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# Histopathology



## Haematological malignancies; the rationale for integrated Haematopathology services, key elements of organisation and wider contribution to patient care.

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Haematological malignancies; the rationale for integrated Haematopathology services, key elements of organisation and wider contribution to patient care.

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For Peer Review

## Abstract

The National Institute of Clinical Excellence (NICE) defined the process of care for haematological malignancies in Improving Outcomes Guidance for Haematological Oncology 2003. The most challenging recommendation has been the requirement to develop integrated laboratory services for accurate diagnosis. This is an area of NICE guidance that has not been fully achieved.

The unified concept of haematological malignancy is recent and based on an understanding of the cellular pathology of the bone marrow and immune systems. Historical UK pathology practice has previously resulted in the separation of laboratory haematology from histopathology and of liquid and tissue specimens. Proposals for re-integration and centralisation with specialist-led, centralised diagnostic and reporting services challenge the fragmented historical model.

Accuracy and certainty of diagnosis remains problematic, particularly applying to lymphomas, with evidence that accuracy of diagnosis is slowly improving but still only approaches 85%. There is a potentially significant human and financial cost of diagnostic errors.

No nationwide, validated and comparable epidemiology/population based data exist for accurate and complete ascertainment of new cases of haematological cancers, service planning or clinical outcomes monitoring.

This article examines the original rationale behind the NICE guidance and outlines the key components and processes of an integrated diagnostic service.

## Introduction

The 1995 Calman-Hine report of oncology services <sup>(1)</sup> in the United Kingdom began a process of service improvement driven by the recognition that UK cancer outcomes were inferior to those achieved in comparable countries <sup>(2-4)</sup>. The approach taken was to re-design the delivery of care around the patient, local multi-disciplinary teams and regional cancer networks. The process of care was later defined by the National Institute of Clinical Excellence (NICE) in Improving Outcomes Guidance for Haematological Oncology 2003 <sup>(5)</sup> and its implementation audited through the Cancer Peer Review process. The process of implementation has been difficult and seven years later, many cancer networks have not complied fully with some of the key recommendations. The most challenging recommendation has been the requirement to develop integrated laboratories for the diagnosis of haematological malignancy and this is an area of NICE guidance that has not been achieved.

The unified concept of haematological malignancy is recent and based on understanding cellular pathology of the bone marrow and immune systems. Historical UK pathology practice has previously resulted in the separation of laboratory haematology from histopathology and separation of liquid and tissue specimens. Proposals for re-integration and centralisation with specialist-led

centralised diagnostic services and reporting<sup>(6)</sup> challenged the historical model with its fragmentation of processes and techniques.

Accuracy and certainty of diagnosis remains an ongoing problem which particularly applies to lymphomas with evidence that concordance of diagnosis for lymphomas is slowly improving but still only approaching 85% in two recent reviews<sup>(7)</sup> (personal communication Byers and Norton 2008). The financial costs of a precise diagnosis are a small fraction of treatment costs and there is a potentially significant human and financial cost of diagnostic errors.

Finally, no nationwide, validated and comparable epidemiology/population based data exist for accurate and complete ascertainment of new cases of haematological cancers, service planning or clinical outcomes monitoring.

This article examines the original rationale behind the NICE guidance and outlines the key components and processes of an integrated diagnostic service.

### Original Rationale and Evidence - NICE guidance 2003

The National Institute for Clinical Excellence laid out the rationale, evidence and recommendations for haemato-oncology services in 'Improving Outcomes in Haematological Cancers – The Manual' in 2003<sup>(5)</sup>.

The NICE guidance clearly identified that the haematological malignancies are a complex group of neoplastic diseases and the current WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues 2008<sup>(8)</sup> identifies over 140 diagnoses and subtypes in 12 major disease groups. Scientific advances have challenged and transformed diagnosis, classification and patient management so that specialist immunophenotyping, cytogenetics and molecular methods have become essential adjuncts to traditional morphology for accurate disease classification. Accurate diagnosis and sub-classification requires integration of the morphological, immunophenotypic and genetic features<sup>(9)</sup>. These techniques are now fundamental not only for diagnosis but also for patient treatment and monitoring in the era of targeted monoclonal antibodies and novel agents for specific molecular abnormalities. Unlike most other solid tumours which are initially biopsied and then surgically removed, there is no second tissue sample for confirmation of most haematological tumours, the bulk of which remains in the patient at the time of treatment. Thus the maximum amount of diagnostic, therapeutic and prognostic information must be generated by the laboratory on the initial biopsy sample.

A central conclusion from NICE was that 'Individual patient management should be based on sound and comprehensive information to define the most appropriate treatment' which recognised that consistency and accuracy of diagnosis was not only the starting point but probably ***'the single most important aspect of improving outcomes in haematological cancers'***.

NICE identified concerns about provision, access and accuracy of diagnosis as a result of heterogeneity of the current services which ranged from single-handed pathologists with little access to specialist diagnostics, through to fully integrated specialist diagnostic laboratories. When key investigations are carried out in multiple separate laboratories there may be reduplication and contradictions in results. There is consistent evidence of a significant level of inaccuracy of diagnosis and that expert review improves diagnostic accuracy. This was derived from audit and reviews which showed significant errors in diagnosis that would affect treatment and these are summarised in Table 1.

*Insert table 1*

Extrapolation of the evidence derived from the Welsh review (up to 5% of patients treated for lymphoma in Wales had benign disease) suggests that annually 400 people might receive an inappropriate cancer diagnosis and unnecessary treatment in England. Cost savings from avoided misdiagnosis in England are unknown but could be substantial. In addition, many more patients may have received sub-optimal treatment because their disease is incorrectly classified.

These problems are by no means limited to the United Kingdom and similar problems in the diagnosis of lymphoma<sup>(14)</sup> and acute leukaemias<sup>(15)</sup> were reported from the USA and support the view that expert review of pathology improves diagnostic accuracy. The financial costs of a precise diagnosis are a small fraction of the cost of treatment and the human cost of diagnostic error is potentially enormous

If progress was to be made as part of the National Cancer Plan, how was this to be achieved? NICE guidance challenged the current organisation of the NHS and made important recommendations about service organisation and delivery. It supported local initial assessment of specimens leading to appropriate referral to identified specialist immunophenotyping, molecular biology and cytogenetics services and facilities. This was incorporated in the Cancer Peer Review measures (1A-248, 249 and 250)<sup>(16)</sup>. The guidance supported the Department of Health's development of clinical networks in pathology across Trusts to build capacity reduce fragmentation and provide enhanced levels of equipment and expertise (Carter Report<sup>(17)</sup>). Finally, it recommended the organisation of clinical and pathology haematological services at network level, with collaboration between networks to achieve economies of scale and with specialist diagnostic services serving one or more networks.

In order to reduce errors, the guidance recommended that every diagnosis should be reviewed by specialists in haematological malignancy. This was to be achieved by integrating the results of specialist tests into a final report with an overall interpretation and diagnostic opinion which is authorised by a single designated pathologist (CPR Measure 1C-122)<sup>(16)</sup>. This is most easily achieved by co-locating all specialist haemato-pathology diagnostic services in single laboratories, having integrated diagnostic processes with a systematic approach to the choice and

sequence of tests and implementing computer software designed to support precise identification of haematological malignancies.

With this way of working, the results can be integrated into a single interpretative report containing all the information relevant to the management of the patient and avoid the duplication and possible contradictions that may arise when these key investigations are carried out in separate laboratories.

Quality of the new organisation and diagnostic systems is assured by all laboratories participating in CPA and external quality assurance schemes as well as a systematic approach to diagnostic testing with a specified range of tests carried out on each sample in a systematic way, following protocols that define order and choice of test. In addition, results of tests were to be integrated and interpreted by experts who work with local haemato-oncology multi-disciplinary teams (MDTs) and provide a specialised service at network level. The MDT is the final quality check confirming that all clinical, imaging and pathology results are concordant.

Of major concern was the fact that there were no precise or reliable figures for incidence or survival rates for the haematological cancers in England and Wales and it is not possible to judge whether clinical outcomes are better or worse than elsewhere in the world. Future service planning for the NHS requires knowledge of incidence and prevalence rates both of which are changing in the UK. Updatable computer software designed to support precise identification of haematological malignancies is required for diagnostic laboratories to facilitate accurate population-based studies of epidemiology and clinical outcomes.

Finally, the guidance identified resource implications for setting up these services which have high capital and revenue costs. Rational selection of diagnostic tests following defined protocols can conserve resource by only selecting tests yielding useful information. There are also substantial economies of scale that can be achieved and obvious economic implications of the current guidance as these specialist laboratories have high capital and revenue costs.

Cost implications of centralising and integrating laboratories varies according to the degree of centralisation already achieved, additional equipment required, inclusion of gene sequencing facilities and size of population served.

Costing exercises predicted national capital set-up costs of approximately £5.8million with annual running costs of £7.5 million were predicted but with cost-effectiveness linked to the size of population served; i.e. a low-cost scenario with an anticipated catchment population of 3 million or more and a high-cost scenario for smaller populations down to 1.5 million.

### **The Integrated Diagnostic Pathway and Report – Clarification of the original NICE guidance**

The original NICE guidance has been misinterpreted by some as simply collating the individual results into a report and at a minimal level, stapling a variety of individual reports together, with or without adding a comment. It is also clear from the NICE guidance that it is inappropriate to have a local report produced and then sent on for “central review” or “integration” into the final diagnostic report. This undermines the integrated diagnostic process and immediacy of access to samples for additional testing as well as the internal validation and quality assurance given by systematic investigation processes. Inevitably it will lead to delays in the turn around of a meaningful, high quality diagnostic report within a time-frame that allows for timely decision making and this will impact on cancer pathways which all trusts are under pressure to comply with.

The underlying principle is that effective working requires an integrated diagnostic pathway and this is what was clearly intended in the original IOG publication. This process is characterised by a single point of access for all samples, registration, initial screening, investigation, reporting and authorisation. It requires a predefined diagnostic pathway that is followed systematically for each specimen type or clinical problem. The design of the pathway includes two components: 1) selection of the most appropriate diagnostic platforms for a particular clinical situation and 2) selection of a panel of investigations for each specimen to provide maximum levels of internal cross-validation using the WHO principle of multi-parameter disease definitions whilst avoiding unnecessary duplication. To achieve this requires comprehensive diagnostic testing facilities, technologies and interpretation (including cytomorphology, histology, immunocytochemistry, flow cytometry, cytogenetics and molecular technologies). This is followed by review of all of the results and compilation within the laboratory of a fully integrated report by senior laboratory staff with appropriate levels of expertise which is then released to the referring clinician. This affords the opportunity for internal validation and cross-checking at source, before a misleading or potentially dangerous report leaves the laboratory. In addition, this should be completed in a timeframe that allows additional investigations to be carried out if inconsistencies or uncertainties remain after the primary investigations have been completed.

An integrated report that includes all information needed for initial patient management should be available at the multidisciplinary meeting (MDM) and the final report should summarise the results of investigations performed, contain an interpretative comment and a final diagnosis using the terminology of the WHO classification/ICDO-3 coding. An effective system of quality assurance should include an audit trail for each sample demonstrating that the diagnostic pathway has been followed, as well as traditional external quality assurance schemes.

In many cases this will require significant re-engineering of existing services to achieve the benefits described below. However, in most cases many of the core resources required to do this will already exist within the network.

## **Review of Rationale and Anticipated Benefits**

The original rationale for the guidance was the recognition that the error rate in the diagnosis of haematological malignancies was unacceptably high and had clinical



consequences. This was based on publications and audit data. Seven years later this data is challenged by some who claim that this is no longer the case. However, there is evidence that the underlying problem, although improving, still remains and this has been confirmed in two recent reviews. The first was an audit carried out in Greater Manchester (A Norton and R Byers 2008) who found the serious and critical error rate to be 15%. This data refers to the diagnosis of lymphoma but similar results would be expected in other diagnostic categories. The second review was undertaken in North London and whilst error rates have fallen between 2003 and 2008, they are still substantial (13-15%) resulting in minor or major changes in treatment or delay in treatment<sup>(7)</sup>. This is the essential context for the following discussion.

### Quality Assurance

These concerns about standards of diagnosis serve to highlight a more fundamental problem that is almost unique to haematological oncology. For most types of cancer, the diagnosis made on an initial biopsy or cytology specimen will result in a secondary operative procedure and specimen which provides independent validation of the original diagnosis. Visualisation of the lesion at endoscopy or operation adds further steps in the diagnostic process contributing to overall confidence in the accuracy of the original diagnosis. For leukaemia and lymphoma a diagnosis made on a pathological specimen will generally lead directly to treatment by chemotherapy or radiotherapy. This may be based primarily on subjective morphological interpretation of cytology preparations or tissue sections by a pathologist. Unless a subsequent review is undertaken serious errors will not be detected. External quality assurance schemes designed to test morphological interpretation are difficult to design for haematopathology given the very large numbers of possible diagnoses. More importantly, by their nature, they are retrospective and based on circulated material to test overall performance rather than detect and prevent errors in 'real time' diagnostic samples. A 'real time' quality assurance scheme should be a target which a network of integrated diagnostic centres could explore and exploit.

Fortunately, recent developments in classification and technology provide a solution to this problem. The WHO classification defines each type of leukaemia and lymphoma in terms of morphology, phenotype, molecular and cytogenetic features and clinical characteristics. If all of the defining features can be demonstrated there is a high probability that the diagnosis is correct. This is the rationale for the integrated diagnostic pathway described above. Technical developments mean that it is now possible to design pathways that contain multiple levels of cross-validation between techniques. Adherence to these pathways is the critical element in diagnostic quality assurance and provides clinician and patient with the level of confidence in the diagnosis that is required before proceeding to treatment. In Haemato-oncology the critical element is the ability to demonstrate that a diagnosis is likely to be correct through a process of internal validation using multiple independent diagnostic techniques. Where this process is absent, particularly where the primary diagnosis is based mainly on subjective assessments, there will be a major weakness in the quality assurance of the whole patient pathway leading to the possibility of undiscoverable errors. As retrospective audit data has demonstrated, these risks are unacceptably high.

A systematic approach to the investigation of suspected leukaemia and lymphoma based around a carefully designed pathway is essential. If this is the approach taken then important entities that cannot be reliably identified by morphology alone will be mis-diagnosed. The problem is not simply a function of morphological interpretation, as shown in a recent European study of the reproducibility of immunocytochemistry<sup>(18)</sup>.

Morphology is no longer a gold standard; though an important starting point it must be complemented by other studies. A very striking example is the recent MRC LY10 trial in Burkitt lymphoma (BL)<sup>(19)</sup>. This is a critical diagnostic area and about 50% of patients entered in the trial were proven not to have Burkitt Lymphoma on review and further investigation. The implications of this data are that half of the patients in the trial had the wrong treatment – in this case expensive and toxic in-patient chemotherapy. The trial took 3 years to recruit approximately 60 patients while the incidence in the UK is about 250 per year (Yorkshire and Humber Haematological Malignancy Research Network data<sup>(20)</sup>). It is very likely that many patients with BL are currently not recognised. This condition is very successfully treated with intensive chemotherapy but not with CHOP-R which is the standard treatment of diffuse large B-cell lymphoma. The specific cause of this problem is the fact that Burkitt Lymphoma cannot be reliably diagnosed by morphology alone and requires systematic use of extended immunophenotyping and FISH investigations.

A similar situation pertains in a number of other types of haematological malignancies. These conditions will only be recognised reliably if a diagnostic pathway designed to sensitively detect them is applied systematically to all specimens in the appropriate setting. This particularly applies to rare, low-frequency tumours.

Finally, the assessment of prognosis is an increasing component of the workload of laboratories engaged in the diagnosis of leukaemia and lymphoma. This includes the identification of prognostic markers at the time the patient presents and the use of monitoring through therapy. This is a highly complex area involving the integration of multiple forms of investigation which should ideally be combined into a single assessment of outcome. The same considerations apply to the assessment of prognosis and response to treatment as for primary diagnosis. Clinically important decisions depend on accurate monitoring during the course of therapy.

### Cost Effectiveness

The traditional approach to the diagnosis of leukaemia and lymphoma is wasteful and often ineffective. If there is no integrated diagnostic pathway samples are often sent to multiple separate laboratories specialising in individual techniques. As a matter of routine, each laboratory carries out its own series of investigations based only on the referral information and which, pre-diagnosis, may be imprecise. The data produced may be irrelevant to the clinical problem or needlessly duplicate information produced in another laboratory. Cost-effectiveness depends on rational choices of investigative techniques, balancing cross-validation against reduplication. There are 3 key examples that illustrate this problem.

(i) The demonstration of genetic abnormalities

This is a central element in the diagnosis of leukaemia and lymphoma. There are many techniques available to demonstrate individual abnormalities and these are often done in different laboratories. In an integrated diagnostic laboratory the most appropriate technique for a particular clinical situation can be selected and unnecessary duplication avoided. This is particularly important in the case of metaphase cytogenetics and other very high-cost techniques. In Leeds, implementation of audit data reduced the use of conventional metaphase cytogenetics by 60% (personal communication, A Jack). For many of these specimens there was no indication for any genetic investigation while for others, a simpler more targeted technique was used in the diagnostic pathway.

#### (ii) Reporting of Bone Marrow Specimens

It is common practice in the UK for the bone marrow aspirate, bone marrow trephine biopsy and flow cytometry to be investigated and reported separately in different departments. Each of these components is required for the final diagnosis and examining each separately is wasteful in time and resources and is clinically ineffective. It has been suggested that reporting a trephine biopsy in isolation requires up to 45 minutes of an histopathologist's time and usually results in further immunocytochemical investigations. An additional 15mins of a consultant haematologist time would be spent separately reporting the aspirate. Reporting the trephine and aspirate together, with flow cytometry data available, reduces the time taken an average of 15-30mins (personal communication, A Jack). The availability of flow cytometry results at the time of reporting greatly reduces the need for immunocytochemistry to around 10% of cases. Even in centres with a small workload this is a very significant cost improvement.

#### (iii) Investigation of Lymph Node Biopsies

Most lymph node biopsies are sent in fixative to Histopathology departments. This precludes the use of flow cytometry and compromises molecular investigations even although these tests may be available in other departments of the same institution. Flow cytometry and molecular studies considerably enhance the quality of diagnosis of nodal lymphoid malignancies by providing a tumour specific phenotype and fast and reliable detection of clonal B-cell populations. The use of modern multi-parameter flow techniques allows much more reliable definition of cellular population compared to a conventional approach based on morphology and immunocytochemistry. This approach is commonplace in other developed countries but not in the UK. As well as improved diagnosis, the reporting time is reduced because flow cytometry is carried out in parallel with the histology processing and the results are available when the tissue sections are examined. A turnaround time of 2-3 days is readily possible.

These three examples represent a major component of haematopathology workload and demonstrate that savings are possible in an integrated model as opposed to separate laboratories based on individual techniques.

A fundamental weakness of the traditional approach is that the onus is placed on the clinician or the MDM to bring together these disparate and sometimes highly

complex pieces of information. In most cases the individuals concerned do not have the experience and competence to do this to the standard required. This issue was raised as a matter of concern in the Carter Report<sup>(17)</sup>. NICE guidance highlighted four levels of diagnostic service clearly demonstrating the national variation in access to diagnostic services (Table2).

*Insert Table 2*

Level 3 and 4 services are still rare.

These problems of effectiveness can be overcome in a fully integrated laboratory and it would be expected that significant savings would also be made by eliminating duplication. However, a fully effective diagnostic integrated haematopathology service requires considerable investment in specialist staff and equipment and this places constraints on the minimum workload that is consistent with cost-effective operation. In this context the benchmarks for cost-effective operation should mean providing the enhanced service at unit costs equal to or less than existing services based on multiple laboratories. This is a complex calculation but is achievable where a laboratory serves a catchment population of 3-4million (Personal communication, A Jack).

### Technical and Organisational Developments

Diagnostic techniques and basic concepts of disease have entered a phase of rapid evolution. This has been driven by an impressive expansion in knowledge which has, in turn, been the result of very high levels of investment in research by government, charities and the commercial sector. These developments promise very significant benefits to patients. Structures within the NHS should be specifically designed to facilitate the introduction of these techniques into clinical practice.

In Haemato-oncology the benefit to patients includes improved certainty and accuracy of diagnosis, the use of minimally invasive techniques, improved assessment of prognosis, risk stratification, the effective use of new targeted therapies and improved disease monitoring following treatment. The service described in this document is particularly suited to the introduction of the new generation of diagnostic techniques through the flexible use of skilled staff and the use of structured diagnostic pathways. Where services are fragmented and uncoordinated, appropriate research and the introduction of new technologies and concepts may be very difficult, not least because of the problems of transferring staff and resource between traditional departments and institutions. This has been clearly demonstrated in the evolution of many services. Underpinning these technical changes is a need for laboratories to have a sufficient critical mass to undertake diagnostic research, technology development and training of scientific and medical staff.

### The Need for Accurate Data

The national datasets for leukaemia and lymphoma are extremely poor and this has been highlighted by Eurocare and others<sup>(21, 22)</sup>. Publishing data on incidence and outcome for all leukaemia and lymphoma patients (current practice in the UK) is effectively meaningless (but costs a lot). The main problems in this area are incomplete ascertainment of all new cases because primary data resides in multiple laboratories and clinical databases and there is a lack of standardised approach to diagnosis. The ability to provide high ascertainment of new cases and detailed datasets that can be used for analysing outcome and service performance is a major benefit of network-based integrated laboratories that extend beyond the direct patient pathway<sup>(23)</sup>. Ascertainment of new cases, as well as follow-up, is required to derive incidence and prevalence data, the latter being an important measure for healthcare planning and resource allocation which cannot be derived from Death Certification Only data. This approach is in line with the National Cancer Intelligence Network initiatives.

The points summarised above demonstrate the benefits of integrated laboratories with effective diagnostic pathways and links to effective population based cancer databases. These anticipated benefits are now much broader and with potentially greater impact across the whole patient pathway, including clinical trials support, research, biobanking, patient outcomes and service planning, than was originally envisaged in the Haematology IOG (Figure 1).

***Insert Figure 1***

### **Key components and processes**

The provision of an integrated diagnostic service, as set out above, is most easily achieved in a single laboratory with a full complement of specialist staff and equipment. It is possible, although much more difficult, to design a compliant service based around multiple laboratories each providing a component of the service. Irrespective of how the service is structured there are a number of essential components:

#### **Organisation**

The service should have clearly defined organisational structures including an identified person responsible for the operation of the service, design of the diagnostic pathway, the use of resources and standards of reporting. The service lead should have formal accountability to the Cancer Network Site Specific Group.

To facilitate organisational management, operation and development, managerial and financial responsibility should rest with a single Trust with defined business planning processes to ensure that diagnostic and therapeutic developments are co-ordinated. The speed of clinical and diagnostic technological development demands effective horizon scanning and funded implementation of new therapeutic and diagnostic technologies.

A key element of organisational and operational quality is achieved through a central reception point for all specimens even if some tests may be performed at a different location. There is a logical flow of samples from registration to initial screening, systematic investigation, reporting and authorisation. There should be a full range of protocols covering sample handling, the diagnostic pathways, compilation of reports and relationships with users. The essential 'glue' that makes this possible is an Information technology (IT) system that regulates the diagnostic pathway, compilation of reports, reporting of diagnoses sub-typed by the WHO leukaemia/lymphoma classification and communication with users. This can be a commercially available system or one produced in-house. Quality is assured at several different levels; Cancer network planning, organisational integrity, systematic investigation protocols, formal accreditation by Clinical Pathology Accreditation (either as a standalone department or as part of haematology) and finally a close interface with the MDT which is the final quality check in the process with the clinicians managing the patient.

### Diagnostic Pathways and Technologies

The diagnostic pathways and protocols that are agreed with networks form part of the network guidelines and be accessible to users. The key diagnostic technologies are flow cytometry, histocytopathology and immunocytochemistry, cytogenetics (including FISH) and molecular genetic PCR based techniques for detection of clonality, chromosomal translocations and mutations.

It is important to realise that these technologies each include a very wide range of options within each category and that many centres in the UK use methods and equipment that could be considered as obsolete (e.g. two colour flow cytometry). The specification of range of acceptable techniques needs to be regularly reviewed. The need for specialist staff is also a critical consideration.

Multiple new technologies are becoming available for routine use. These include advanced 8-10 colour flow cytometry, gene expression profiling, whole genome copy number analysis and new generation high throughput sequencing. These will have a substantial impact on the nature of the service provided to patients. These technologies are capital intensive but with potential for savings in staff and recurrent costs. If implemented in centres with a high workload then there is potential to contain or reduce overall unit costs. To realise these savings, obsolete methods of investigation will need to be discarded, again emphasising the need for a coordinated approach to integrated diagnostic pathways rather than the current ad hoc approach found in many areas. Diagnostic centres need sufficient capital and capacity to fund, research, develop, evaluate and implement these new technologies in the setting of increasing clinical requirements for diagnostic sub-classification, cellular prognostic factors, targeted treatment planning (eg detection of BCR/ABL mutations in CML for Tyrosine Kinase resistance and p53 deletion in Chronic lymphocytic Leukaemia) and detection of minimal residual disease. Laboratory services need to be flexible to accommodate rapid implementation of new technologies, maintain platforms of technology research feeding diagnostic services and have capital investment capability. Associated with this is the need for changes in staffing skills mix.

## Interface with Clinical Haemato-oncology

The specialist diagnostic laboratory should be fully integrated with the clinical services and must be able to provide support to multi-disciplinary teams within the network. There should be clearly identifiable contacts for discussion of clinical problems and defined mechanisms for ensuring consultation with users on the organisation and performance of the service. Modern IT systems can provide secure electronic data repositories for results lookup and customised e-mails alerts to clinicians when results become available.

## Conclusions

There are very significant quality improvements to be gained from implementing this service model. The central requirement is to demonstrate that diagnoses are correct through following a systematic protocol for investigation and reporting. Financial savings are also possible both from improved efficiency of the diagnostic process and from reduction in error. These financial gains are only achievable by centralised services where the effects of relatively high fixed costs are offset by a high workload and correspondingly low unit costs. Experience in several centres has shown that services can be provided by a centralised facility serving more than one network whilst maintaining a high level of integration with clinical services. This is fully consistent with the approach outlined in the Carter Report<sup>(17)</sup> and more recently in the NHS Confederation document 'Dealing with the Downturn'<sup>(24)</sup>.

To make real progress with implementation of the diagnostic aspects of NICE guidance requires a national approach to achieve uniformity of quality and equity of access to modern diagnostic technologies and expertise. This would best be achieved through the establishment of a national network collaborative with a national outline specification for the service and a revised set of Cancer Peer Review measures.

Such an approach would provide clarity of organisation, operation and function, coordinate and support development of services and reduce fragmentation. There is a need to build capacity and access with enhanced equipment and expertise as well as stimulate collaboration to achieve economies of scale, improved purchasing power and cost-effectiveness. On a national scale is it possible to implement innovative 'real-time' quality assurance schemes appropriate for malignant haematopathology to improve and assure quality of diagnostic pathways. Improved ascertainment of diagnostic data for epidemiological studies and service provision linked to population-based databases concords with the National Cancer Intelligence Network and Cancer Plan initiatives. A minimum critical mass of resources is required to maintain the research, education and training for the future needs of the service together with a strong linkage between clinical and diagnostic elements to maintain progress in patient care.



For Peer Review

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Table 1. Summary of lymphoma histology audits and reviews from 'Improving Outcomes in Haematological Cancers – The Manual' 2003

<b>All Wales Lymphoma Pathology Review Panel</b> <sup>(10)</sup>	2 year central review of 275 lymph nodes(1998-2000)	Major diagnostic discordance in 20% of cases: -5 cases diagnosed as benign were lymphoma. -13 cases diagnosed as lymphoma were benign or a non-haematological malignancy. -15cases changed from NHL to HL or vice versa. -16 cases of NHL assigned to a different prognostic group. -21% diagnosed as lymphoma but no REAL classification -17 cases would have had a change in management strategy and first-line treatment was altered in 12.
<b>Lancashire Hospital</b> <sup>(11)</sup>	Regional centre review	-36% had major discrepancies
<b>NE England audit</b> <sup>(12)</sup>	100 lymph nodes	-26% diagnostic discrepancy rate that would have changed management
<b>Scottish and Newcastle Group</b> <sup>(13)</sup>	574 cases of Hodgkin Lymphoma	-28% had revised histological subtype and a resulting change in management in 10%

