Public Health England

Protecting and improving the nation's health

Case mix adjusted 30-day mortality post systemic anti-cancer therapy rates

A companion brief to support the interpretation of this data

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Summary

In June 2020, the National Cancer Registration and Analysis Service (NCRAS) team at Public Health England (PHE) produced a workbook documenting case mix adjusted 30-day mortality post systemic anti-cancer therapy (SACT) rates (CMAR) for four tumour sites. These CMAR were calculated for NHS trusts and the workbook was circulated to all trusts. The data is case mix adjusted to allow for comparisons to be made between trusts and within trusts over time. Trusts were able to request NHS numbers of patients who had died within 30 days of receiving SACT at their trust. We developed this information to support clinical governance at trusts and potentially identify areas where clinical care could be improved. We provided all trusts with the opportunity to comment on their data.

Background

In 2016, the SACT team at PHE published a paper in the Lancet Oncology providing 30-day mortality post SACT rates for breast and lung cancer. NHS trusts, NHS England and the clinical community fed back to PHE that this work had been beneficial in terms of setting a national benchmark, identifying variation in clinical practice between trusts and identifying areas where patient care could have been improved. This information helped to inform advancements to clinical practice.

In December 2018, the SACT team released a workbook to trusts providing crude rates for 30-day mortality post SACT for all cancers combined and breakdowns for Acute Myeloid Leukaemia, Breast, Colon, Children's Teenagers and Young Adults (CTYA), Small Cell Lung Cancer, Non-Small Cell Lung Cancer, Upper Gastro-Intestinal Oesophageal.

Feedback generated from this release highlighted the need for 30-day mortality data which was more timely to support clinical audit, as well as case-mix adjusted which would facilitate the comparison of performance between trusts. Unfortunately, these two needs cannot be met in a single data feed. Case mix adjusted data cannot be produced soon enough after treatment activity to support clinical audit as it requires linkage to cancer registry data to provide supplementary patient information which operates at an 18-month time lag, and additional analytical time to conduct the work. Furthermore, for rarer cancer types, case mix adjustment may only be possible when several years of data have accrued to provide sufficient patient number to support analysis. The SACT team have therefore met these two needs through two outputs: the Rapid Data Review (RDR) and the CMAR. The RDR provides a quarterly data feed to all NHS trusts in England providing key information on patients who died within 30 days of receiving SACT at their trust. This aims to inform 'mortality and morbidity' meetings and develop communications between trusts on initiatives undertaken to reduce 30-day mortality. The CMAR produces 30-day mortality post SACT rates that are adjusted for key variables which means that rates can be compared between trusts and within trusts over time.

Workbook

The workbook is based on routine data submitted by NHS trusts to the SACT dataset and includes patients diagnosed with cancer in England between 2010 and 2017 and treated with SACT in all NHS trusts in England between January 2017 and December 2018[1]. The period of treatment activity used varies depending on the cancer type studied (see Table 2) and patients were only included if they received their latest treatment during the treatment period (i.e. patients still receiving treatment in 2019 were excluded). Each patient was allocated to the trust where they received their final treatment, regardless of any prior treatment received at other trusts.

Table 1. ICD-10 code, morphology code and treatment activity covered for each cancer site

Cancer site	ICD-10 code and morphology code	Period of treatment activity
Lung	Non-Small Cell Lung Cancer: • ICD-10: C33-C34, C37-C39 • Morphology: M8012/3, M8013/3, M8046/3, M8050/3, M8070/3, M8070/6, M8071/3, M8072/3, M8074/3, M8075/3, M8140/3, M8140/6, M8200/3, M8240/3, M8246/3, M8249/3, M8250/3, M8253/3, M8255/3, M8260/3, M8263/3, M8310/3, M8370/3, M8470/3, M8480/3, M8481/3, M8490/3, M8520/3, M8550/3, M8560/3, M8574/3, M8575/3 Small Cell Lung Cancer: • ICD-10: C33-C34, C37-C39 • Morphology: M8002/3, M8041/3, M8042/3, M8044/3, M8045/3 Unknown morphology: • ICD-10: C33-C34, C37-C39 • Morphology not recorded	Jan 2018 – Dec 2018
Cancer of Unknown Primary (CUP)	C77-C80	Jan 2017 – Dec 2018
Gastric	Small Intestine Cancer: • ICD-10: C17 Stomach Cancer: • ICD-10: C16	Jan 2017 – Dec 2018
Pancreatic	C25	Jan 2017 – Dec 2018

The cancer registry is a database of information about cancer patients collected directly from hospitals. The SACT dataset collects systemic anti-cancer therapy activity from all NHS England providers. For the purposes of the analysis, patients were selected from the cancer registry data. This cohort of patients was then linked to SACT data to retrieve the latest

[1] All patients treated during the selected time frame were included – not only those who started treatment during the period of interest.

treatment records for these patients. Certain restrictions were applied to the data to ensure that the appropriate patients and treatment data were selected for each cancer site. These restrictions mean that some trusts may have no data included in the workbook because their patients and patients' treatment activity did not fit the criteria applied. The restrictions applied to the data are outlined below.

Tumour restrictions

- Diagnosis was restricted to tumours diagnosed between 2010 and 2017.
- Patients whose most recent cancer diagnosis was one of the cancer sites of interest were selected. If patients had more than one tumour diagnosed on the same day, the tumour in cancer groups we were analysing was selected.

It is important to note that in some cases, the cancer diagnosis recorded in the cancer registry may differ from that recorded by the trust. This is particularly important for cancers that are more difficult to define, such as CUP. Further details on this are provided in Q10 of the FAQ document.

If you would like support in improving the quality of the data feed into the cancer registry then please contact a member of the National Disease Registration Service Data Improvement Team. Contacts are listed below by region:

Northern and Yorkshire – Karen Graham Karen.Graham@phe.gov.uk
North West – Paul Stacey Paul.Stacey@phe.gov.uk
East Midlands – Simon Cairnes Simon.Cairnes@phe.gov.uk
West Midlands and Oxford- Gemma Feeney Gemma.Feeney@phe.gov.uk
London – Katrina Sung Katrina.Sung@phe.gov.uk
Eastern – Marianne Mollett Marianne.Mollett@phe.gov.uk
South West – James Withers James.Withers@phe.gov.uk

Data completeness restrictions

- Trusts with less than 70% completeness for the following key variables: stage[2]; performance status; and co-morbidity score were excluded from the analysis. Please note that these variables were sourced from the SACT dataset, the Cancer Outcomes and Services Dataset (COSD) and Hospital Episodes Statistics (HES) data. The cancer types were selected for analysis on the basis that less than 20% of trusts would be excluded using the 70% completeness threshold.

Age restrictions

- The cohort was restricted to those aged 18+.

Treatment restrictions

For the purposes of the analysis, and to ensure treatment data was relevant to the cancer site, the following rules were applied when linking SACT data to the cohort of patients identified from the registry:

1. For those patients with only one cancer diagnosed, all treatment records within the relevant time frame were selected.
2. For those patients with more than one cancer diagnosed, treatment records were selected if they fit the following criteria:

[2] For the Cancer of Unknown primary analysis, the data completeness threshold was only applied to performance status and co-morbidity score due to lack of staging data for this site.

    - Within the relevant time frame (January 2017- December 2018).
    - The first three characters of the primary diagnosis recorded in SACT for that treatment record matched the first three characters of the cancer site identified in the registry.
3. For those patients with treatment records that did not fall within categories 1 and 2 outlined above, records were selected if they were within the relevant time frame and fell within 31 days before and 183 days after the diagnosis of interest. This ensures that treatment given soon after diagnosis is included for those patients where the diagnosis codes recorded in the cancer registry are not an exact match to those recorded in SACT. This is particularly relevant for some cancers such as cancer of unknown primary where coding of the cancer site sometimes differs between data sources. The decision to restrict based on the time between treatment and diagnosis is in accordance with the standard operating procedure for linking treatment tables to the cancer registration data in analysis system, published here. Please note that the ICD-10 and morphology codes selected may differ from the standard operating procedure referenced. The codes used for this work were selected in accordance with previous releases of 30-day mortality post SACT rates.

Non-harmful, supportive treatments, hormones and non-chemo drugs as well as records submitted in error were excluded from the analysis. The regimen names of those excluded treatments are listed below. These were selected for exclusion in consultation with pharmacists.

- Not Chemo
- Trial
- Anagrelide
- Anti-Histamines
- Anti-Emetics
- APML
- B12
- Bisphosphonates
- Denosumab
- Folinic Acid
- GCSF
- Hepatoblastoma
- Ibandronic Acid
- Lanreotide
- Medroxyprogesterone
- Megestrol
- Octreotide
- Pamidronate
- Pasireotide
- Progesterone
- Retinoblastoma
- Sandostatin
- Signifor
- Somatuline
- Somatostatin
- Steroid
- Stilboestrol
- Stilbestrol

- Triple Intrathecal
- Vitamin
- Zoledronic Acid

Communication of the workbook

The SACT helpdesk at PHE (SACT@phe.gov.uk) compiled a list of named contacts at each NHS trust including the SACT uploader, lead cancer clinician, the regimen mapper, CEO and medical director, unless otherwise notified.

The workbook was sent to these named contacts. There was no patient identifiable data included in the workbook. Trusts were invited to request the NHS numbers of patients in their data who had died within 30 days of receiving SACT. NHS numbers were only provided via secure means following a request from a trust. This aims to restrict the circulation of this sensitive information to individuals who intend to use it for clinical audit and local governance processes.

We informed the trusts that we would be making the workbook publicly available in late summer 2020 and invited them to provide a statement for inclusion in this companion report. The workbook will be published on the SACT website (http://www.chemodataset.nhs.uk/) and will be publicised through a range of channels, including the SACT and the National Disease Registration Service (NDRS) newsletters.

Interpretation of the data

Case-mix adjusted mortality post SACT rates are reported in this workbook. Each trust will see and treat a wide variety of patients depending on the population they serve and the services they provide. The case-mix adjusted rates take into account these differences by producing rates that are based on an average group of patients as opposed to the trust's own group of patients. The rates can then be compared between trusts. This was done using statistical modelling (in this case, a mixed effects logistic regression model).

The following variables were adjusted for in the analysis:

- Performance status at diagnosis
- Stage at diagnosis[3]
- Co-morbidity score[4]
- Index of multiple deprivation
- Gender
- Ethnicity[5]
- Age calculated as of the 1st January 2018
- Hospital trusts (as a random effect[6])

These variables were chosen because they are known to influence 30-day post SACT mortality and because they are available in the data and have better completeness compared with other variables that could be included. It is important to note that due to the absence of any information on critical factors such as patient choice and clinical factors such as liver function tests, the case-mix adjustment may not fully correct for the differences in case load between trusts.

The funnel plot[7] presented in the workbook is a means of visualising 30-day mortality post-SACT rates for the eligible[8] trusts in England.

- The volume of patients is on the horizontal axis. The more patients treated by your trust, the further to the right your trust will be.
- The 30-day mortality post-SACT is on the vertical axis. The higher the mortality post SACT rate at your trust, the further up the graph it will appear.
- The solid red horizontal line shows the average mortality post SACT rate of all trusts.

[3] This was not adjusted for in the Cancer of Unknown primary analysis due to lack of staging data for this site. For patients who had more than one tumour of interest diagnosed on the same day (e.g. two diagnoses of C16 for gastric cancer site analysis), the tumour record with the highest stage was selected.
[4] The co-morbidity score relates to the Charlson comorbidity score derived using inpatient Hospital Episode Statistics data from 27 to 3 months prior to cancer diagnosis, with the same methodology as described by Maringe *et al.*
[5] Grouped into White and non-White categories for analysis as there were insufficient numbers in the other ethnic groups for robust analysis.
[6] In a model, a random effect is usually a grouping factor (e.g. general practice, school, university), in this case the trust, for which we are trying to control and which we expect to be influencing the pattern of 30-day mortality.
[7] More information on funnel plot uses and interpretation can be found here.
[8] See data completeness restrictions.

- Your trust is indicated by the yellow diamond, other trusts are represented by the blue diamonds.
- The dotted lines represent the ±2 standard deviations (SDs) (roughly equivalent to 95% confidence intervals); the dashed lines represent the ±3 standard deviations (SDs) (roughly equivalent to 99.8% confidence intervals). They are higher on the left because when a trust treats a smaller number of patients, chance will have a greater impact on the rate, and therefore the confidence intervals will be wider to reflect this.

The confidence intervals presented in the workbook reflect the distribution of trust mortality post SACT rates around the national average. The workbook highlights the mortality post SACT rates for ±2 standard deviations (SDs) (roughly equivalent to 95% confidence intervals) and ±3 standard deviations (SDs) (roughly equivalent to 99.8% confidence intervals). Trusts with rates above the upper, +3SD will be identified as outliers.

- Trusts with rates above the upper, +3SD have a significantly higher than average 30-day post SACT mortality rate.
- Trusts with rates below the lower, −3SD have a significantly lower than average 30-day post SACT mortality rate.
- Trusts with rates within the confidence limits have an average 30-day post SACT mortality rate.

Trusts with no data

Some trusts had 'no data' in the workbook. This means that they had no activity data for patients being treated for the particular cancer site for the time period, who fit the inclusion criteria. Strict criteria were applied to the data for this work and so there are a few reasons why a trust may have no data in the workbook. Examples of this include:

- Patients were still receiving treatment after the period of interest (e.g. in 2019)
- Patients were treated with regimens that were excluded from the analysis
- Patients received their last treatment at a different trust
- We were not able to match the patient's diagnosis in the registry to that of the trust and the patient's treatment fell outside of the diagnosis-to-treatment time window

The table below presents those trusts with no data in the analysis, by cancer site.

Table 2. Trusts with no data, by cancer site

Trust name	Lung	Pancreas	Gastric	CUP
Ashford And St Peter's Hospitals NHS Foundation Trust	No data	No data	No data	No data
Barnsley Hospital NHS Foundation Trust	No data	No data	No data	No data
Basildon And Thurrock University Hospitals NHS Foundation Trust	No data	No data	No data	No data
Bolton Hospital NHS Foundation Trust		No data	No data	
Chelsea And Westminster Hospital NHS Foundation Trust		No data		No data
Chesterfield Royal Hospital NHS Foundation Trust		No data	No data	
Countess Of Chester Hospital NHS Foundation Trust	No data	No data	No data	
Croydon Health Services NHS Trust	No data	No data	No data	No data
Doncaster And Bassetlaw Hospitals NHS Foundation Trust	No data	No data	No data	No data
East Cheshire NHS Trust	No data	No data	No data	No data
Epsom And St Helier University Hospitals NHS Trust	No data	No data	No data	No data
Homerton University Hospital NHS Foundation Trust		No data		No data
King's College Hospital NHS Foundation Trust		No data	No data	
Kingston Hospital NHS Foundation Trust	No data	No data	No data	No data
Lewisham And Greenwich NHS Trust		No data	No data	
Manchester University NHS Foundation Trust		No data	No data	
Medway NHS Foundation Trust		No data	No data	No data
Mid Cheshire Hospitals NHS Foundation Trust				No data

North Bristol NHS Trust		No data	No data	No data
Pennine Acute Hospitals NHS Trust		No data	No data	No data
Salford Royal NHS Foundation Trust	No data	No data	No data	No data
Sandwell And West Birmingham Hospitals NHS Trust	No data			No data
Sherwood Forest Hospitals NHS Foundation Trust		No data		No data
South London Healthcare NHS Trust	No data	No data	No data	No data
Southport And Ormskirk Hospital NHS Trust	No data	No data	No data	No data
St Helens And Knowsley Hospitals NHS Trust	No data	No data	No data	No data
Stockport NHS Foundation Trust		No data	No data	No data
Surrey And Sussex Healthcare NHS Trust		No data	No data	No data
Tameside And Glossop Integrated Care NHS Foundation Trust	No data	No data	No data	No data
The Hillingdon Hospital NHS Foundation Trust	No data	No data	No data	No data
The Rotherham NHS Foundation Trust	No data	No data	No data	No data
Warrington And Halton Hospitals NHS Foundation Trust	No data	No data	No data	No data
West Hertfordshire Hospitals NHS Trust	No data	No data		No data
Weston Area Health NHS Trust	No data			
Wirral University Teaching Hospital NHS Foundation Trust	No data	No data	No data	No data
Wrightington, Wigan And Leigh NHS Foundation Trust	No data	No data	No data	No data
Wye Valley NHS Trust	No data	No data	No data	No data

Excluded trusts and outlying trusts

The table below presents those trusts that were found to be outliers for the 30-day post SACT mortality rates and those trusts that were excluded based on the 70% data completeness threshold[9] for each cancer site included in the analysis.

Table 3. Trusts that were outliers[10] for the 30-day post SACT mortality rates and trusts excluded based on the 70% completeness threshold[11], by cancer site

Trust name	Lung	Pancreas	Gastric	CUP
Blackpool Teaching Hospitals NHS Foundation Trust	Outlier	Excluded	Excluded	
Bolton Hospital NHS Foundation Trust	Excluded			
Calderdale And Huddersfield NHS Foundation Trust		Excluded		
Chelsea And Westminster Hospital NHS Foundation Trust			Excluded	
Dorset County Hospital NHS Foundation Trust		Excluded	Excluded	Excluded
East Kent Hospitals University NHS Foundation Trust			Outlier	
East Suffolk And North Essex NHS Foundation Trust	Excluded	Excluded	Excluded	Excluded
Gloucestershire Hospitals NHS Foundation Trust		Excluded	Excluded	Excluded
Hull University Teaching Hospitals NHS Trust		Excluded	Excluded	Excluded
King's College Hospital NHS Foundation Trust				Excluded
Liverpool University Hospitals NHS Foundation Trust				Excluded
London North West University Healthcare NHS Trust	Excluded	Excluded	Excluded	Excluded
Medway NHS Foundation Trust	Excluded			
Northern Devon Healthcare NHS Trust		Excluded		
Pennine Acute Hospitals NHS Trust	Excluded			
Royal Cornwall Hospitals NHS Trust	Outlier	Excluded	Excluded	Excluded
Sandwell And West Birmingham Hospitals NHS Trust		Excluded	Excluded	

[9] Trusts with less than 70% completeness for the following key variables: stage at diagnosis; performance status; and co-morbidity score were excluded from the analysis. For the Cancer of Unknown primary analysis, the data completeness threshold was only applied to performance status and co-morbidity score due to lack of staging data for this site. Please note that these variables were sourced from the SACT dataset, the Cancer Outcomes and Services Dataset (COSD) and Hospital Episodes Statistics (HES) data.

[10] Outliers referred to in the table are those trusts with 30-day post SACT mortality rates above the upper +3SD.

[11] Trusts excluded based on the 70% completeness threshold are referred to as ‘Excluded’ in the table.

Sherwood Forest Hospitals NHS Foundation Trust			Excluded	
Stockport NHS Foundation Trust	Excluded			
The Dudley Group NHS Foundation Trust				Excluded
The Princess Alexandra Hospital NHS Trust	Excluded	Excluded	Excluded	Excluded
The Royal Wolverhampton NHS Trust	Excluded	Excluded	Excluded	Excluded
University Hospitals Plymouth NHS Trust				Excluded
Walsall Healthcare NHS Trust			Excluded	Excluded
Weston Area Health NHS Trust		Excluded	Excluded	Excluded
Worcestershire Acute Hospitals NHS Trust		Outlier		
Yeovil District Hospital NHS Foundation Trust		Excluded		Excluded
York Teaching Hospital NHS Foundation Trust		Excluded	Excluded	Excluded

Trust comments

Trusts were invited to comment on their results. We received the following comments:

Bedford Hospital NHS Trust

We have reviewed the individual 7 cases with advanced lung cancer, who died between January- December 2018.

This is to confirm that the patients were treated appropriately with approved cancer systemic treatments.

The cause of death was carefully reviewed and assessed by all consultants and found to be progressive disease for all patients.

This is to confirm that there were no deaths attributable to SACT.

3 deaths were due to rapid progression of the disease, due to a change in biology of the cancer.

In summary, these were deaths were attributable to progressive disease, with no relation to SACT administration prior to death.

Blackpool Teaching Hospitals NHS Foundation Trust

Thank you for the opportunity to review the 30-day mortality post-SACT analysis for those patients who had their final treatment in 2018. We note that Blackpool Teaching Hospitals NHS Foundation Trust stands as an outlier for the lung cancer dataset.

Within the Trust every patient death within 30 days of receiving SACT has their care reviewed at the Oncology or Haematology SACT Mortality Meeting, along with a determination as to whether treatment was given appropriately and whether the death was causally related to the SACT.

From the 2018 dataset, 19 lung cancer patients were identified. The majority (11) of these patients were receiving palliative immunotherapy and died soon after starting treatment. Sometimes the death appeared to be from disease progression but there were also cases of unexpected deaths from other or unknown causes. This raises the question of whether too many patients with advanced cancer were being treated at the end of life. One way to assess this would be to determine the overall survival (from start of treatment to death) of the cohort of patients treated in 2018. For the cohort treated with first-line pembrolizumab at any time in 2018 we have calculated the median overall survival to be 20.9 months. This is comparable to the 20.0 months overall survival calculated from the final analysis of the phase 3 KEYNOTE-042 trial for first-line pembrolizumab in patients with high PD-L1 expression.

We also identified 3 patients treated with SACT who died following admission with neutropenic sepsis. All of these patients were treated promptly with antibiotics as per local sepsis guidelines although the longest door-to-needle time was recorded at 66 minutes.

Overall the standard of care for these patients was rated as good and the time to antibiotic administration was not considered to have contributed to the patients' deaths.

We look forward to the analysis of future cohorts especially as the indications for the use of immunotherapy in advanced lung cancer increase.

East Kent Hospitals University NHS Foundation Trust

East Kent Hospitals University NHS Foundation Trust is grateful to NCRAS for supplying details of the cases identified in the audit. Our upper GI oncology lead has reviewed the identified 8 cases in detail, and confirms that most of the identified gastric and small bowel cancers deaths within 30 days of administered systemic anticancer treatment were attributed to disease progression. In 3 of the cases the decision to discontinue chemotherapy due to disease progression had been taken in conjunction with the patient some time prior to the date of death. Additionally, one case was enrolled into a chemotherapy trial but did not commence chemotherapy due to rapid disease deterioration before the treatment course could commence, and hence should not have been included in the SACT data. The data for the Trust is likely to also be skewed by a reduction in the denominator of cases captured for East Kent, as good prognosis patients treated with imatinib for GIST and somatostatin analogues for small bowel neuroendocrine tumours are not captured in our SACT data.

Royal Cornwall Hospitals NHS Trust

In July 2020 Public Health England alerted RCHT that it was a statistical outlier for patients with Lung cancer who were treated in 2017-18 and who died within 30 days of Systemic Anti-Cancer Therapy (SACT).

Detailed case analysis of the 17 of 18 cases correctly identified (1 case died 72 days after last SACT and was removed from analysis) shows that of these deaths 4 (23.5%) died of other illnesses, not their cancer, and 13/17 (76.5%) died due to rapid progression of their cancer despite treatment. All patients had a performance score of 1 or 2 at the time of treatment. Additionally, no deaths were deemed to be attributable to side effects or toxicity from the treatment. The department reviews all patients who die during cancer treatment in a monthly mortality review and undertake regular audit of outcomes from patients receiving treatment. Arising from this the department is currently reviewing different Frailty Indexes as a better surrogate for decision making than performance score.

West Suffolk NHS Foundation Trust

This is a group of patients (lung & gastric) who have complex conditions and the numbers of diagnosed patients vary year to year, which can affect the overall %.

We have a robust system of ensuring peer review for any patients who have a Performance Status of 3 or above. The service adopted M&M reviews over 12 years ago. These are reviewed monthly with reflections on each patients case, which allows any learning to be taken forward. From these we are aware that most of these patients died from progressive disease rather than their SACT.

Worcestershire Acute Hospitals NHS Trust

The national SACT team has provided Worcestershire Acute Hospitals NHS Trust the patient data associated with the publication of the 30 day mortality report for pancreas patients for the period 2017/2018. The Trust has now had the opportunity to review and validate the data and 52% of the patients included in the published report were not administered treatment within 30 days of their death. When these patients are removed from the data the Trust are confident it would not be in an outlying position.

Unfortunately the published data cannot be amended, however the Trust would like to reassure patients that treatment for pancreatic cancer is in line with national guidance. The Trust will put in place measures to validate future SACT data prior to submission.

The corrected data is tabulated below:

Findings	**Patient numbers**
Never started chemotherapy, but was prescribed	4
Treatment delayed beyond 30 days but still prescribed	5
Died within 30 days of treatment	8

If you have any questions regarding this work, please contact the SACT Helpdesk (SACT@phe.gov.uk).