

**Scottish Cancer Taskforce**

**National Cancer Quality Steering Group**

**Lymphoma**

**Clinical Quality Performance Indicators**

**Engagement Document**

**August 2017**

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# 1. National Cancer Quality Programme

Better Cancer: Ambition and Action (2016)1 details a commitment to delivering the national cancer quality programme across NHSScotland, with a recognised need for national cancer QPIs to support a culture of continuous quality improvement. Addressing variation in the quality of cancer services is pivotal to delivering improvements in quality of care. This is best achieved if there is consensus and clear indicators for what good cancer care looks like.

Small sets of cancer specific outcome focussed, evidence based indicators are in place for 18 different tumour types. These are underpinned by patient experience QPIs that are applicable to all, irrespective of tumour type. These QPIs ensure that activity is focussed on those areas that are most important in terms of improving survival and individual care experience whilst reducing variation and supporting the most effective and efficient delivery of care for people with cancer. QPIs are kept under regular review and are responsive to changes in clinical practice and emerging evidence.

A programme to review and update the QPIs in line with evolving evidence is in place as well as a robust mechanism by which additional QPIs will be developed over the coming years.

## 1.1 Quality Assurance and Continuous Quality Improvement

The ultimate aim of the programme is to develop a framework, and foster a culture of, continuous quality improvement, whereby real time data is reviewed regularly at an individual Multi Disciplinary Team (MDT)/Unit level and findings actioned to deliver continual improvements in the quality of cancer care. This will be underpinned and supported by a programme of regional and national comparative reporting and review.

NHS Boards will be required to report against QPIs as part of a mandatory, publicly reported, programme at a national level. A rolling programme of reporting is in place, with approximately three national tumour specific reports published annually. National reports include comparative reporting of performance against QPIs at MDT/Unit level across NHSScotland, trend analysis and survival. This approach will help overcome existing issues relating to the reporting of small volumes in any one year.

In the intervening years tumour specific QPIs are monitored on an annual basis through established Regional Cancer Network and local governance processes, with analysed data submitted to Information Services Division (ISD) for inclusion in subsequent national reports. This approach ensures that timely action is taken in response to any issues that may be identified through comparative reporting and systematic review.

# 2. Quality Performance Indicator Development Process

The QPI development process was designed to ensure that indicators are developed in an open, transparent and timely way. The development process can be found in appendix 1.

The Lymphoma QPI Development Group was convened in March 2012, chaired by Mr Matthew Barber, Consultant Surgeon. Membership of this group included clinical representatives drawn from the three regional cancer networks, Healthcare Improvement Scotland, ISD and patient/carer representatives. Membership of the development group can be found in appendix 2.

# 3. QPI Formal Review Process

As part of the National Cancer Quality Programme a systematic national review process has been developed, whereby all tumour specific QPIs published are subject to formal review following 3 years analysis of comparative QPI data.

Formal review of the Lymphoma QPIs was undertaken in May 2017. A Formal Review Group was convened, chaired by Mr Matthew Barber, Consultant Surgeon. Full membership of this group can be found in appendix 3.

The formal review process is clinically driven with comments sought from specialty specific representatives in each of the Regional Cancer Networks for discussion at the initial meeting. This review builds on existing evidence using expert clinical opinion to identify where new evidence is available.

During formal review QPIs may be removed and replaced with new QPIs. Triggers for doing so include significant change to clinical practice, targets being consistently met by all Boards and publication of new evidence.

Any new QPIs have been developed in line with the following criteria:

* **Overall importance** – does the indicator address an area of clinical importance that would significantly impact on the quality and outcome of care delivered?
* **Evidence based** – is the indicator based on high quality clinical evidence?
* **Measurability** – is the indicator measurable i.e. are there explicit requirements for data measurement and are the required data items accessible and available for collection?

# 4. Format of the Quality Performance Indicators

QPIs are designed to be clear and measurable, based on sound clinical evidence whilst also taking into account other recognised standards and guidelines.

* Each QPI has a **short title** which will be utilised in reports as well as a fuller **description** which explains exactly what the indicator is measuring.
* This is followed by a brief overview of the **evidence base and rationale** which explains why the development of this indicator was important.
* The measurability **specifications** are then detailed; these highlight how the indicator will actually be measured in practice to allow for comparison across NHSScotland.
* Finally a **target** is indicated, this dictates the level which each unit should be aiming to achieve against each indicator.

In order to ensure that the chosen target levels are the most appropriate and drive continuous quality improvement as intended they will be kept under review and revised as necessary, if further evidence or data becomes available.

Rather than utilising multiple exclusions, a tolerance level has been built into the QPIs. It is very difficult to accurately measure patient choice, co-morbidities and patient fitness therefore target levels have been set to account for these factors. Further detail is noted within QPIs where there are other factors which influenced the target level.

Where ‘less than’ (<) target levels have been set the rationale has been detailed within the relevant QPI. All other target levels should be interpreted as ‘greater than’ (>) levels.

# 5. Supporting Documentation

A national minimum core dataset and a measurability specification document have been developed in parallel with the indicators to support the monitoring and reporting of Lymphoma QPIs. The updated document will be implemented for patients diagnosed with lymphoma on, or after, 1st October 2017.

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| ***Revision to inclusion criteria:*** |  ***Exclude Small Lymphocytic Lymphoma (SLL) from the dataset.*** |

# 6. Quality Performance Indicators for Lymphoma

## QPI 1 – Radiological Staging

|  |  |
| --- | --- |
| **QPI Title:** | Patients with lymphoma should be evaluated with appropriate imaging to detect the extent of disease and guide treatment decision making. |
| **Description:** | Proportion of patients with lymphoma undergoing treatment with curative intent who undergo Computed Tomography (CT) scanning of the chest, abdomen and pelvis or PET CT scanning prior to treatment, within 2 weeks of radiology request, and where the report is available within 3 weeks of radiology request.**Please note:** The specifications of this QPI are separated to ensure clear measurement of the following:1. Patients with lymphoma undergoing treatment with curative intent who are evaluated with appropriate imaging;
2. Patients with lymphoma undergoing treatment with curative intent who are evaluated with appropriate imaging within 2 weeks of radiology request; and
3. Patients with lymphoma undergoing treatment with curative intent who are evaluated with appropriate imaging where the report is available within 3 weeks of radiology request.
 |
| **Rationale and Evidence:** | Accurate staging is important to ensure appropriate treatment is delivered and futile interventions avoided. CT is recommended as the initial imaging investigation for all patients with lymphoma to detect extent of disease and guide treatment decision making. This should include CT of the chest, abdomen and pelvis. CT neck should also be undertaken where clinically appropriate. Intravenous contrast should be utilised unless contraindicated2. |
| **Specification (i):** | **Numerator:** | Number of patients with lymphoma undergoing treatment with curative intent who undergo CT of chest, abdomen and pelvis or PET CT scanning prior to treatment. |
| **Denominator:** | All patients with lymphoma undergoing treatment with curative intent. |
| **Exclusions** | * Patients who refuse investigation.
* Patients with primary cutaneous lymphoma.
 |
| **Specification (ii):** | **Numerator:** | Number of patients with lymphoma undergoing treatment with curative intent who undergo CT of chest, abdomen and pelvis or PET CT scanning prior to treatment and within 2 weeks of radiology request. |
| **Denominator:** | All patients with lymphoma undergoing treatment with curative intent who undergo CT of chest, abdomen and pelvis or PET CT scanning prior to treatment. |
| **Exclusions** | * None.
 |

(Continued overleaf…)

**QPI 1 – Radiological Staging (continued)**

|  |  |  |
| --- | --- | --- |
| **Specification (iii)** | **Numerator:****Denominator:****Exclusions** | Number of patients with lymphoma undergoing treatment with curative intent who undergo CT of chest, abdomen and pelvis or PET CT scanning prior to treatment where the report is available within 3 weeks of radiology request.All patients with lymphoma undergoing treatment with curative intent who undergo CT of chest, abdomen and pelvis or PET CT scanning prior to treatment.* None.
 |
| **Target:** | Specification (i): 95%The tolerance within this target is designed to account for patients with B-cell lymphoproliferative disorders that do not necessarily require extensive imaging.Specifications (ii) and (iii): 90% The tolerance within this target is designed to account for situations where imaging may be delayed due to factors of patient fitness or patient choice.  |

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| ***Revisions:*** | ***Target for specification (i) increased to 95%.*** ***Denominator for specification (ii) and (iii) changed to focus on those who have undergone CT/PET CT prior to treatment. Removed exclusions from (ii) and (iii) as no longer required due to denominator change.******Specification (iii) added – Patients undergoing CT/PET CT scanning prior to treatment with report available within 3 weeks of radiology request.*** |

## QPI 2 – Treatment Response

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| --- | --- |
| **QPI Title:** | Patients with Diffuse Large B Cell Lymphoma (DLBCL) who are treated with curative intent should have their response to treatment evaluated with appropriate imaging. |
| **Description:** | Proportion of patients with DLBCL who are undergoing chemotherapy treatment with curative intent, who have their response to treatment evaluated with Computed Tomography (CT) scan of the chest, abdomen and pelvis or PET CT scan. |
| **Rationale and Evidence:** | CT scanning is recommended as the most appropriate method of response assessment following chemotherapy for DLBCL2 as treatment response may not be clinically obvious.Evidence suggests that mid-treatment evaluation is best practice, unless there is a good clinical response to treatment2. Measurement of this is however not specifically included within this QPI.  |
| **Specification:** | **Numerator:** | Number of patients with DLBCL who are undergoing chemotherapy treatment with curative intent who undergo CT of chest, abdomen and pelvis or PET CT at end of chemotherapy treatment[[1]](#footnote-1). |
| **Denominator:** | All patients with DLBCL who are undergoing chemotherapy treatment with curative intent. |
| **Exclusions** | * Patients who died during treatment.
 |
| **Target:** | 90%The tolerance within this target is designed to account for the fact that some patients will have a good clinical response to chemotherapy and will therefore not require an end of treatment scan. It also accounts for those patients who may not complete chemotherapy treatment due to factors of fitness.  |

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| ***Revisions:*** | ***No change to QPI.*** |

## QPI 3 – Positron Emission Tomography (PET CT) Staging

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| **QPI Title:** | Patients with Classical Hodgkin Lymphoma (CHL) should be evaluated with PET CT scanning to detect the extent of disease and guide treatment decision making. |
| **Description:** | Proportion of patients with Classical Hodgkin Lymphoma undergoing treatment with curative intent who undergo PET CT scan prior to first treatment, within 2 weeks of radiology request, and where the report is available within 3 weeks of radiology request.**Please note:** The specifications of this QPI are separated to ensure clear measurement of the following:1. Patients with Classical Hodgkin Lymphoma undergoing treatment with curative intent who undergo PET CT scan prior to first treatment;
2. Patients with Classical Hodgkin Lymphoma undergoing treatment with curative intent who undergo PET CT scan prior to first treatment and within 2 weeks of radiology request; and
3. Patients with Classical Hodgkin Lymphoma undergoing treatment with curative intent who undergo PET CT scan prior to first treatment where the report is available within 3 weeks of radiology request.
 |
| **Rationale and Evidence:** | Accurate staging is important to ensure appropriate treatment is delivered and futile interventions avoided. All newly diagnosed patients with CHL being considered for curative therapy should have a baseline PET CT scan3.A whole body PET CT scan is recommended for the diagnosis of CHL to assess the extent of disease and therefore identify the most appropriate treatment option4. |
| **Specification (i):** | **Numerator:** | Number of patients with CHL undergoing treatment with curative intent who undergo PET CT prior to treatment. |
| **Denominator:** | All patients with CHL undergoing treatment with curative intent. |
| **Exclusions** | * Patients who refuse investigation.
 |
| **Specification (ii):** | **Numerator:** | Number of patients with CHL undergoing treatment with curative intent who undergo PET CT prior to treatment and within 2 weeks of radiology request. |
|  | **Denominator:** | All patients with CHL undergoing treatment with curative intent who undergo PET CT prior to treatment. |
|  | **Exclusions** | * None.
 |

(Continued overleaf…)

**QPI 3 – Positron Emission Tomography (PET CT) Staging (continued)**

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| **Specification (iii):** | **Numerator:****Denominator:****Exclusions:** | Number of patients with CHL undergoing treatment with curative intent who undergo PET CT prior to treatment where the report is available within 3 weeks of radiology request.All patients with CHL undergoing treatment with curative intent who undergo PET CT prior to treatment.* None.
 |
| **Target:** | 95% The tolerance within this target is designed to account for situations where patients are not fit enough to undergo all investigations prior to commencing treatment.  |

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| ***Revisions:*** | ***Denominator for specifications (ii) and (iii) changed to focus on those who have undergone PET CT prior to treatment. Removed exclusions from (ii) and (iii) as no longer required due to denominator change.******Specification (iii) added to QPI for patients with Classical Hodgkin Lymphoma (CHL) undergoing PET CT prior to treatment where the report is available within 3 weeks of radiology request.*** |

## QPI 4 – Cytogenetic Testing

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| **QPI Title:** | Patients with Burkitt Lymphoma and Diffuse Large B-Cell Lymphoma (DLBCL) should have MYC[[2]](#footnote-2) testing as part of diagnostic process, to identify those who may require central nervous system (CNS) prophylaxis and alternative treatment.  |
| **Description:** | Proportion of patients with Burkitt Lymphoma and DLBCL undergoing treatment with curative intent who have MYC testing as part of the diagnostic process. **Please note:** The specifications of this QPI are separated to ensure clear measurement of the following:1. Patients with Burkitt Lymphoma and DLBCL undergoing chemotherapy treatment with curative intent who have MYC results reported prior to first treatment; and
2. Patients with Burkitt Lymphoma and DLBCL undergoing chemotherapy treatment with curative intent who have MYC results reported within 3 weeks of commencing treatment.
 |
| **Rationale and Evidence:** | Classical cytogenetic or Fluorescence in Situ Hybridization (FISH) analysis is essential for the diagnosis of Burkitt lymphoma5.Rearrangements of MYC in DLBCL are a strong prognostic factor and will guide treatment options and provide important information to help inform patients and carers about the nature of the disease and prognosis7. Deregulation of MYC in DLBCL, as occurs in translocations involving the long arm of chromosome 8, is highly associated with aggressive disease and a poor prognosis. Detection of such a translocation by FISH is an important prognostic factor and will often lead to a change in management7. Cases approaching 100% ki67 and with deregulation of p53 (p53+ p21-) need to be investigated for MYC rearrangements to exclude Burkitt lymphoma6. Rearrangements of MYC, particularly in association with t(14;18) remain a strong prognostic factor in DLBCL7.  |
| **Specification (i):** | **Numerator:** | Number of patients with Burkitt Lymphoma and DLBCL undergoing chemotherapy treatment with curative intent who have MYC results reported prior to treatment. |
| **Denominator:** | All patients with Burkitt Lymphoma and DLBCL undergoing chemotherapy treatment with curative intent. |
| **Exclusions** | * No exclusions.
 |

(Continued overleaf)

**QPI 4 – Cytogenetic Testing (continued)**

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| **Specification (ii):** | **Numerator:** | Number of patients with Burkitt Lymphoma and DLBCL undergoing chemotherapy treatment with curative intent who have MYC results reported within 3 weeks of commencing treatment. |
| **Denominator:** | All patients with Burkitt Lymphoma and DLBCL undergoing chemotherapy treatment with curative intent. |
| **Exclusions** | * No exclusions.
 |
| **Target:** | Specification (i): 60%Specification (ii): 85% The tolerance within this target accounts for situations where there is no fresh tissue for cytogenetic analysis and there is insufficient tissue for FISH studies. Furthermore, MYC testing may not be appropriate if patients are not suitable for more intensive treatment, i.e. for factors of fitness or due to co-morbidities. |

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| ***Revisions:*** | ***QPI separated into 2 parts – wording has been revised in specification (i) to specifically state chemotherapy treatment.*** ***Specification (ii) added to focus on the availability of MYC results within 3 weeks of commencing treatment (chemotherapy) with more challenging target (85%).***  |

## QPI 5 – Lymphoma MDT

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| **QPI Title:** | Patients with lymphoma should be discussed by a multidisciplinary team following diagnosis. |
| **Description:** | Proportion of patients with lymphoma who are discussed at MDT meeting within 8 weeks of diagnosis. |
| **Rationale and Evidence:** | Evidence suggests that patients with cancer managed by a multi-disciplinary team have a better outcome. There is also evidence that the multidisciplinary management of patients increases their overall satisfaction with their care8.Discussion prior to definitive treatment decisions being made provides reassurance that patients are being managed appropriately. Within this QPI an 8 week from diagnosis timeframe has been utilised as the QPI Group agreed that, due to the complex referral and diagnostic pathway for patients with lymphoma, this was the most appropriate time period in which patients should be discussed at MDT.  |
| **Specifications:** | **Numerator:**  | Number of patients with lymphoma discussed at the MDT within 8 weeks of diagnosis. |
| **Denominator:**  | All patients with lymphoma. |
| **Exclusions:**  | * Patients who died before first treatment.
* Patients with primary cutaneous lymphoma.
 |
| **Target:** | 90%The tolerance within this target is designed to account for situations where additional complex diagnostic testing requires to be undertaken.  |

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| ***Revisions:*** | ***QPI updated to measure patients with lymphoma who are discussed at MDT meeting within 8 weeks of diagnosis (increased from 6 weeks).******Target increased from 85% to 90%.*** |

## QPI 6 – Treatment for Follicular Lymphoma and Diffuse Large B-Cell Lymphoma

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| --- | --- |
| **QPI Title:** | Patients with symptomatic advanced\* follicular lymphoma and Diffuse Large B Cell Lymphoma (DLBCL) should undergo treatment with anti-B cell monoclonal antibody therapy[[3]](#footnote-3) in combination with chemotherapy. |
| **Description:** | Proportion of patients with follicular lymphoma and DLBCL undergoing treatment with chemotherapy who receive anti-B cell monoclonal antibody therapy. |
| **Rationale and Evidence:** | Patients with symptomatic advanced stage follicular lymphoma and DLBCL should receive rituximab in combination with chemotherapy as this increases response to chemotherapy and provides a progression free, and overall, survival benefit 2,9. Rituximab in combination with chemotherapy is recommended for the treatment of patients with symptomatic advanced stage follicular lymphoma 2,9.Rituximab is recommended for use in NHSScotland by the Scottish Medicines Consortium. When added to a number of different chemotherapy regimens it produced statistically significant improvements in survival when compared with chemotherapy regimens alone10. \* As it is difficult to accurately identify those patients with symptomatic advanced follicular lymphoma, the number of patients with follicular lymphoma undergoing chemotherapy is being utilised as a proxy measure for symptomatic advanced disease. |
| **Specifications:** | **Numerator:** | Number of patients with follicular lymphoma and DLBCL who receive chemotherapy in combination with anti-B cell monoclonal antibody therapy. |
| **Denominator:** | All patients with follicular lymphoma and DLBCL who receive chemotherapy. |
| **Exclusions** | * Patients who refuse chemotherapy.
* Patients enrolled in clinical trials.
 |
| **Target:** | 95%The tolerance within this target accounts for that fact that due to co-morbidities and fitness levels not all patients will require or be suitable for anti-B cell monoclonal antibody therapy.  |

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| ***Revisions:*** | ***QPI wording updated to remove reference to rituximab and replace with anti-B cell monoclonal antibody therapy.******Footnote added regarding current practice in relation to rituximab.*** |

## QPI 10 – Primary Cutaneous Lymphoma

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| --- | --- |
| **QPI Title:** | Patients with primary cutaneous lymphoma should be discussed at a specialist MDT meeting. |
| **Description:** | Proportion of patients with primary cutaneous lymphoma who are discussed at a specialist MDT meeting which includes representation from pathology, dermatology, oncology ± haemato-oncology. |
| **Rationale and Evidence:** | A specialist MDT for patients with primary cutaneous lymphoma facilitates clinico-pathological correlation, which is very important in this group of conditions where treatment is multi-faceted. Furthermore it allows for consolidation of expertise in this rare condition which will help develop robust diagnosis and management. |
| **Specifications:** | **Numerator:** | Number of patients with primary cutaneous lymphoma who are discussed at a specialist MDT meeting. |
| **Denominator:** | All patients with primary cutaneous lymphoma. |
| **Exclusions** | * No exclusions.
 |
| **Target:** | 95%  |

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| ***Revisions:*** | ***No changes to QPI.*** |

## QPI 11 – Hepatitis and HIV Status

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| --- | --- |
| **QPI Title:** | Virological testing for Human Immunodeficiency Virus (HIV), hepatitis B and C should be undertaken for patients undergoing anti-B cell monoclonal antibody therapy[[4]](#footnote-4).  |
| **Description:** | Proportion of patients with lymphoma undergoing anti-B cell monoclonal antibody therapy who have hepatitis B, hepatitis C and HIV status checked prior to treatment. |
| **Rationale and Evidence:** | Clinical assessment and virological testing for HIV, hepatitis B and C should be undertaken for all patients as part of the diagnostic process and in all patients considered at risk of virus reactivation 2 4. All patients who are found to be hepatitis B should receive the appropriate anti-viral prophylaxis and those found to be HIV positive should receive appropriate anti-retroviral treatment before commencing treatment.  |
| **Specifications:** | **Numerator:** | Number of patients with lymphoma undergoing anti-B cell monoclonal antibody therapy who have hepatitis B, C and HIV status checked prior to treatment. |
| **Denominator:** | All patients with lymphoma undergoing anti-B cell monoclonal antibody therapy. |
| **Exclusions** | * No exclusions.
 |
| **Target:** | 95% The tolerance within this target accounts for situations where patients undergo other treatments prior to anti-B cell monoclonal antibody therapy.  |

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| ***Revisions:*** | ***Target lowered from 100% to 95%.******QPI wording updated to remove reference to rituximab and replace with anti-B cell monoclonal antibody therapy.******Footnote added regarding current practice in relation to rituximab.*** |

## QPI 12 – Treatment Response in Hodgkin Lymphoma

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| --- | --- |
| **QPI Title:** | Patients with advanced Hodgkin Lymphoma who receive treatment with ABVD[[5]](#footnote-5) chemotherapy should have early assessment of response by appropriate imaging. |
| **Description:** | Proportion of patients with advanced Hodgkin Lymphoma (stage 2B and above) who receive ABVD chemotherapy treatment, that have their treatment evaluated with PET CT scan after 2 cycles of chemotherapy.  |
| **Rationale and Evidence:** | PET CT demonstrates a higher level of accuracy compared with contrast CT scan and is therefore the most appropriate method of response assessment following chemotherapy in lymphoma patients11. Interim PET CT is recommended for patients with advanced Hodgkin Lymphoma undergoing treatment with ABVD chemotherapy as this is an indicator of predicted treatment success when continuing treatment11,12. Evidence suggests that the optimal timing for PET CT to be carried out is following 2 cycles of ABVD chemotherapy11.  |
| **Specification:** | **Numerator:** | Number of patients with advanced Hodgkin Lymphoma (stage 2B and above) who receive ABVD chemotherapy treatment that undergo PET CT scan after 2[[6]](#footnote-6) cycles of chemotherapy. |
| **Denominator:** | All patients with advanced Hodgkin Lymphoma (stage 2B and above) who receive ABVD chemotherapy treatment. |
| **Exclusions** | * Patients who died during treatment.
 |
| **Target:** | 80%The tolerance within this target is designed to account for those patients who may not complete ABVD chemotherapy treatment due to factors of fitness. It also accounts for those patients where PET CT may not be appropriate as the result will not alter management due to co-morbidities or fitness.  |

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| ***Revisions:*** | ***NEW QPI*** |

## QPI 13 – Maintenance Therapy for Follicular Lymphoma

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| **QPI Title:** | Patients with follicular lymphoma undergoing R-Chemotherapy[[7]](#footnote-7) should receive maintenance therapy with rituximab. |
| **Description:** | Proportion of patients with follicular lymphoma undergoing treatment with R-Chemotherapy who receive maintenance therapy with rituximab. |
| **Rationale and Evidence:** | Maintenance treatment with rituximab can prolong the time until relapse and delay the need for more treatment2.It is recommended that patients with follicular lymphoma responding to first line rituximab based chemotherapy should receive rituximab maintenance therapy as this has progression free survival benefits2,13 . |
| **Specifications:** | **Numerator:** | Number of patients with follicular lymphoma who undergo treatment with R-Chemotherapy who receive maintenance therapy with rituximab. |
| **Denominator:** | All patients with follicular lymphoma who undergo treatment with R-Chemotherapy. |
| **Exclusions** | * Patients who refuse chemotherapy.
* Patients enrolled in clinical trials.
* Patients who died before chemotherapy treatment.
 |
| **Target:** | 90%The tolerance within this target accounts for the fact that some patients will not respond to chemotherapy treatment and therefore not be appropriate for maintenance therapy with rituximab. Maintenance therapy may also not be suitable due to co-morbidities and fitness levels.  |

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| ***Revisions:*** | ***NEW QPI*** |

## QPI 14 – Clinical Trial Access

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| ***Revisions:*** | ***This QPI which is applicable to all tumour sites is currently under review.*** ***The revised Clinical Trial Access QPI will be included within the final Lymphoma QPI document.***  |

# 7. Survival

Improving survival forms an integral part of the national cancer quality improvement programme. Lymphoma survival analysis will be reported and analysed on a 3 yearly basis by Information Services Division (ISD). The specific issues which will be addressed will be identified by an expert group ahead of any analysis being undertaken, as per the agreed national cancer quality governance and improvement framework.

The Lymphoma Cancer QPI Group has identified, during the QPI development process, the following issues for survival analysis:

* 2 and 5 year overall survival

To ensure consistent application of survival analysis, it has been agreed that a single analyst on behalf of all three regional cancer networks undertakes this work. Survival analysis will be scheduled as per the national survival analysis and reporting timetable, agreed with the National Cancer Quality Steering Group and Scottish Cancer Taskforce. This reflects the requirement for record linkage and the more technical requirements of survival analyses which would make it difficult for individual Boards to undertake routinely and in a nationally consistent manner.

# 8. Areas for Future Consideration

The Lymphoma QPI Groups have not been able to identify sufficient evidence, or determine appropriate measurability specifications, to address all areas felt to be of key importance in the treatment of lymphoma, and therefore in improving the quality of care for patients affected by lymphoma.

The following areas for future consideration have been raised across the lifetime of the Lymphoma QPIs:

* Timely Hickman line insertion and maintenance of Hickman lines.
* Histology minimum panels for diagnosis of lymphoma.
* Production of final integrated report for all patients with lymphoma before treatment
* Access to a specific cancer nurse specialist.

# 9. Governance and Scrutiny

A national and regional governance framework to assure the quality of cancer services in NHSScotland has been developed; key roles and responsibilities within this are set out below. Appendices 4 and 5 provide an overview of these governance arrangements diagrammatically. The importance of ensuring robust local governance processes are in place is recognised and it is essential that NHS Boards ensure that cancer clinical audit is fully embedded within established processes.

## 9.1 National

* Scottish Cancer Taskforce
	+ - Accountable for overall national cancer quality programme and overseeing the quality of cancer care across NHSScotland.
		- Advising Scottish Government Health and Social Care Directorate (SGHSCD) if escalation required.
* Healthcare Improvement Scotland
	+ - Proportionate scrutiny of performance.
		- Support performance improvement.
		- Quality assurance: ensure robust action plans are in place and being progressed via regions/Boards to address any issues identified.
* Information Services Division (ISD)
* Publish national comparative report on tumour specific QPIs and survival for three tumour types per annum and specified generic QPIs as part of the rolling programme of reporting.

## 9.2 Regional – Regional Cancer Networks

* Annual regional comparative analysis and reporting against tumour specific QPIs.
* Support national comparative reporting of specified generic QPIs.
* Identify and share good practice.
* In conjunction with constituent NHS Boards identify regional and local actions required to develop an action plan to address regional issues identified.
* Review and monitoring of progress against agreed actions.
* Provide assurance to NHS Board Chief Executive Officers and Scottish Cancer Taskforce that any issues identified have been adequately and timeously progressed.

## 9.3 Local – NHS Boards

* Collect and submit data for regional comparative analysis and reporting in line with agreed measurability and reporting schedule (generic and tumour specific QPIs).
* Utilise local governance structures to review performance, develop local action plans and monitor delivery.
* Demonstrate continual improvements in quality of care through on-going review, analysis and feedback of clinical audit data at an individual multidisciplinary team (MDT) or unit level.

# 10. How to participate in the engagement process

In order to ensure wide inclusiveness of clinical and management colleagues from across NHSScotland, patients affected by lymphoma and the wider public, several different methods of engagement are being pursued:

**Professional groups, health service staff, voluntary organisations and individuals:**

* Wide circulation of the draft documentation for comment and feedback.

**Patient representative groups:**

* Organised patient focus group sessions to be held.

## 10.1 Submitting your comments

You can submit your comments on the Revised Lymphoma QPIs via the Scottish Government Consultation Hub (website link below):

<https://consult.scotland.gov.uk/west-of-scotland-cancer-network/lymphoma-cancer-qpi>

All responses should be submitted by **Monday 11th September 2017.**

**If you require any further information regarding the engagement process please use the email address below.**

Email: **LymphomaQPIPublicEngagement@gov.scot**

## 10.2 Engagement feedback

At the end of the engagement period, all comments and responses will be collated for review by the Lymphoma Formal Review Group. Those who have participated in the engagement process will receive an overview of the changes made and a copy of the final Lymphoma QPI document.11. References

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#

# 12. Appendices

## Appendix 1: QPI Development Process

**Preparatory Work and Scoping**

The preparatory work involved the development of a structured briefing paper by Healthcare Improvement Scotland. This paper took account of existing, high quality, clinical guidance and provided a basis for the development of QPIs.

The scope for development of Lymphoma QPIs and a search narrative were defined and agreed by the Lymphoma QPI Development Group. The table below shows the final search criteria used in the literature search.

|  |  |
| --- | --- |
| Inclusion | Exclusion |
| *Topics* (**population/patient**): * Hodgkin’s Lymphoma, primary cutaneous lymphoma and non-Hodgkin’s Lymphoma.

*Topics* **(intervention)**: * Diagnosis
* Staging
* Imaging
* CNS prophylaxis
* Treatment of disease (including treatment with curative and non-curative intent)

Follow up management of disease | *Topics:* prevention, screening, communication, information sharing and support and palliative/end of life care. |
| Adults only (16 years of age or over) |  |
| Date: 2005 to present day  |  |
| Language: English only |  |

**Table 1 – Lymphoma Search Criteria**

A systematic search was carried out by Healthcare Improvement Scotland using selected websites and two primary medical databases to identify national and international guidelines.

Thirteen guidelines were appraised for quality using the AGREE II instrument. The instrument assesses the methodological rigour and precision used when developing a guideline. Two of the guidelines were not recommended for use. Of the remaining eleven guidelines, all were recommended for use.

**Indicator Development**

The Lymphoma QPI Development group defined evidence based, measurable indicators with a clear focus on improving the quality and outcome of care provided.

The Group developed QPIs using the clinical recommendations set out in the briefing paper as a base, ensuring all indicators met the following criteria:

* **Overall importance** – does the indicator address an area of clinical importance that would significantly impact on the quality and outcome of care delivered?
* **Evidence based** – is the indicator based on high quality clinical evidence?
* **Measurability** – is the indicator measurable i.e. are there explicit requirements for data measurement and are the required data items accessible and available for collection?

**Engagement Process**

A wide clinical and public engagement exercise was undertaken as part of development in May 2013 where the Lymphoma QPIs, along with accompanying draft minimum core dataset and measurability specifications, were made available on the Scottish Government website. During the engagement period clinical and management colleagues from across NHSScotland, patients affected by lymphoma cancer and the wider public were given the opportunity to influence the development of Lymphoma QPIs.

Draft documentation was circulated widely to professional groups, health service staff, voluntary organisations and individuals for comment and feedback.

Following the engagement period all comments and responses received were reviewed by the Lymphoma Cancer QPI Development Group and used to produce and refine the final indicators.

## Appendix 2: Lymphoma QPI Development Group Membership (2012)

##

| **Name** | **Designation** | **Cancer Network/Base** |
| --- | --- | --- |
| Matthew Barber | Consultant Breast Surgeon (CHAIR) | SCAN |
| Iain Andrews | Consultant Radiologist | WoSCAN (Gartnavel General Hospital, Glasgow) |
| Kathy Burton | Cancer Audit Manager | SCAN (Queen Margaret Hospital, Fife) |
| Dominic Culligan | Consultant Haematologist  | NOSCAN (Aberdeen Royal Infirmary) |
| Susan Cumming | Haematology Audit/ MDT Co-ordinator | NOSCAN (Raigmore Hospital, Inverness) |
| Cathy Dowdle | Advanced Nurse Practitioner | WoSCAN (Beatson West of Scotland Cancer Centre) |
| John Good | Patient Representative |  |
| John Goodlad | Consultant Pathologist | SCAN (Western General Hospital, Edinburgh) |
| Bob Jackson | Consultant Pathologist | WoSCAN (Southern General Hospital, Glasgow)  |
| Simon Jackson | Consultant Radiologist | SCAN (Western General Hospital, Edinburgh) |
| Neil Kernohan | Consultant Pathologist | NOSCAN (Ninewells Hospital, Dundee) |
| Mike Leach | Consultant Haematologist | WoSCAN (Beatson West of Scotland Cancer Centre) |
| Graham Macdonald | Consultant Clinical Oncologist | NOSCAN (Aberdeen Royal Infirmary) |
| Jean MacKenzie | Patient Representative |  |
| Pam McKay | Consultant Haematologist | WoSCAN (Beatson West of Scotland Cancer Centre) |
| Jean McKnight | Haematology Research Nurse | SCAN (Western General Hospital, Edinburgh) |
| David Meiklejohn | Consultant Haematologist | NOSCAN (Ninewells Hospital, Dundee) |
| Brian Murray | Principal Information Development Manager | ISD |
| Noelle O’Rourke | Consultant Clinical Oncologist | WoSCAN (Beatson West of Scotland Cancer Centre) |
| Norman Pratt | Head of Laboratory Services, Human Genetics Unit | NOSCAN (Ninewells Hospital, Dundee) |
| Iona Scott | Project Manager | WoSCAN |
| Fiona Scott | Consultant Haematologist | SCAN (Western General Hospital, Edinburgh) |
| Evelyn Thomson | Regional Manager (Cancer) | WoSCAN |
| Heather Whately | Charge Nurse - Haematology | NOSCAN (Ninewells Hospital, Dundee) |
| Heather Wotherspoon | MCN Manager/Audit Facilitator  | WoSCAN |

## Appendix 3: Lymphoma QPI Formal Review Group Membership (2017)

| **Name** | **Designation** | **Cancer Network/Base** |
| --- | --- | --- |
| Matthew Barber | Consultant Breast Surgeon (CHAIR) | SCAN |
| David Meiklejohn | Clinical Lead | NOSCAN |
| Pam McKay | Clinical Lead | WoSCAN |
| Fiona Scott | Clinical Lead | SCAN |
| Carol Marshall | Information Manager | WoSCAN |
| Jennifer Doherty | National Cancer Quality Programme Co-ordinator | WoSCAN |
| Lorraine Stirling | Project Officer | WoSCAN |

SCAN - South East Scotland Cancer Network

NOSCAN - North of Scotland Cancer Network

WoSCAN - West of Scotland Cancer Network

## Appendix 4: 3 Yearly National Governance Process & Improvement Framework for Cancer Care

*This process is underpinned by the annual regional reporting and governance framework (see appendix 6).*

|  |  |
| --- | --- |
| **Development of nationally agreed QPIs, dataset and measurability** | **1. National QPI Development Stage*** QPIs developed by QPI development groups, which include representation from Regional Cancer Networks, Healthcare Improvement Scotland, ISD, patient representatives and the Cancer Coalition.
 |
| **Data collection, analysis, reporting and publication*****Satisfactory performance***  | **2. Data Analysis Stage:*** NHS Boards and Regional Cancer Advisory Groups (RCAGs)\* collect data and analyse on yearly basis using nationally agreed measurability criteria and produce action plans to address areas of variance, see appendix 6.
* Submit yearly reports to ISD for collation and publication every 3 years.
* National comparative report approved by NHS Boards and RCAGs.
* ISD produce comparative, publicly available, national report consisting of trend analysis of 3 years data and survival analysis.
 |
| **Expert Review Group convened to review results****Where required, if significant variance identified** | **3. Expert Review Group Stage (for 3 tumour types per year):*** Expert group, hosted by Healthcare Improvement Scotland, review comparative national results.
* Write to RCAGs highlighting areas of good practice and variances.
* Where required NHS Boards requested to submit improvement plans for any outstanding unresolved issues with timescales for improvement to expert group.
* Improvement plans ratified by expert group and Scottish Cancer Taskforce.
 |
| **Improvement Support** | **4. Improvement Support Stage:*** Where required Healthcare Improvement Scotland provide expertise on improvement methodologies and support.
 |
| **If progress acceptable****Monitoring****If progress not acceptable** | **5. Monitoring Stage:*** RCAGs work with Boards to progress outstanding actions, monitor improvement plans and submit progress report to Healthcare Improvement Scotland.
* Healthcare Improvement Scotland report to Scottish Cancer Taskforce as to whether progress is acceptable**.**
 |
| **Action if failure to progress improvement** | **6. Escalation Stage:*** If progress not acceptable, Healthcare Improvement Scotland will visit the service concerned and work with the RCAG and Board to address issues.
* Report submitted to Scottish Cancer Taskforce and escalation with a proposal to take forward to Scottish Government Health Department.
 |

\*In the South and East of Scotland Cancer Network (SCAN) the Regional Cancer Planning Group is the equivalent group to Regional Cancer Advisory Group (RCAG).

## Appendix 5: Regional Annual Governance Process and Improvement Framework for Cancer Care

|  |  |
| --- | --- |
| **Regional implementation of nationally agreed QPIs** | **1. Regional QPI Implementation Stage:*** National cancer QPIs and associated national minimum core dataset and measurability specifications, developed by QPI development groups.
* Regional implementation of nationally agreed dataset to enable reporting of QPIs.
 |
| **Data collection, analysis, reporting and publication*****Satisfactory performance***  | **2. Data Analysis Stage:*** NHS Boards collect data and data is analysed on a yearly basis using nationally agreed measurability criteria at local/ regional level.
* Data/results validated by Boards and annual regional comparative report produced by Regional Networks.
* Areas of best practice and variance across the region highlighted.
* Yearly regional reports submitted to ISD for collation and presentation in national report every 3 years.
 |
| **Results reviewed by RCAGs** | **3. Regional Performance Review Stage:*** RCAGs\* review regional comparative report.
* Regional or local NHS Board action plans to address areas of variance developed.
* Appropriate leads identified to progress each action.
* Action plans ratified by RCAGs.
 |
| **If progress acceptable****Monitoring** | **4. Monitoring Stage:*** Where required, NHS Boards monitor progress with action plans and submit progress reports to RCAGs.
* RCAGs review and monitor regional improvement.
 |
| **Improvement Support****If progress not acceptable** | **5. Improvement Support Stage:*** Where required Healthcare Improvement Scotland maybe requested to provide expertise to NHS Boards/RCAGs on improvement methodologies and support.
 |
| **Action if failure to progress improvement** | **6. Escalation Stage:*** If progress not acceptable, RCAGs will escalate any issues to relevant Board Chief Executives. If progress remains unacceptable RCAGs will escalate any relevant issues to Healthcare Improvement Scotland.
 |

\*In the South and East of Scotland Cancer Network (SCAN) the Regional Cancer Planning Group is the equivalent group to Regional Cancer Advisory Group (RCAG).

## Appendix 6: Glossary of Terms

|  |  |
| --- | --- |
| **Asymptomatic** | Having no symptoms. You are considered asymptomatic if you:* Have recovered from an illness or condition and no longer have symptoms.
* Have an illness or condition (such as early stage high blood pressure or glaucoma) but do not have symptoms.
 |
| **Burkitt Lymphoma**  | An aggressive (fast-growing) type of B-cell non-Hodgkin lymphoma that occurs most often in children and young adults. The disease may affect the jaw, central nervous system, bowel, kidneys, ovaries, or other organs. There are three main types of Burkitt lymphoma (sporadic, endemic, and immunodeficiency related). |
| **Central Nervous System (CNS)** | The brain and spinal cord. |
| **Chemotherapy** | The use of drugs that kill cancer cells, or prevent or slow their growth. |
| **Chromosome** | Part of a cell that contains genetic information. |
| **Classical Hodgkin Lymphoma (CHL)** | The most common type of Hodgkin lymphoma. |
| **Clinical Trials** | A type of research study that tests how well new medical approaches or medicines work. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease. |
| **CNS prophylaxis** | Treatment given to prevent spread of disease to the central nervous system. |
| **Combined modality treatment**  | The treatment of a disease or condition by several different means simultaneously or sequentially. |
| **Co-morbidity** | The condition of having two or more diseases at the same time. |
| **Computed Tomography (CT)**  | An x-ray imaging technique, which allows detailed investigation of the internal organ of the body.  |
| **Contraindication/ Contraindicated** | A symptom or medical condition that makes a particular treatment or procedure inadvisable because a person is likely to have a bad reaction. |
| **Curative intent** | Treatment which is given with the aim of curing the cancer. |
| **Cytogenetics**  | The study of chromosomes and chromosomal abnormalities. |
| **Cytotoxic** | Toxic to cells. This term is used to describe drugs which kill cancer cells or slow their growth. |
| **Dermatology** | A branch of medicine concerned with the study and treatment of disorders of the skin. |
| **Diagnosis** | The process of identifying a disease, such as cancer, from its signs and symptoms. |
| **Diffuse Large B-Cell lymphoma (DLBCL)** | A type of B-cell non-Hodgkin lymphoma (cancer of the immune system) that is usually aggressive (fast-growing). It is the most common type of non-Hodgkin lymphoma, and is marked by rapidly growing tumours in the lymph nodes, spleen, liver, bone marrow, or other organs. |
| **Fluorescence in situ hybridization (FISH)** | Provides researchers with a way to visualize and map the genetic material in an individual's cells, including specific genes or portions of genes. This is important for understanding a variety of chromosomal abnormalities and other genetic mutations. |
| **Follicular Lymphoma**  | A type of non-Hodgkin lymphoma that is usually indolent (slow-growing) divided into 3 separate grades (1, 2 and 3). |
| **Grading** | The degree of malignancy of a tumour, i.e. how closely the cancer cells look like normal cells. |
| **Haemato-oncology** | A branch of medicine concerned with the study and treatment of cancers of the blood and blood-forming tissues. |
| **Hepatitis B**  | A virus that causes hepatitis (inflammation of the liver). It is carried and passed to others through the blood and other body fluids. |
| **Hepatitis C**  | A virus that causes hepatitis (inflammation of the liver). It is carried and passed to others through the blood and other body fluids. Although patients who are infected with hepatitis C virus may not have symptoms, long-term infection may lead to cirrhosis (scarring of the liver) and liver cancer. These patients may also have an increased risk for certain types of non-Hodgkin lymphoma. |
| **Hickman line** | A fine plastic cannula inserted under the skin of your chest into a vein to allow administration of drugs and repeated blood samples.  |
| **Hodgkin Lymphoma** | Cancer of the lymphatic system. There are 2 main types of Hodgkin lymphoma; classical Hodgkin lymphoma and nodular lymphocyte predominant Hodgkin lymphoma. |
| **Human Immunodeficiency Virus (HIV)**  | The cause of acquired immunodeficiency syndrome (AIDS). |
| **Imaging**  | Medical imaging is process used to create images of the body for clinical purposes.  |
| **Immunohistochemistry (IHC)** | A technique used to identify specific molecules in different kinds of tissue. The tissue is treated with antibodies that bind the specific molecule. These are made visible under a microscope by using a colour reaction, a radioisotope, colloidal gold, or a fluorescent dye. Immunohistochemistry is used to help diagnose diseases, such as cancer, and to detect the presence of micro organisms. It is also used in basic research to understand how cells grow and differentiate (become more specialized). |
| **Intravenous contrast** | A substance administered directly into the bloodstream to enhance the visibility of structures on imaging. |
| **Lymphatic system** | Complex network of tubes (lymphatic vessels), glands (lymph nodes) and other organs including the spleen. |
| **Lymphoma**  | Cancer of the lymphatic system. There are two main types of lymphoma – Hodgkin Lymphoma and non-Hodgkin Lymphoma. |
| **Mediastinal** | Relating to the mediastinum, the space in the chest cavity between the 2 pleural sacs. |
| **Multi-disciplinary team meeting (MDT)** | A meeting which is held on a regular basis, which is made up of participants from various disciplines appropriate to the disease area, where diagnosis, management, and appropriate treatment of patients is discussed and decided. |
| **MYC**  | MYC is a regulator gene located on chromosome 8.  Deregulation of MYC in diffuse large B-cell lymphoma, as occurs in translocations involving the long arm of chromosome 8, is highly associated with aggressive disease and a poor prognosis. Detection of such a translocation by Fluorescent in-situ hybridisation (FISH) is an important prognostic factor and will often lead to a change in management.  |
| **Nodal** | Relating to lymph nodes. |
| **Non-Hodgkin Lymphoma**  | Cancer of the lymphatic system. There are two main groups – high grade which are aggressive and fast growing and low grade which are slow growing. High grade lymphomas include: Diffuse Large B Cell Lymphoma (DLBCL), Peripheral T-cell Lymphoma, Burkitt’s Lymphoma, Mantle Cell Lymphoma and AIDS-related lymphoma. Low grade or indolent lymphomas include: Follicular Lymphomas, Waldenstrom’s Lymphoma and Marginal Zone Lymphomas. |
| **Oncology** | The study of the biology and physical and chemical features of cancers. Also the study of the causes and treatment of cancers. |
| **Pathology/Pathological** | The study of disease processes with the aim of understanding their nature and causes. This is achieved by observing samples of fluid and tissues obtained from the living patient by various methods, or at post mortem. |
| **Positron Emission Tomography - Computed Tomography (PET-CT)** | A highly specialised imaging technique used to produce a computerised image of metabolic activity of body tissues. It may be used to diagnose a cancer, show what stage it is, or see how well you are responding to treatment. |
| **Primary cutaneous lymphoma** | A rare type of non-Hodgkin lymphoma that presents in the skin with no evidence of extracutaneous disease at the time of diagnosis. |
| **Prognosis** | An assessment of the expected future course and outcome of a person’s disease. |
| **Prognostic Factors** | Factors, such as staging, tumour type or deprivation that may influence treatment effectiveness and outcomes. |
| **Prophylaxis** | An intervention used to prevent an unwanted outcome. |
| **Radiological** | The use of imaging technologies (such as ultrasound and magnetic resonance imaging) to diagnose or treat disease. |
| **Radiotherapy** | The use of radiation to treat disease. |
| **Rituximab**  | Rituximab belongs to a group of cancer drugs known as monoclonal antibodies. Monoclonal antibodies recognise and lock on to specific proteins on the surface of cancer cells. This helps the body's immune system recognise the cancer cells and destroy them. Monoclonal antibodies are sometimes called targeted therapies because they target cancer cells.  |
| **Scottish Medicines Consortium (SMC)** | The purpose of the SMC is to accept for use those newly licensed drugs that clearly represent good value for money to NHSScotland. SMC analyses information supplied by the drug manufacturer on the health benefits of the drug and justification of its price.  |
| **Staging** | Process of describing to what degree cancer has spread from its original site to another part of the body. Staging involves clinical, surgical and pathology assessments. |
| **Survival** | The percentage of people in a study or treatment group who are alive for a certain period of time after they were diagnosed with or treated for a disease, such as cancer. |
| **Symptomatic** | Having to do with symptoms, which are signs of a condition or disease. |
| **Systemic Anti Cancer Therapy (SACT)** | Treatment of cancer using drugs which prevent the replicationor growth of cancer cells. This encompasses biological therapies and cytotoxic chemotherapy. |
| **Translocation** | A genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. Sometimes pieces from two different chromosomes will trade places with each other.  |
| **Virological Testing** | Used to diagnose infection, and most importantly guide treatment decisions and assess the virological response to antiviral therapy. |

1. Within the measurement of this QPI, CT scans within 3 months of the final cycle of chemotherapy, or final fraction of radiotherapy in patients undergoing combined modality treatment, will be classified as an end of treatment scan. [↑](#footnote-ref-1)
2. MYC is a regulator gene located on chromosome 8.  9 [↑](#footnote-ref-2)
3. At time of publication, rituximab is the only anti-B cell monoclonal antibody therapy approved by the Scottish Medicines Consortium (SMC) for first line treatment of lymphoma. [↑](#footnote-ref-3)
4. At time of publication, rituximab is the only anti-B cell monoclonal antibody therapy approved by the Scottish Medicines Consortium (SMC) for first line treatment of lymphoma. [↑](#footnote-ref-4)
5. ABVD is a chemotherapy regimen which includes Doxorubicin, Bleomycin, Vinblastine and Dacarbazine. [↑](#footnote-ref-5)
6. PET CT Scans should be carried out after day 15 of the 2nd cycle and before day 1 of the 3rd cycle of chemotherapy treatment. [↑](#footnote-ref-6)
7. R-Chemotherapy is a chemotherapy regimen that includes rituximab. Examples include but are not limited to R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone), R-CVP (rituximab, cyclophosphamide, vincristine, and prednisolone), and R-bendamustine (rituximab and bendamustine). [↑](#footnote-ref-7)