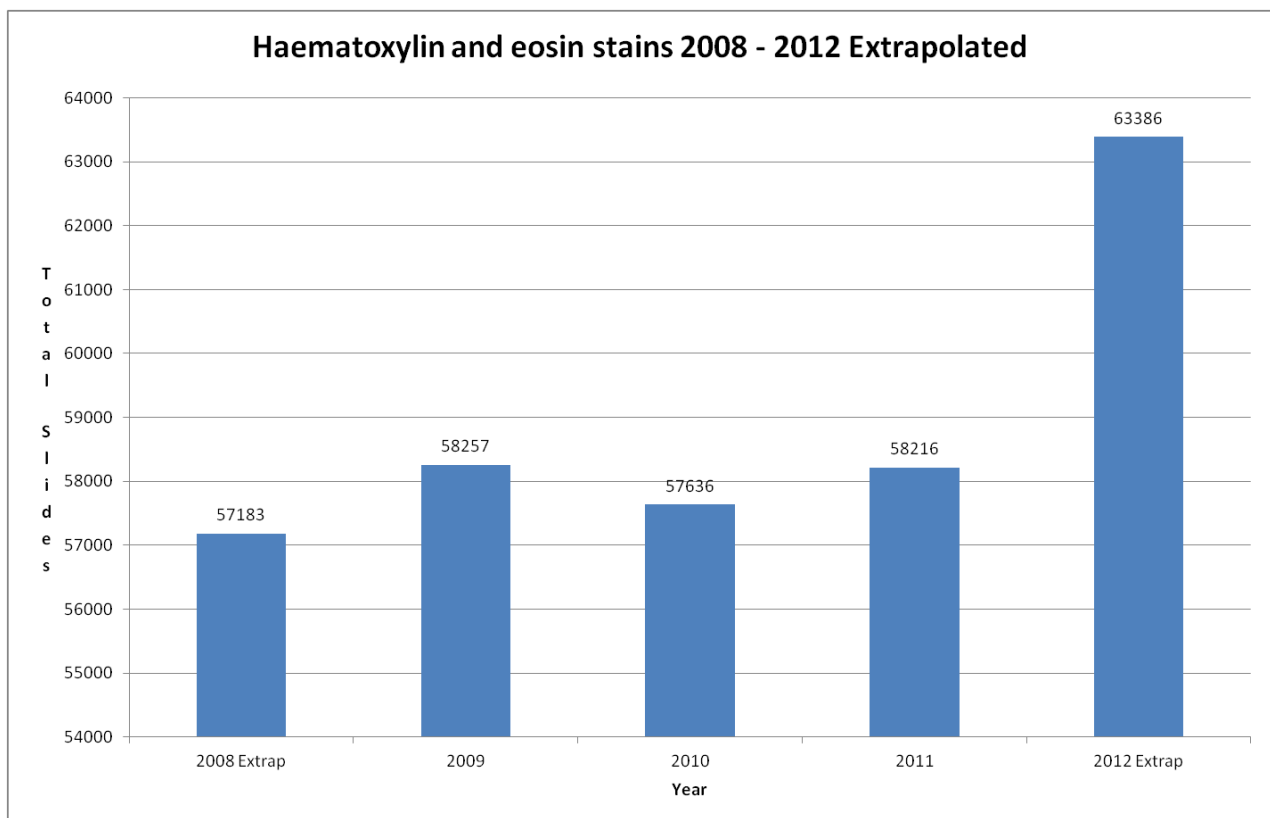
Internal quality control is managed by a BMS. Distributed to pathologists in Nottingham. In-house there is a supermarket system. Slides are tracked on the LIMS.

### Routine staining

The Tribune (Surgipath) staining machine is used for all haematoxylin and eosin (H&E) staining. This machine looked ancient but was only five years old. This piece of equipment had been awaiting repair for nearly two weeks at the time of this visit. The cellular pathology laboratory were reliant on hand staining.

H&E stains are procured from Surgipath. The Tribune has a reagent management system. The H&E is performed as a regressive stain. An independent engineer maintains the machine

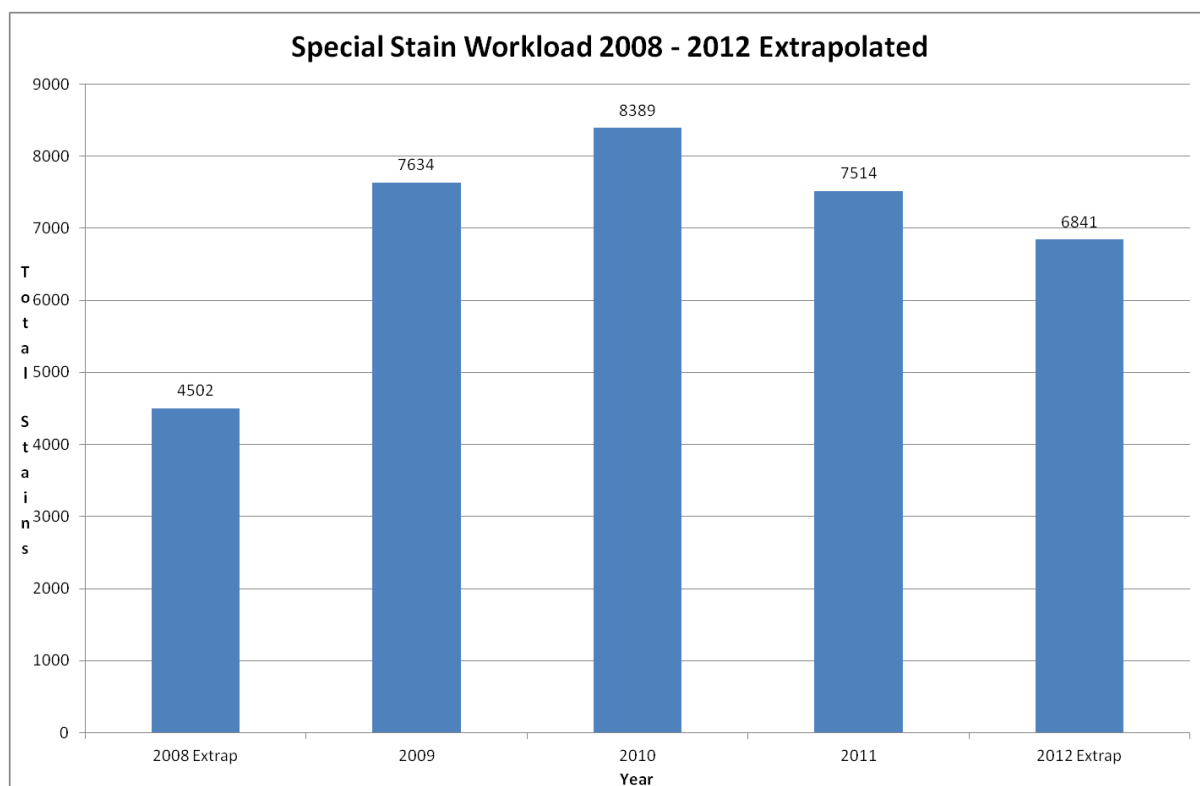
**Figure 19 Routine haematoxylin and eosin staining 2008–2012**



## Special stains

Special stains take place in a separate room. Stains are mainly made up in house by BMS using quality stains from VWR. The special stain workload for the last five years is shown in Figure 20.

**Figure 20 Special stain workload 2008–2012**



There is currently an ongoing research project on osteoarthritis. This takes up valuable laboratory. It was originally funded by Astra Zeneca but the investigation team were unsure as to whether it is still funded. The NHS laboratory staff cut the sections for the research assistant in return for the assistant providing Band 2 duties such as slide filing.

## Immunohistochemistry (IHC)

Previously the laboratory used the manual Shandon Sequenza 2006 – 11 with a domestic pressure cooker for antigen retrieval or protease mediated retrieval as an alternative for some antigens. Tris citrate buffer pH 6 used in antigen retrieval is made up in house for 45–60 minutes incubation. From January 2012, the department has had the Intellipath (Menarini) installed to replace the manual Sequenza. All controls ran on this machine so far were validated with the assistance of one of the consultants. The intention is to run all remaining control material and validate over the next few months. The department has owned the Intellipath since April 2012. There was good on-site training for four staff and on-site validation provided by Menarini. Slides are dried over night at 60°C. On the same day are hot plated for one hour. Sections are taken to water manually prior to immune labelling. Use off-board antigen retrieval pressure cooker. Laboratory has used protease on flat bed manual method but now retrieving on the Intellipath with protease. Commercial buffers are not checked for pH. Use either pH 6.0 or 9.0 buffers. pH 6.0 is used routinely. The department made the decision to use Menarini bulk buffers to provide a robust method on the Menarini machine avoiding in-house induced variation.

IHC testing has been off-site since early 2011. In-house the laboratory is comparing ID5 and 6F11 on the new machine. Oestrogen and progesterone receptor labelling has not yet been tried on the new machine. They will also be using freshly sectioned composite block for ER control. Control material is now sourced at the time of cut-up instead of discard, improving the over fixation problem.

For most antibodies the staff follow the suppliers recommendations. The Intellipath is not a closed system and it offers the ability to tweak protocols to ensure best staining. The machine operates bar code driven protocols. There is no LIMS interface.

Daily housekeeping utilises the machine's on-board reagent management system and cleaning protocol. After 200 slides have been processed, the machine must be cleaned as it will not proceed until completed. The immunostainer has a warranty for 12 months from April 2012.

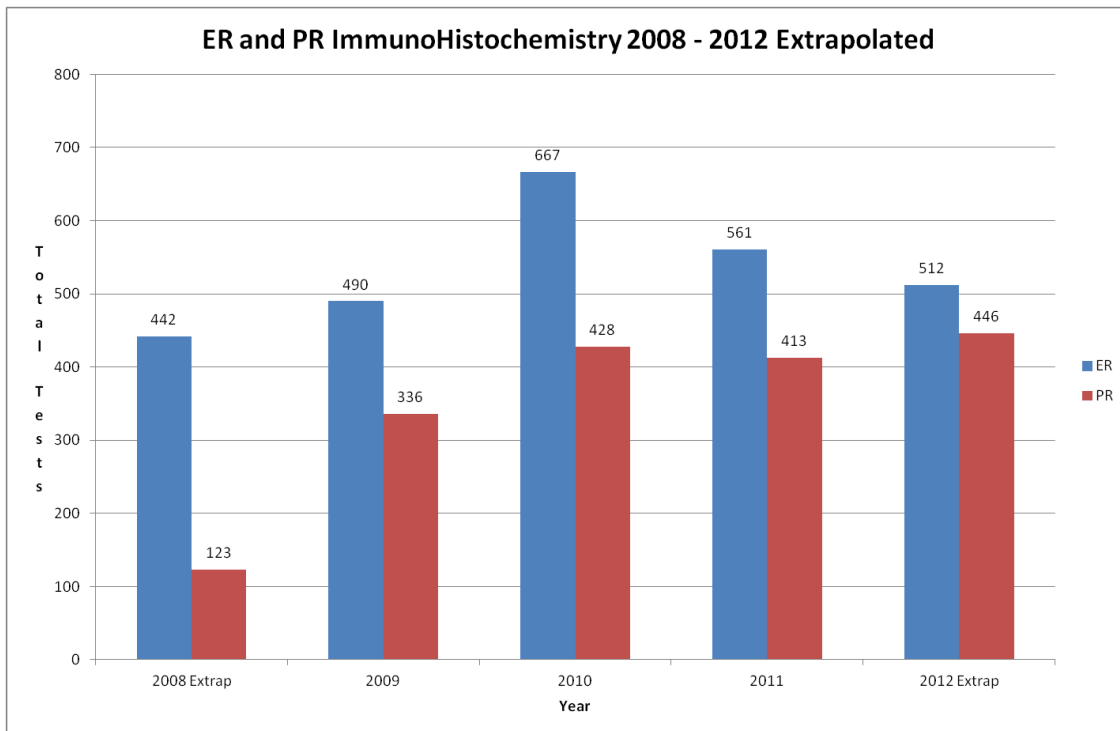
There is currently a Band 6 taking an interest in the IHC since the senior BMS stepped down recently.

There are problems with taking TTF-1 controls as the laboratory has been unable to obtain surgical lung tissue locally. They have approached Nottingham for help.

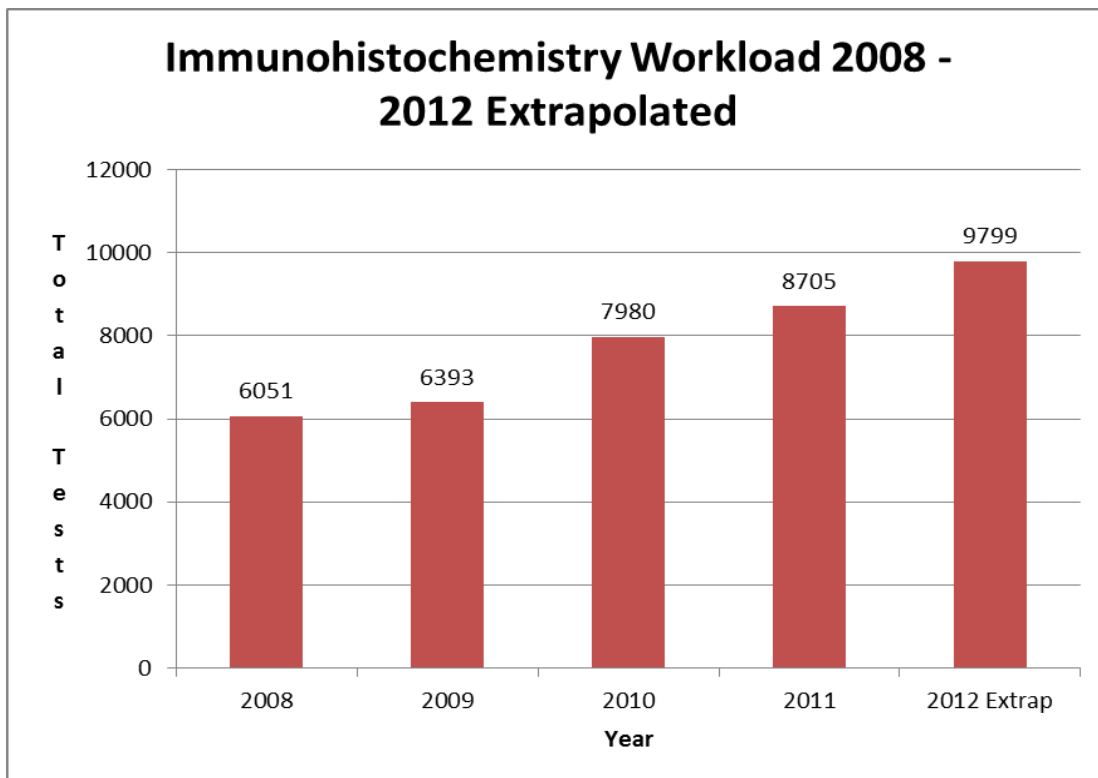
There is no air conditioning in IHC laboratory and therefore no adequate ambient temperature control during the process. This wasn't picked up in any CPA assessment. This would be a problem during temperature extremes, such as a hot summer. It was noted how hot the ambient temperature was during the visit in December.

Currently there are requests for five or six Oestrogen receptor requests/week. Figure 21 shows the ER and PR workload for 2008–2012, and Figure 22 all immunohistochemistry tests.

**Figure 21 Oestrogen (ER)and Progesterone Receptor (PR) Workload 2008 – 2012 extrapolated**



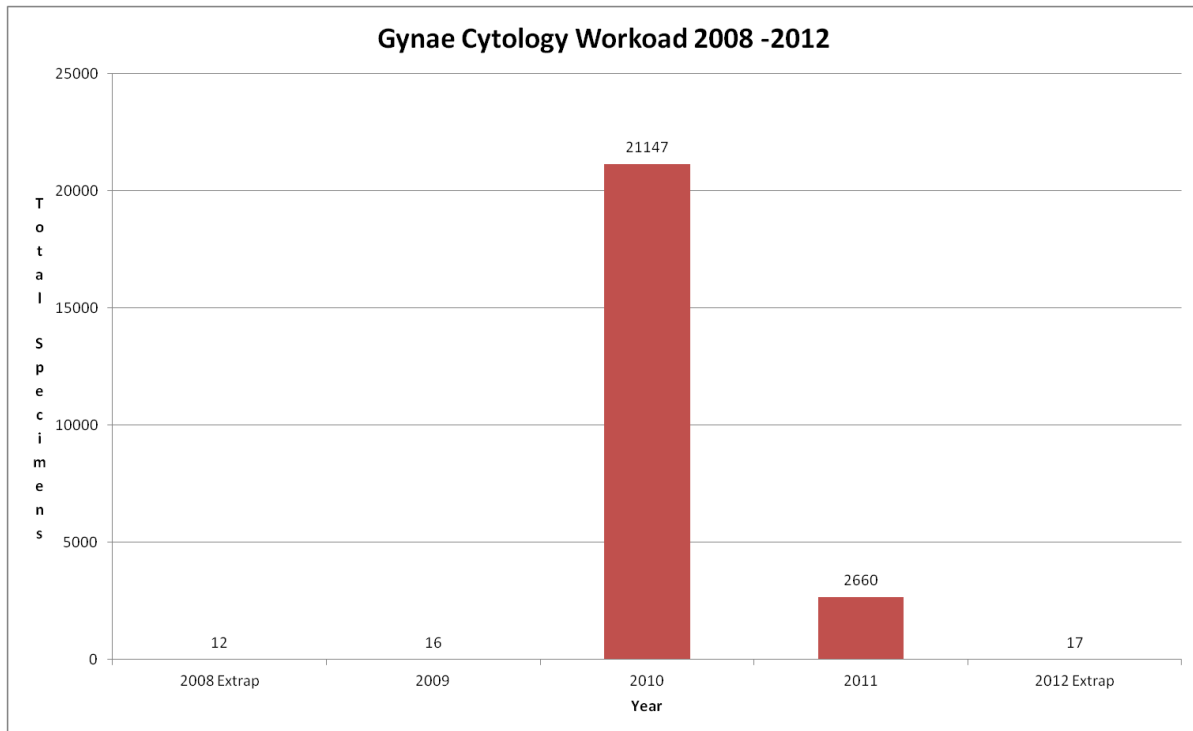
**Figure 22 Total IHC workload for the last 5 years**



**Table 2 The following were not included in Figure 5 as coded differently or not ER**

	2008 Extrap.	2009	2010	2011	2012 Extrap.
<b>Breast – therapeutic marker</b>	21	16	5	6	7
<b>Breast diagnostic marker</b>	46	14	22	14	19
<b>Breast HER2 status</b>	0			181	253
<b>Breast hormone receptor</b>	0		129	267	259

**Figure 23 LBC workload (Incomplete data available)**



Liquid-based cytology (LBC) service moved to Derby County Hospital 18 months ago. The old cytology screening laboratory is currently used for sorting investigation cases. Future use has not yet been decided.

**Category B1 non-gynae cytology laboratory**

Non-gynae cytology and andrology. Andrology is off site at Newark Hospital. Some BMS staff rotate through non-gynae cytology and andrology. There are no rapid access clinics. There are parathyroid frozen sections eight–ten times per year. No other frozen sections.

Non-gynae cytology workload for 2008–2012 is shown in Figure 24. Andrology workload is shown in Figure 25.

Figure 24 Non-gynae cytology specimens 2008–2012

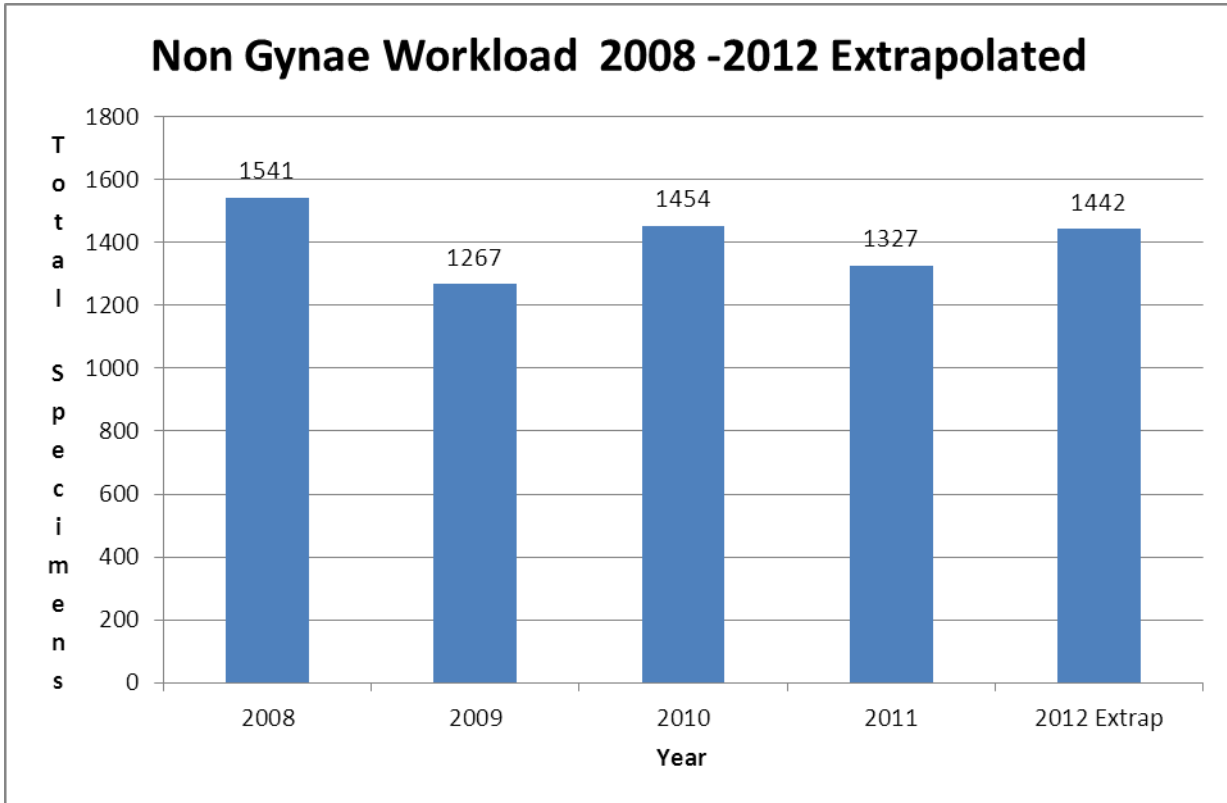
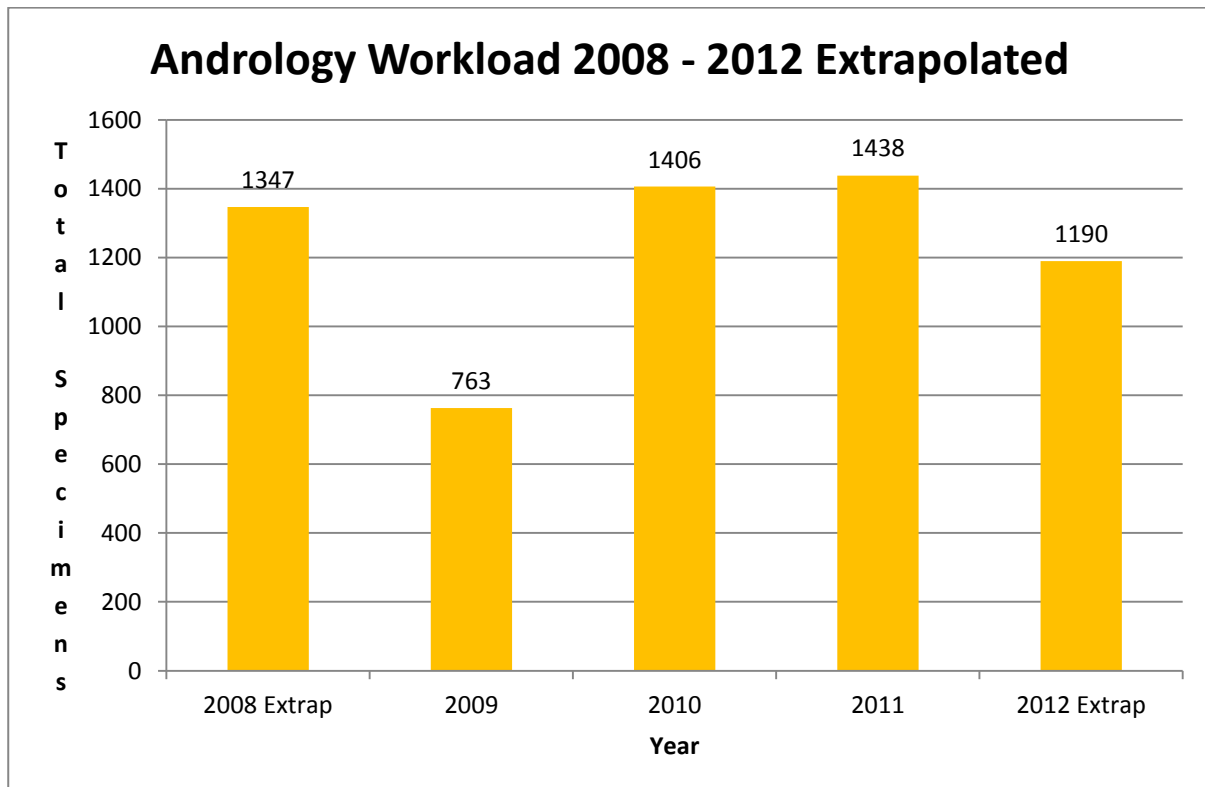


Figure 25 Andrology specimen workload 2008–2012





## Slide and block storage

All slides retained for 10 years. Blocks are retained for more than 30 years at present reducing to 30 years. Four years of slides are retained on-site.

## Staffing

2000 Department had three consultant histopathologists, two left to move to Nottingham.

2002 Department had one consultant histopathologist on-site with two locums to cover. Sending work to Pathlore. There was no clinical lead. The substantive consultant had health issues that may have made it more difficult to recruit.

2007 Two substantive consultant histopathologists were appointed. Breast reporting by Nottingham also came on site for dissection, attend MDT meetings and to report cases and ERs. Laboratory manager issued monthly survey on technical work including the IHC sent to Nottingham. No significant problems identified. Four Nottingham consultant histopathologists synchronised with MDTs. Sent sections over for reporting until Dr S Gill started 2007. No formal agreement. BMS were doing biopsy transfer.

The current establishment is listed in Table 3.

**Table 3 Current cellular pathology staffing levels**

	2010/11		2011/12		2012/13 ytd 31/10/2012	
	Budget WTE	Actual WTE	Budget WTE	Actual WTE	Budget WTE	Actual WTE
<b>Consultant B Pay</b>	4.10	4.10	3.40	4.10	4.10	4.10
<b>Staff Grade Officer B Pay</b>	0.00	0.00	1.00	0.00	0.00	0.00
<b>Band 8c Scientist B Pay</b>	0.00	0.00	1.00	0.00	0.00	0.00
<b>Band 8a Pathology Mgr B Pay</b>	1.00	1.00	1.00	1.00	1.00	1.00
<b>Band 7 Spec BMS Dep Lead B Pay</b>	1.86	1.86	1.86	0.86	0.87	0.86
<b>Band 6 Specialist BMS B Pay</b>	3.43	2.93	3.43	2.93	2.93	2.93
<b>Band 5 BMS B Pay</b>	3.00	3.00	3.00	3.00	4.00	4.00
<b>Band 3 MLA B Pay</b>	3.40	3.40	3.40	3.33	3.40	3.40
<b>Band 2 MLA B Pay</b>	2.50	2.50	3.00	2.00	2.43	1.43
<b>Band 4 A&amp;C B Pay</b>	0.67	0.67	0.67	0.00	0.00	0.00
<b>Band 3 A&amp;C B Pay</b>	1.53	1.53	1.53	1.53	1.53	1.53
<b>Band 2 A&amp;C B Pay</b>	0.98	0.98	0.99	0.49	1.49	1.00
	22.47	21.97	24.28	19.24	21.75	20.25

The laboratory was asked for the impact of endoscopy business case increase in workload and identified the need for 0.5 WTE band, 5/6 BMS which is yet to be funded. This has been entered on the risk register (score 20).

Current Vacancies:

Band 7 – 1.0 WTE (includes Quality Officer role)

Band 5 – 2.0 WTE

Band 2- 1.0 WTE

A&C 2 – 0.9 WTE

Bank staff currently used in the office

Locums in laboratory covering three vacancies: three BMS HPC registered (plus one BMS for the week of the CQC/RCPATH visit)

A fifth consultant post proposed by the Trust and approved by The Royal College of Pathologists, is not yet funded. Staff were advised to revisit the business case and update it. Note: This would enable repatriation of all work currently sent to Nottingham for reporting.

### **Training**

There is a dedicated training officer in each dept. All courses requested funded (including congress, IHC 2010 Oxford course, non gynae cytology). Unfortunately releasing staff to attend was a problem. The Pathology Training Officer supported bids for funding of all courses.

There has been a recent change of Pathology Training Officer. There are some concerns as to whether there would be the same level of support for training bids. Internal training by pathologists would be ideal but not realised.

### **Meetings**

There are regular governance, senior staff, technical, quality and staff daily huddle meetings that are attended by consultant and laboratory staff. There is also a system of 'sticky notes' on the noticeboard where staff can post suggestions and issues.

### **Quality Management**

There is a Pathology Quality Manager. Q-Pulse supports the quality management system. The department currently has a vacancy for a Band 7 whose role includes a Quality Officer responsibility. The current Cellular Pathology Manager is caretaking this function.

There were communication problems between histopathologists and the laboratory staff when problems were highlighted but not actioned promptly or appropriately. There is now a shared drive system in place that is used to report and identify problem cases for investigation. A spreadsheet populated by the histopathologists, including actions planned and taken by the laboratory.

There are regular monthly audits of technical External Quality Assessment (EQA) reports. All EQA reports are recorded onto Q-Pulse. Actions are documented against non-conformities.

The general view of staff is that the department needs the vacancies to be filled. Four cellular pathology staff were lost through Mutually Agreed Resignation Scheme (MARS) with the resulting vacancies covered by locums.

The departmental quality system requires further improvement in particular with more staff training required in the use of Q-Pulse with non-compliance reporting.

### **Procurement**

In 2010, Dr S Ibrahim developed IHC by offering support in tender specification. The specification was written but the procurement of a new machine was halted after funding had been identified. Some validation of antibodies had been carried out using the loan machine which was subsequently purchased.

### **IT support**

Extraction of data from Winpath is by the Pathology IT Manager. Reliance on one person is problematic in a service that must be proactive in using data to respond to the changing needs of the service. It would be helpful to train someone from the cellular pathology staff to extract data.

## Mortuary

There are sufficient body storage spaces and autopsy tables to accommodate present workload. The viewing gallery and chapel of rest facilities adequate. Generally clean and tidy.

**Table 4 Mortuary staffing**

Mortuary Staffing	2010/12		2011/12		2012/13	
	Budget WTE	Actual WTE	Budget WTE	Actual WTE	Budget WTE	Actual WTE
Band 6 MTO B Pay	1.00	1.00	1.00	1.00	1.00	1.00
Band 5 MTO B Pay	1.00	0.67	1.00	0.67	0.67	0.67
Band 4 MTO Trainee B Pay	1.35	1.35	1.34	1.35	1.66	1.67
Total	3.35	3.02	3.34	3.02	3.33	3.34

## Mortuary workload

A public mortuary service is provided.

650 coroners and 10 hospital post mortems are carried out per annum.

Out-of-hours service is provided for police identifications.

Plans to improve mortuary layout had been drawn up but not yet funded.

## 7.5 List of documentation reviewed

Number	Title
1	Professor Robert E Mansel's investigation report on oestrogen receptor negative patients at Sherwood Forest Hospitals NHS Trust
2	Letter to all organisations from Professor Sir Bruce Keogh - DH, 8 Oct 2012
3	KM Pathology services staffing, Sept 2012
4	The Histopathology organisational structure at King Mill Hospital
5	A copy of the spreadsheet referred to in the investigation report
6	A time line showing the NEQAS checking of slides 2004 - 2012
7	An email from KM Pathology Services Manager to clarify why the above timeline ends in February 2012
8	CQC - summary of visit to the pathology lab at King's Mill Hospital 15 10 2012
9	Root Cause Analysis investigation of the under reporting of ER positive. Progress Update. Sherwood Forest Hospitals NHS Foundation Trust, 6 November 2012.
10	Timeline of events (not same as in RCA project plan) following publication of east midlands pathology booklet
11	Various UK NEQAS ICC and SIH immunohistochemistry journals
12	UK NEQAS ICC participants manual 2012-2013
13	Email from NEQAS Director on 17 10 2012 offering details from UK NEQAS on process for UKNEQAS breast hormonal receptors module (plus participants manual attached)
14	ER negative patient review action project plan from KM
15	East Midlands Cancer Network report - Peer review June 2012
16	Various EQA emails TR/PQ and others
17	Estrogen Receptor Status by Immunohistochemistry Is superior to Ligand-binding Assay for predicting response to adjuvant Endocrine Therapy in Breast Cancer J Clin Oncol 17:144-1481 1999
18	Immunohistochemical detection of steroid receptors: a working protocol. J Clin Pathol 2000;53:634-35
19	East Midlands Pathology Booklet: An audit of individuals and departmental pathology performance 2004-2010
20	East Midlands Pathology Booklet 2012: An audit of individual and departmental pathology performance 2008-2011
21	CPA assessment report, Department of Cellular Pathology KM 2007
22	CPA surveillance report, 2009 KM
23	CPA report final, may 2011 KM
24	CPA report 2011 overview KM
25	23 clinical audit reports from KM histopathology department, 2009-2012
26	KM - Trust risk register
27	Risk register for pathology department at KM
28	ER NEQAS May 2012 and Sept 2012 - KM
29	GEN NEQAS May 2012 and Sept 2012 -KM
30	HTA licence and site visit inspection report for KM Dec 2010
31	Review of ER Status of screen detected invasive cancer in Scotland, 2008-11
32	List of breast cases per annum at KM, 2008-12
33	KM Directorate budget broken down to the level of histopathology for the last 3 years.
34	Copy of hormone receptor data in East Midlands Region
35	Various KM NEQAS reports
36	Internal Quality Control records KM
37	Internal Quality Control records for histology KM
38	Quality Manual Cellular Pathology KM, Nov 2012
39	Time line of ICC of ER Issues and Improvements KM
40	Timeline of Immunohistochemistry Quality Control, Issues raised and Actions KM
41	Annual management review - pathology KM 2006, 2007, 2009, 2010 & 2011

42 Divisional governance minutes (12 months) KM

43 Divisional governance report 2001-2012 (total 10) KM

44 KM Pathology Clinical Governance terms of reference and minutes for 2012

45 KM Quality managers report 2012 x3

46 Governance and Quality Assurance SOP KM, June 2012

47 KM SOPs x24

48 KM User surveys x4

49 KM Pathology SMT terms of reference and minutes 2011-2012 x10

50 KM Pathology quality group terms of reference and minutes 2012 x9

51 KM Senior Staff, Cellular Pathology Meeting 2011-2012 x16

52 KM Histology Technical Staff Meeting x12

53 KM Quality Reports 2012 x3

54 KM Incidents request x18

55 Histopathology and immunohistochemistry development plans KM 2008 2009 x3

56 KM Laboratory managers meeting terms of reference and notes x34

57 KM Departmental IHC meeting notes Aug 2012

58 NEQAS Director emails

59 NEQAS director presentation

60 E Midlands Regional Co-ordinator email and 3 documents

61 The NHS Litigation Authority (NHSLA) Circular 02/02 Apologies and Explanations

62 NHSBSP No. 44: 2009. Guidelines for Managing Incidents in the Breast Screening Programme

63 NHSBSP No 60 Consolidated guidance on standards for the NHS breast screening programme

64 NHSBSP No 50 Guidelines for non operative diagnostic procedures and reporting in breast cancer screening. Non operative diagnosis Sub group of the national coordinating group for breast screening pathology

65 NHSBSP No 57 External quality assessment scheme for breast screening histopathology. General description and Standard Operating procedures

66 Quality assurance Guidelines for Breast Pathology services Second edition NHSBSP Publication No 2 July 2011:4.7.7

67 NHS Breast Screening Programme and Association of Breast Surgery: Breast Pathology QA: Review of ER status of screen-detected invasive cancer. Being Open NPSA Alert, 19 Nov 2009

68 Patient Safety Alert: NPSA/2009/PSA003, Nov 2009

69 An independent external review of the breast screening unit at East Lancashire NHS Trust. FG Burns, Jan 2011

70 Report on a review of breast imaging at Altnagelvin Hospital, Belfast City Hospital and Antrim Area 2002-2005, Jan 2006

71 Achieving the Vision of Excellence in Quality: Recommendations for the English NHS system of quality Improvements, IHI, 2008

72 Production, Dissemination, and Use of Evidence Reviews and Guidelines in Australia

73 Development and Use of Practice Guidelines in The Netherlands

74 Production, Dissemination, and Use of Evidence Reviews, Guidelines, and Directives in Germany

75 Improving Outcomes: A Strategy for Cancer. Second annual report 2012

76 Quality oversight in Britain - findings, observations and recommendations for a new model, JCI Consulting. 2008

77 Developing, Dissemination and Assessing Standards the National Health Service. An Assessment of Current Status Opportunities for Improvement, Rand. 2008

78 United Kingdom National Co-ordinating Committee for Breast Pathology. Various Minutes.

79 NHSBSP No 58 Guidelines for pathology reporting in breast disease. A joint document inc. third edition of the NHSBSP guidelines for pathology reporting in Breast screening and the second edition of the RCPATH dataset for breast cancer histopathology

80 Detection and management of outliers. Guidance prepared by the National Clinical Audit Advisory Group. DH. Jan 2011.

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- 82 Paper on Validation and Quality Control for IHC from NSH Symposium, Sep 2010  
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- 83 Quality of Life of Cancer Survivors in England. Report of a pilot survey using Patients  
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- 94 Shaping policy: the Canadian Cancer Society and the Hormone Receptor Testing  
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- 95 Breast Cancer Testing scandal shines spotlight on black box of clinical laboratory  
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## 8 Glossary of terms

### 8.1 Organisations

#### **The Royal College of Pathologists**

The Royal College of Pathologists is a professional membership organisation committed to setting and maintaining professional standards and to promoting excellence in the teaching and practice of pathology.

[www.rcpath.org](http://www.rcpath.org)

#### **The Institute of Biomedical Science (IBMS)**

The IBMS is the professional body for those who work within the field of biomedical science. Its principal aims are: to represent its members; set standards of behaviour for its members; enable career development; educate its members; promote biomedical science to the public and award qualifications.

[www.ibms.org](http://www.ibms.org)

#### **Care Quality Commission**

The Care Quality Commission is the independent regulator of all health and social care in England.

[www.cqc.org.uk/public](http://www.cqc.org.uk/public)

#### **NHS Breast Screening Programme (NHS BSP)**

The NHS Breast Screening Programme provides free breast screening every three years for all women aged 50 and over. It began inviting women for screening in 1988 and national coverage was achieved by the mid-1990s. The NHS Breast Screening Programme is nationally coordinated. It sets national standards which are monitored through a national quality assurance network.

[www.cancerscreening.nhs.uk/breastscreen](http://www.cancerscreening.nhs.uk/breastscreen)

#### **United Kingdom Accreditation Service (UKAS)**

The United Kingdom Accreditation Service is the sole national accreditation body recognised by government to assess, against internationally agreed standards, organisations that provide certification, testing, inspection and calibration services.

[www.ukas.com](http://www.ukas.com)

#### **Clinical Pathology Accreditation (UK) Ltd (CPA)**

CPA is a provider of accreditation services to the health sector. CPA is a non-profit distributing organisation that acts in the public interest. It assesses and declares the competence of medical laboratories in the public and independent sector, and External Quality Assessment (EQA) Schemes in the UK and overseas. Accreditation is voluntary. In 2009 CPA became a wholly owned subsidiary of UKAS.

[www.cpa-uk.co.uk](http://www.cpa-uk.co.uk)

#### **UK National External Quality Assurance Schemes (UK NEQAS)**

UK NEQAS is one of many EQA providers in the UK. It facilitates optimal patient care by providing a comprehensive external quality assessment service in laboratory medicine. Through education and the promotion of best practice, it helps ensure that the results of investigations are reliable and comparable wherever they are produced. It is composed of a network of 390 schemes, operating from 26 centres. The services cover qualitative and interpretative investigations in reproductive science, cellular pathology, clinical chemistry, genetics, haematology, immunology and microbiology.

[www.ukneqas.org.uk](http://www.ukneqas.org.uk)

### **National Quality Assurance Advisory Panels (NQAAP)**

The National Quality Assurance Advisory Panels receive information from external quality assessment (EQA) providers on poor performance. There are a total of six panels in pathology disciplines:

- Chemical Pathology Panel
- Genetics Panel
- Haematology Panel
- Histopathology and Cytopathology Panel
- Microbiology Panel
- Reproductive Sciences Panel.

All National Quality Assurance Panels report to the Joint Working Group for Quality Assurance in Pathology, which reports to the Professional Performance Panel of The Royal College of Pathologists.

### **Joint Working Group for Quality Assurance in Pathology (JWGQA)**

The Joint Working Group for Quality Assurance in Pathology is a multidisciplinary group accountable to The Royal College of Pathologists for the oversight of performance in external quality assessment (EQA) schemes and monitoring of the EQA performance of clinical laboratories in the UK. This is achieved via discipline-specific panels (NQAAP – see above), which report to the Joint Working Group. In turn, the Joint Working Group will work with failing laboratories, but is also bound to report persistent poor performance to the Care Quality Commission.

[www.rcpath.org/committees/intercollegiate-and-joint-committees/joint-working-group-for-quality-assurance-in-pathology/joint-working-group-for-quality-assurance-in-pathology.htm](http://www.rcpath.org/committees/intercollegiate-and-joint-committees/joint-working-group-for-quality-assurance-in-pathology/joint-working-group-for-quality-assurance-in-pathology.htm)

### **Medicines and Healthcare products Regulatory Agency (MHRA)**

The Medicines and Healthcare products Regulatory Agency (MHRA) is the Government agency that is responsible for ensuring that medicines and medical devices work, and are acceptably safe. The MHRA is an executive agency of the Department of Health.

## **8.2 Technical, medical or and scientific terminology**

### **Cellular pathology**

Cellular pathology describes the group of pathology specialties that look at changes in cells and tissues using a microscope to make a diagnosis. The tissue might come from a biopsy, a smear or from a post-mortem examination. The branches of cellular pathology include histopathology, forensic pathology, paediatric pathology, neuropathology, and cytology. Cellular pathology also includes 'molecular pathology', which involves looking at the DNA and proteins that make up a tissue to work out what disease is present and how to treat it.

### **Histopathology**

Histopathology is the study of diseased tissue, for example, breast lumps or specimens of bowel removed because of suspected cancer, including examination under the microscope.

### **Breast pathology**

A specialised area of histopathology concerned with the diagnosis of breast disease.

### **Histopathologist**

A histopathologist is a medically qualified doctor specialising in the microscopic study of diseased tissue.



### **Biomedical scientist**

A biomedical scientist is a science graduate, not medically qualified, working in laboratories in pathology specialties such as histopathology.

### **Immunohistochemistry (IHC)**

Immunohistochemistry (IHC) is a test used by histopathologists to detect specific molecules on the cells in tissues.

Immunohistochemistry testing works by identifying antigens (e.g. proteins) in cells of a tissue sample, by using antibodies that bind specifically to antigens in the tissue. In the case of breast cancer, it is used to show whether or not the cancer cells have hormone receptors on their surface.

### **Immunocytochemistry (ICC)**

Immunocytochemistry is a test used by histopathologists on samples of intact cells that have had most, if not all, of their surrounding extracellular matrix removed. Immunohistochemistry testing works by identifying antigens (e.g. proteins) in cells, by using antibodies that bind specifically to antigens in the sample.

### **The difference between immunohistochemistry and immunocytochemistry**

Immunocytochemistry is similar to immunohistochemistry. Immunocytochemistry is used to identify the presence of a specific protein or antigen in *cells* (cultured cells, cell suspensions), where as immunohistochemistry is used to identify the presence of a specific protein or antigen in *tissues*.

### **Clinical records**

Clinical records include any information relating to the care or treatment of any current or former patient, including notes made by clinical staff, correspondence between clinicians, clinical photographs, video and audio recording, pathology results.

### **Control Cell lines**

These are cells grown in the laboratory that are known to be positive eg for ER and used to confirm that a method such as ER testing has worked successfully and to enable standardisation of a particular laboratory technique such as immunohistochemistry.

### **Interpretative external quality assessment**

The purpose of interpretative histopathology EQA schemes, for consultant histopathologists, is to provide CPD material to participation in periodic slide circulations in general or specialist histopathology practice. Individual response are reported back to the scheme organisers and performance are reviewed against that of peers participating in the scheme.

### **Allred scores**

This scoring system is named for the doctor who developed it. The system looks at what percentage of cells test positive for hormone receptors, along with how well the receptors show up after staining (called 'intensity'). This information is then combined to score the sample on a scale from zero to eight. The higher the score, the more receptors were found and the easier they were to see in the sample.

## **8.3 NHS terminology**

### **Clinical audit**

The NHS Clinical Governance Support team define clinical audit in their *Practical Clinical Audit Handbook* as: "a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and the implementation of change. Put more simply: clinical audit is all about measuring the

quality of care and services against agreed standards and making improvements where necessary”.

**Clinical governance**

Clinical governance is a systematic approach to maintaining and improving the quality of patient care within a healthcare system.

**Internal quality control**

Internal quality control is a means to check that test results are reliable by detecting, reducing and correct deficiencies in a laboratory's internal analytical process prior to the release of patient results. It improves the quality of the results reported by the laboratory.