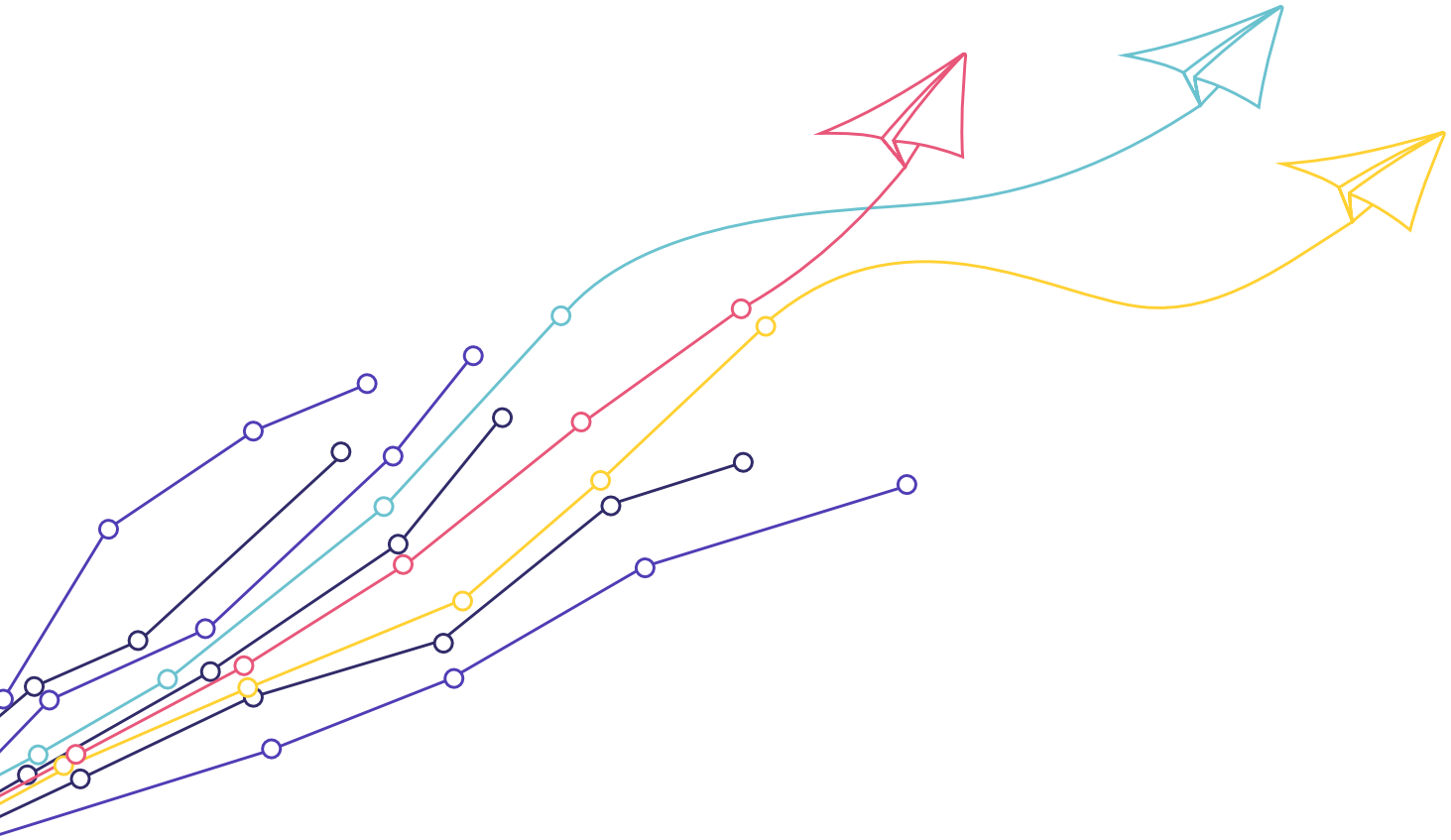
Pancreatic Cancer UK



Variation in pancreatic cancer care and treatment

August 2020

Introduction

People living with and affected by pancreatic cancer have long reported unacceptable differences in the treatment and services they experience in different areas of the UK. Depending on where someone diagnosed with pancreatic cancer receives care, their experience can be very different – there can be different diagnostic pathways, different standards of care and different approaches to treatment.

At the beginning of 2018, for the first time, NICE guidelines were published for the diagnosis and management of pancreatic cancer – in publishing the guidelines, NICE observed "wide variation in practice". The COVID-19 pandemic has also further highlighted and exacerbated the variation in treatment and care for pancreatic cancer that has long existed across the UK.

To date there has been little attention given to exploring or explaining variations in care, treatment and outcomes within the UK. This report is a preliminary analysis of publicly available pancreatic cancer data, benchmarking the current available data for pancreatic cancer and highlighting variation in incidence, mortality, stage, treatment and survival.

The majority of both the academic and routine national output data contained within this report focuses on England. Treatment and stage data for England are published by the National Cancer Registration and Analysis Service (NCRAS), with granular breakdown by Cancer Alliance and Clinical Commissioning Group (CCG), allowing detailed comparisons to be made across England. We are keen to work further with Scotland, Wales and Northern Ireland to develop and analyse more data to better understand variation in care across all areas of the UK.

For the purposes of this report, we have not identified better or worse performing regions, as it is not currently possible to explain the causes of the observed variation. Without adjustments for clinical, patient and demographic characteristics, we cannot determine the extent to which variation is unjustified or unwarranted. This report aims to set the groundwork for further quantifying variation and to start a conversation about the causes of variation in pancreatic cancer care and treatment so that we can better understand where unjustified variation exists and start to standardise care to reduce health inequalities.

The COVID-19 pandemic has brought together the pancreatic cancer clinical community to share learning and experience. There is now an opportunity, as we move forward from the COVID-19 pandemic, to facilitate national collaboration to better understand variation in pancreatic cancer care and build consensus on optimal pancreatic cancer treatment and care.

Pancreatic Cancer UK will work with partners across the clinical and charity sector to collect, analyse and publish more data to better quantify variation at all levels. This will transform our understanding of the landscape of pancreatic cancer treatment and care, and lead to the adoption of best practice across the country, which will ultimately improve care, treatment, and outcomes for everyone diagnosed with pancreatic cancer.

Through 2020 - 2021, the All-Party Parliamentary Group on Pancreatic Cancer (APPGPC) will launch an inquiry to explore the variation in pancreatic cancer treatment, care and outcomes, with evidence submitted and collated from across the pancreatic cancer community. This will be the first step towards starting to better understand variation: allowing best practice to be identified, highlighting areas of concern and building consensus on optimal pancreatic cancer treatment and care.

Executive summary

Pancreatic cancer is the deadliest common cancer, with one in four people dying within a month and less than 7% surviving for five years – a figure that has barely changed in four decades.[1]

Treatments for pancreatic cancer are limited, with surgery the only potentially curative treatment, however, fewer than 1 in 10 people will receive surgery.[2] Most people are diagnosed too late to receive treatment, with 7 in 10 people not receiving any active treatment, and instead only receiving palliative care and best supportive care.

These statistics are staggeringly poor and unparalleled among most common cancers, yet unwarranted variation in treatment and care further worsens outcomes for people with pancreatic cancer. Addressing this variation is essential to standardising treatment and care across the country, improving local and national outcomes and bringing the UK survival outcomes in line with other countries.

Pancreatic cancer treatment and care can be, as described by one patient, "a bit of a lottery with high stakes" with some "drugs available in certain areas but not others and some oncologists willing to try different combinations, while others won't."

Geographically, variation in treatment and care exists at all levels. There is international survival variation across developed countries, regional treatment variation across Cancer Alliances, and local variation in clinical practice between hospitals.

Despite poor outcomes globally, the UK still lags behind the rest of the world, ranking 29th out of 33 countries for five-year survival;[3] in part due to lower early diagnosis and surgery rates than many other developed countries.

Five-year survival in other nations can be almost two times higher than the UK, but even within that poor national figure, further regional differences in survival persist, with one-year survival for pancreatic cancer ranging from 21.3% to 29.1% and five-year survival ranging from 4.8% to 10.6% across Cancer Alliances.[4]

Yet the data shows that the variation in treatment and care is not only dependent on geographical location. It also varies for different groups: between young and old, between patients with operable and inoperable pancreatic cancer, and between specialist centres and secondary care.

The principal drivers of this variation are complex and unclear. A picture further clouded by the absence of consistent minimum data standards, incomplete staging data and lack of published detailed regional data, which make it difficult to understand observed variation and compare outcomes.

More can and must be done to reduce health inequalities and variation, to improve outcomes for people with pancreatic cancer and align survival rates with the best in the world. Ultimately, teasing out where and why variation exists is essential to standardising outcomes and improving care and treatment for everyone with pancreatic cancer.

1 CONCORD-3, Lancet 2018 (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)33326-3/fulltext)

2 NCRAS, Treatment 2013-2015

3 CONCORD-3, Lancet 2018 (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)33326-3/fulltext)

4 https://www.gov.uk/government/publications/geographic-patterns-of-cancer-survival-in-england-adults-diagnosed-2013-to-2017-and-followed-up-to-2018/geographical-patterns-of cancer-survival-in-england-adults-diagnosed-2013-to-2017-and-followed-up-to-2018

International variation

There is significant international variation across a range of outcomes for pancreatic cancer. Five-year survival for pancreatic cancer in the UK has only increased from 3.7% in 2000-2004 to 6.8% in 2010-2014 **(Figure 1)**. Despite poor outcomes globally, the UK lags behind the rest of the world, ranking 29th out of 33 countries for five-year survival.[5]

There is also variation in 5-year survival within the UK. England has the highest 5-year survival in the UK, with a 5-year survival of 7.0% compared to 6.2% in Northern Ireland, 5.7% in Wales and 5.6% in Scotland.[6]

Other developed countries also have better early stage diagnosis, with diagnosis at stage one and stage two ranging from 23% in the Netherlands to 32.4% in the USA, compared to only 18.2% in England.[7,8] The proportion of people with pancreatic cancer who receive surgery in England is also lower than other nations, with surgery rates in the USA, Netherlands, Belgium, Norway and Denmark 1.5 to 2 times higher than in England.[9,10]

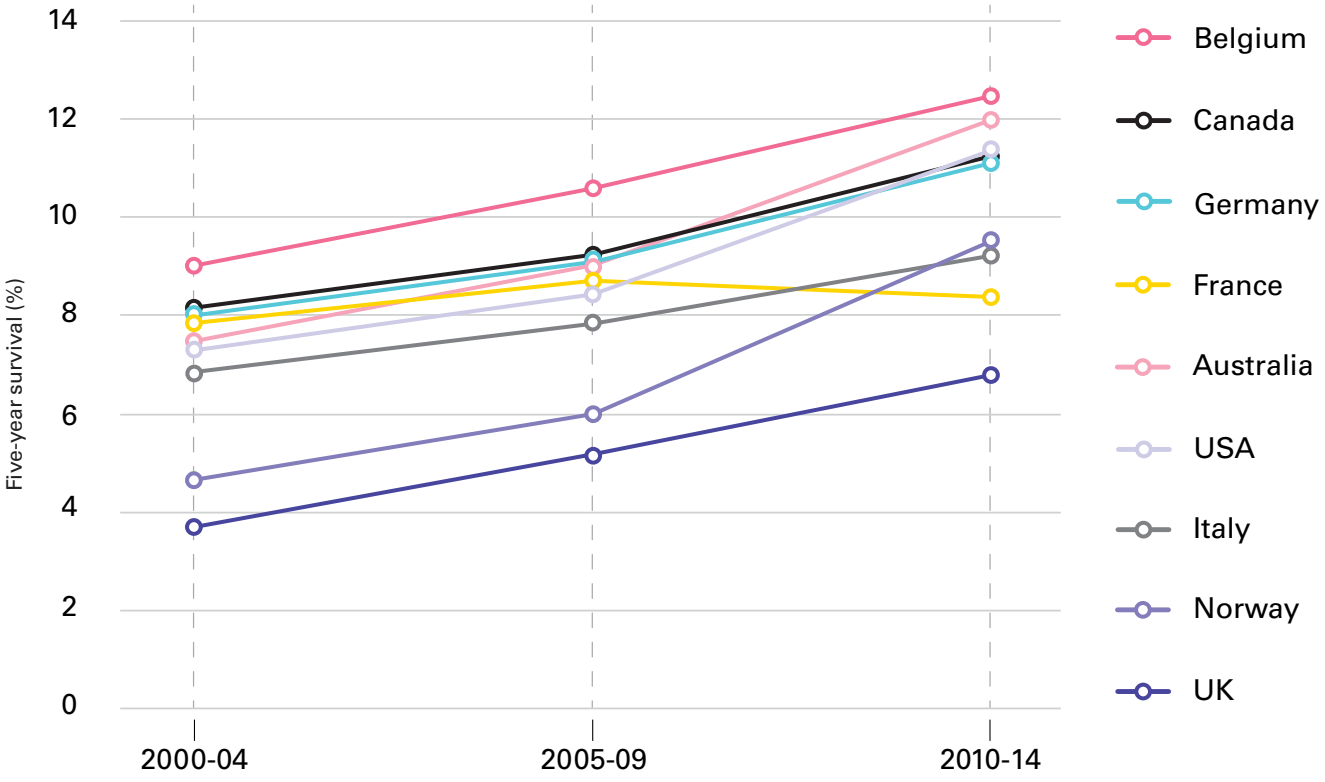


Figure 1: Five-year survival trend for pancreatic cancer between 2000-2004 and 2010-2014. Data adapted after CONCORD-3.

5 CONCORD-3, 2018. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)33326-3/fulltext
6 CONCORD-3, 2018. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)33326-3/fulltext
7 https://www.ncbi.nlm.nih.gov/pubmed/29158237
8 http://www.ncin.org.uk/publications/survival_by_stage
9 https://www.ncbi.nlm.nih.gov/pubmed/29158237, Patients diagnosed during 2013-2014
10 NCRAS, Treatment 2013–2015, http://www.ncin.org.uk/view?rid=3460. Accessed in August 2018

Incidence

There were 8,829 pancreatic cancer cases diagnosed in 2017 in England and the overall age standardised incidence rate was 17.18 per 100,000 people.[11] Across the 195 Clinical Commissioning Groups (CCGs), the age standardised incidence rates ranged from 9.4 to 30.9 per 100,000 people.

Each point on the funnel plot below represents a single Clinical Commissioning Group (CCG) - the NHS bodies responsible for planning and commissioning healthcare services in a local area in England **(Figure 2)**.[12]

There is expected normal random variation in incidence between CCGs with most falling within the control limits (inner dashed lines). However, some CCGs lie outside the inner dashed lines, suggesting there may be real significant differences in incidence. It is important to start to understand the factors underlying this unexpected variation.

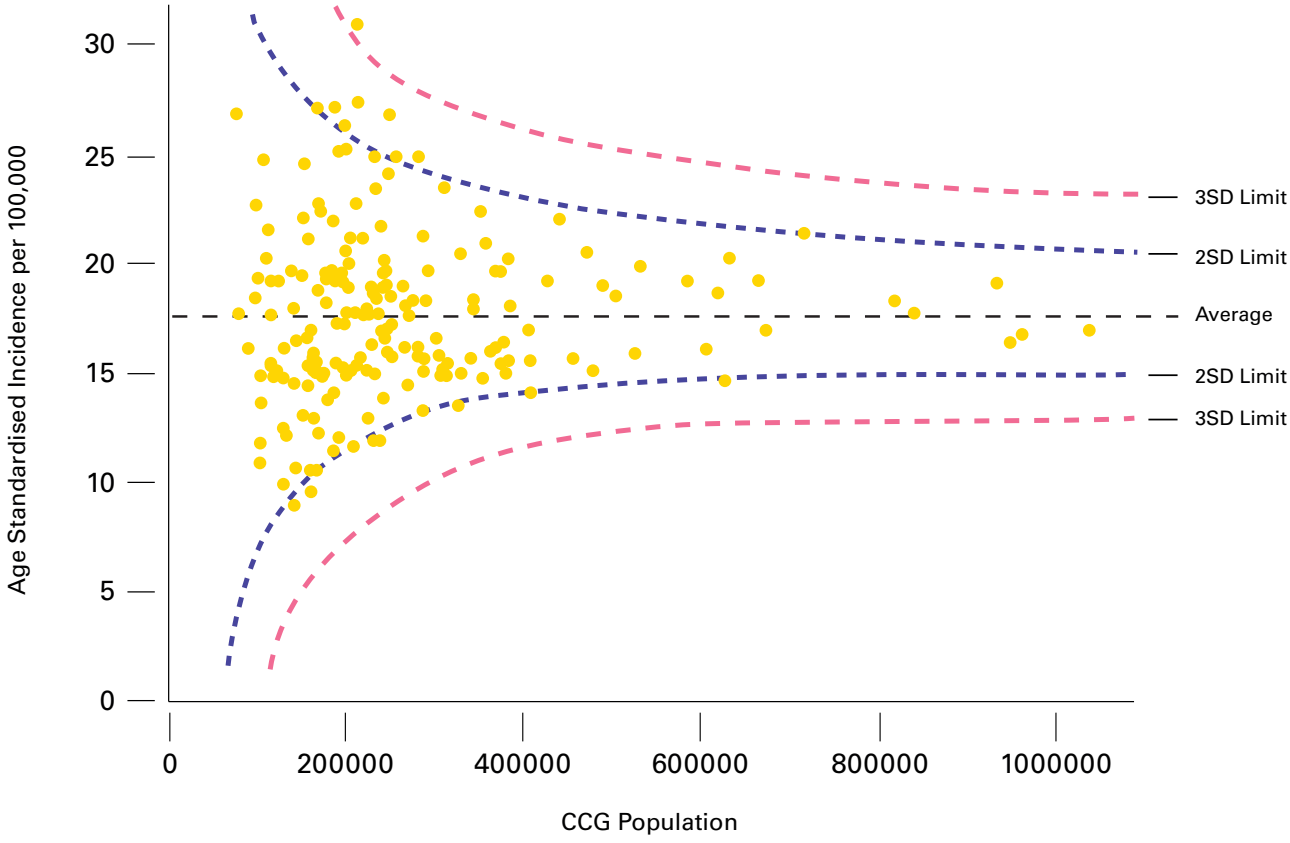


Figure 2: Funnel plot showing the variation in age standardised incidence per 100,000 across the Clinical Commissioning Groups in England (2017). CCGs that lie outside the inner dashed lines (2SD) have unexpected variation and may have real differences in incidence and not random variation. CCGs that lie outside the outer dashed lines (3SD) are more likely to have significant variation in incidence.

11 https://www.cancerdata.nhs.uk/incidence/age_standardised_rates

12 https://improvement.nhs.uk/resources/funnel-plot-tool/

Mortality

There were 7,869 pancreatic cancer deaths in 2017 in England and the overall age standardised mortality rate was 15.30 per 100,000 people.[13] The age standardised mortality rates ranged from 8.1 to 23.7 per 100,000 people across the 195 Clinical Commissioning Groups (CCGs) in England **(Figure 3)**.

There is expected random variation in mortality between CCGs with most falling within the control limits (inner dashed lines). However, some CCGs lie outside the inner dashed lines, suggesting there may be real significant differences in mortality. It is important to understand where significant variation in mortality exists and start to explore the underlying reasons for this.

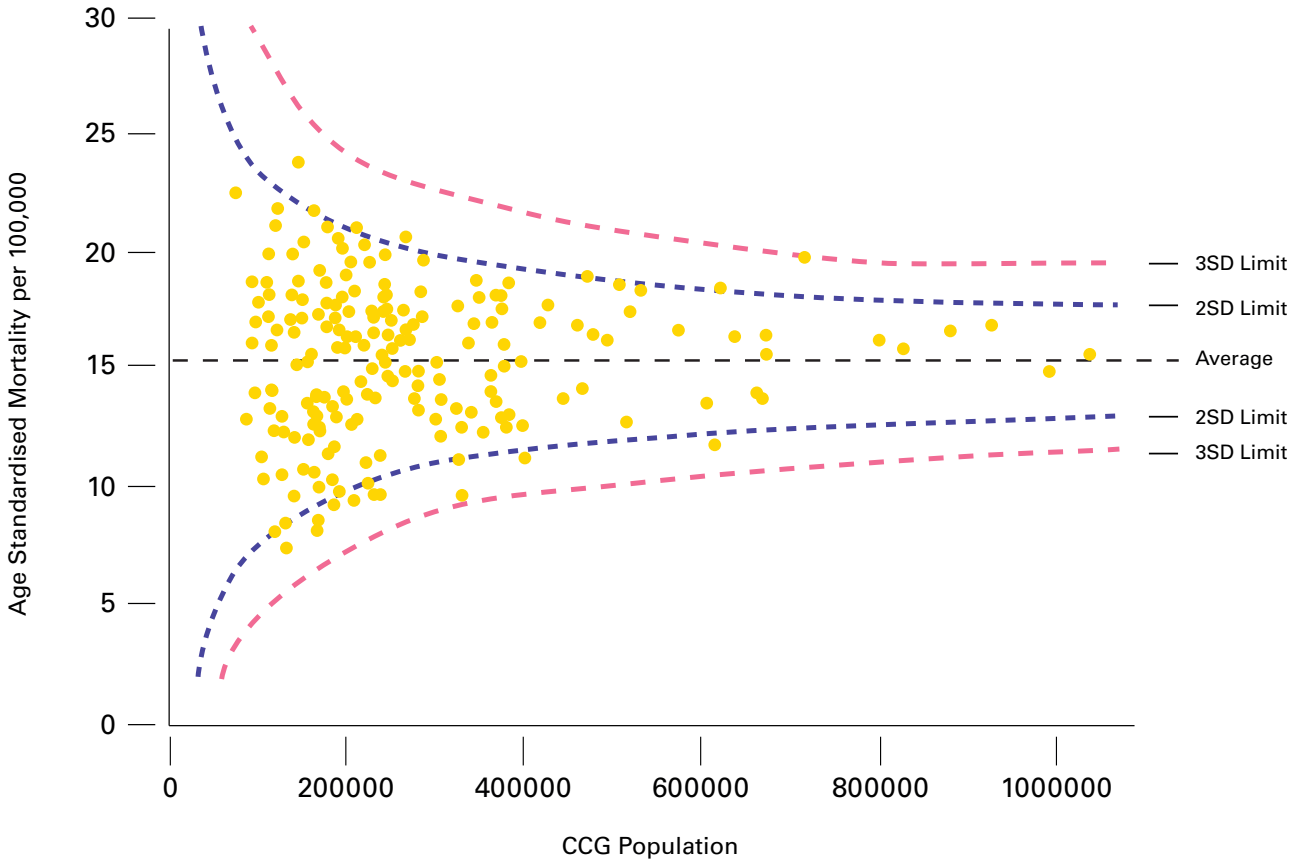


Figure 3: Funnel plot showing the variation in age standardised mortality per 100,000 across the Clinical Commissioning Groups in England (2017).[14] CCGs that lie outside the inner dashed lines (2SD) have unexpected variation and may have real differences in mortality and not random variation. CCGs that lie outside the outer dashed lines (3SD) are more likely to have significant variation in mortality.

13 https://www.cancerdata.nhs.uk/mortality/age_standardised_rates

14 https://improvement.nhs.uk/resources/funnel-plot-tool/

Staging

Stage at diagnosis is an essential parameter for the management of pancreatic cancer as earlier diagnosis offers the opportunity for people to receive potentially curative surgery and defines the treatment options available.

Early diagnosis is crucial to improve survival outcomes for people with pancreatic cancer; with one-year survival in those diagnosed at an early stage six times higher than one-year survival in those diagnosed at stage 4.[15]

The NHS long-term plan[16] has set an ambition for 75% of all cancers to be diagnosed at an early stage, by 2028, however, currently only 18.2% of people with pancreatic cancer are diagnosed at stage one and stage two and 60.9% are diagnosed at stage three and stage four **(Figure 4).** Substantial variation exists within that national figure across CCGs, with the proportion of pancreatic cancer cases diagnosed at an early stage ranging from 2.4% to 46.7% across CCGs. **(Figure 5)**.[17]

All patients with pancreatic cancer should be staged, except in circumstances where patients are too ill for staging investigations; however, 20.9% of pancreatic cancer cases across England in 2017 had no reported stage.[18] When analysed at the CCG level, this can be as high as 63% of cases missing stage data. Staging data completeness is essential to understand variation in care for pancreatic cancer and the incompleteness of staging data affects the interpretation of local data.

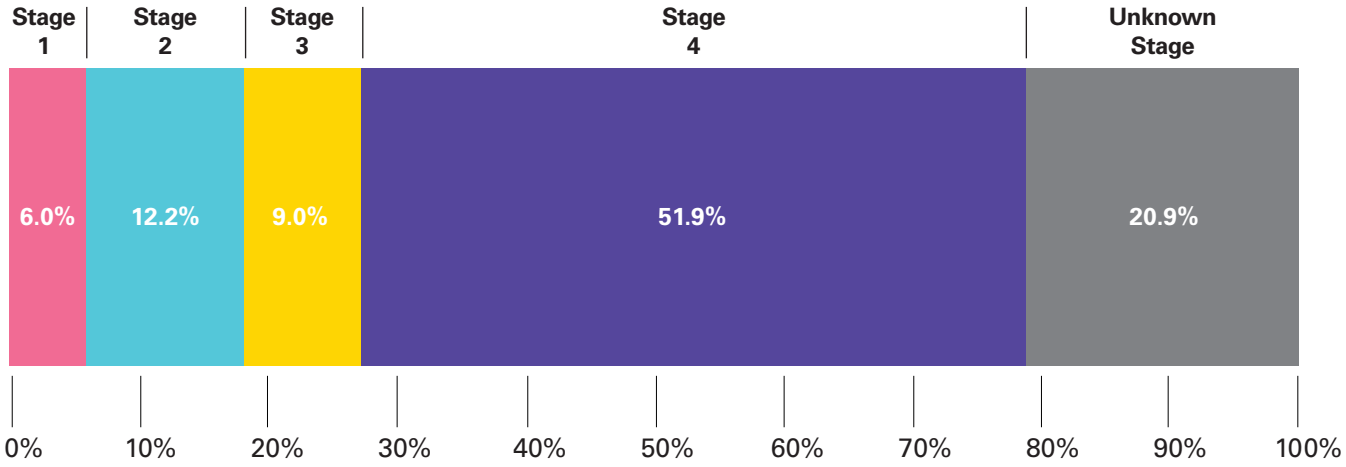


Figure 4: Graph representing the stage at diagnosis profile for people with pancreatic cancer in England (2015-2017)[18]

15 https://www.pancreaticcancer.org.uk/media/1775493/new-insights-on-pancreatic-cancer.pdf
16 https://www.longtermplan.nhs.uk/publication/nhs-long-term-plan/
17 http://www.ncin.org.uk/publications/survival_by_stage
18 http://www.ncin.org.uk/publications/survival_by_stage

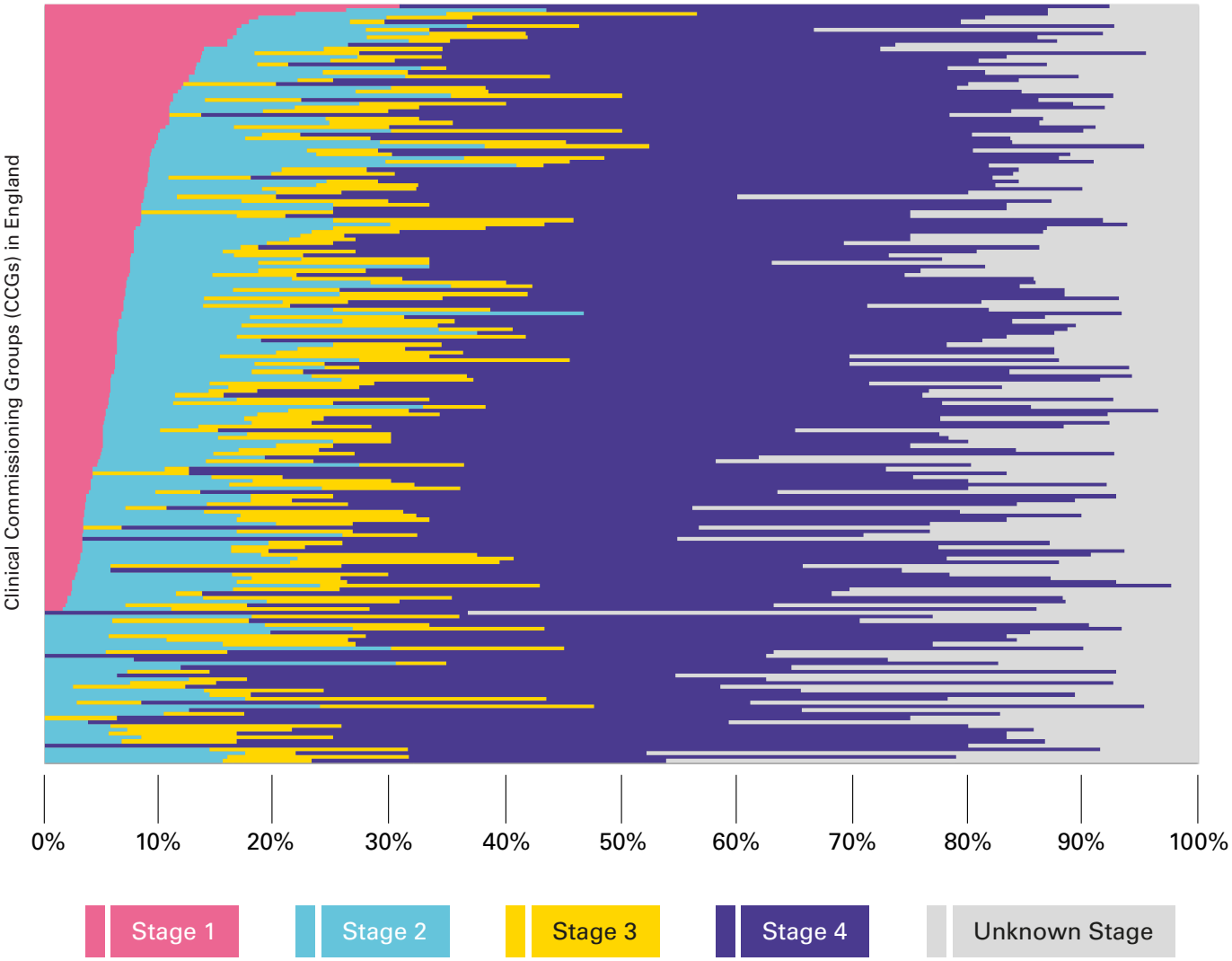


Figure 5: Graph representing the stage profile for pancreatic cancer across all CCGs (2017)[20]

Although there is variation in the stage profile across CCGs **(Figure 5)**[19], the interpretation of this variation is limited, as the numbers are small when analysing staging data at the CCG level and is impacted by the degree of staging data completeness. The variation in stage profile could reflect different provision in primary care (access to GPs, referral pathways and diagnostic pathways), slower patient presentation to primary care, demographic differences or inconsistent data reporting.

> "It took 11 months from the time I went to see my GP until the time I got diagnosed. If this had been picked up sooner it would have saved me a lot of unnecessary suffering where I felt in isolation."

19 http://www.ncin.org.uk/publications/survival_by_stage

20 http://www.ncin.org.uk/publications/survival_by_stage

Survival

The national average across England for pancreatic cancer survival is 25.4% for one-year survival and 7.3% for five-year survival (2013 – 2017).[21]

Cancer Alliances are supra-regional bodies in England that are responsible for local transformation of cancer diagnosis, treatment and care; with both decision-making power and accountability for outcomes, they represent a meaningful and useful structural level to compare and analyse data across England.

Across Cancer Alliances in 2013 – 2017, the age standardised one-year survival for people with pancreatic cancer ranges from 29.1% to 21.3%, and the five-year survival ranges from 10.6% to 4.8%. There is more relative variability in five-year survival than one-year survival between Cancer Alliances, with a two-fold difference between the five-year survivals in the lowest performing Cancer Alliance compared to the highest performing Cancer Alliance.[22]

The Cancer Alliance survival data is consistent with academic data from the London School of Hygiene and Tropical Medicine (LSHTM), which also showed significant variation in survival outcomes across the 23 HepatoPancreatoBiliary (HPB) regions in England (areas covered by HPB specialist centres and their referring NHS Trusts). Across the HPB regions, the one-year survival for people with pancreatic cancer ranges from 16.1% to 36.4%, and five-year survival ranges from 1.7% to 7.6% in 2010-2013.[23]

Less variation in one-year survival was observed when only looking at patients who received surgery among the 23 HPB regions, with one-year survival for those who have had surgery ranging from 62.3% to 83.3%, with variation in the expected range and no upper or lower outliers observed. This suggests that more of the variation in survival may exist in the inoperable patient population, where the one-year survival for inoperable pancreatic cancer ranges between 11.2% and 31.0%.

Combined, this data shows that real variation exists in survival outcomes across England for pancreatic cancer, however, it does not reveal the underlying reasons or factors influencing the survival variation. Survival is dependent on multiple factors including quality of treatment, stage at diagnosis, local provision of care and the clinical and demographic characteristics of the local population. Further research is needed to address why differences exist in survival outcomes across Cancer Alliances and HPB centres across England.

21 https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed

22 https://www.gov.uk/government/publications/geographic-patterns-of-cancer-survival-in-england-adults-diagnosed-2013-to-2017-and-followed-up-to-2018/geographical-patterns-of-cancer-survival-in-england-adults-diagnosed-2013-to-2017-and-followed-up-to-2018

23 https://www.sciencedirect.com/science/article/pii/S1424390320300302

Surgery

Surgery, either alone or with chemotherapy, is the only treatment with curative intent for pancreatic cancer so minimising unjustified variation is critical to improving survival outcomes.

The proportion of people receiving surgery in England is 9.7%, ranging from 7% to 13.5% across Cancer Alliances (2013 - 2015).[24] The funnel plot **(Figure 6)** shows that there is unexpected variation in surgery rates between Cancer Alliances, with some Cancer Alliances outside the inner dashed lines.

A study across the 23 HPB regions in England has also showed substantial variation in the proportion of people receiving surgery, with the surgery rate ranging from 5.1% to 19.6% (2010 – 2013).25 Although there is observed variation in access to surgery across England, this could reflect regional differences in stage at diagnosis, age, co-morbidities, the proportion of missing data or differences in clinical approach and practice.

The national data also shows that only 38% of people diagnosed at stage one and two receive surgery which does not fit with the clinical experience. More research is needed to understand these inconsistencies between national data and clinical experience. Older people are also much less likely to receive surgery, although this may in part be explained by co-morbidity.

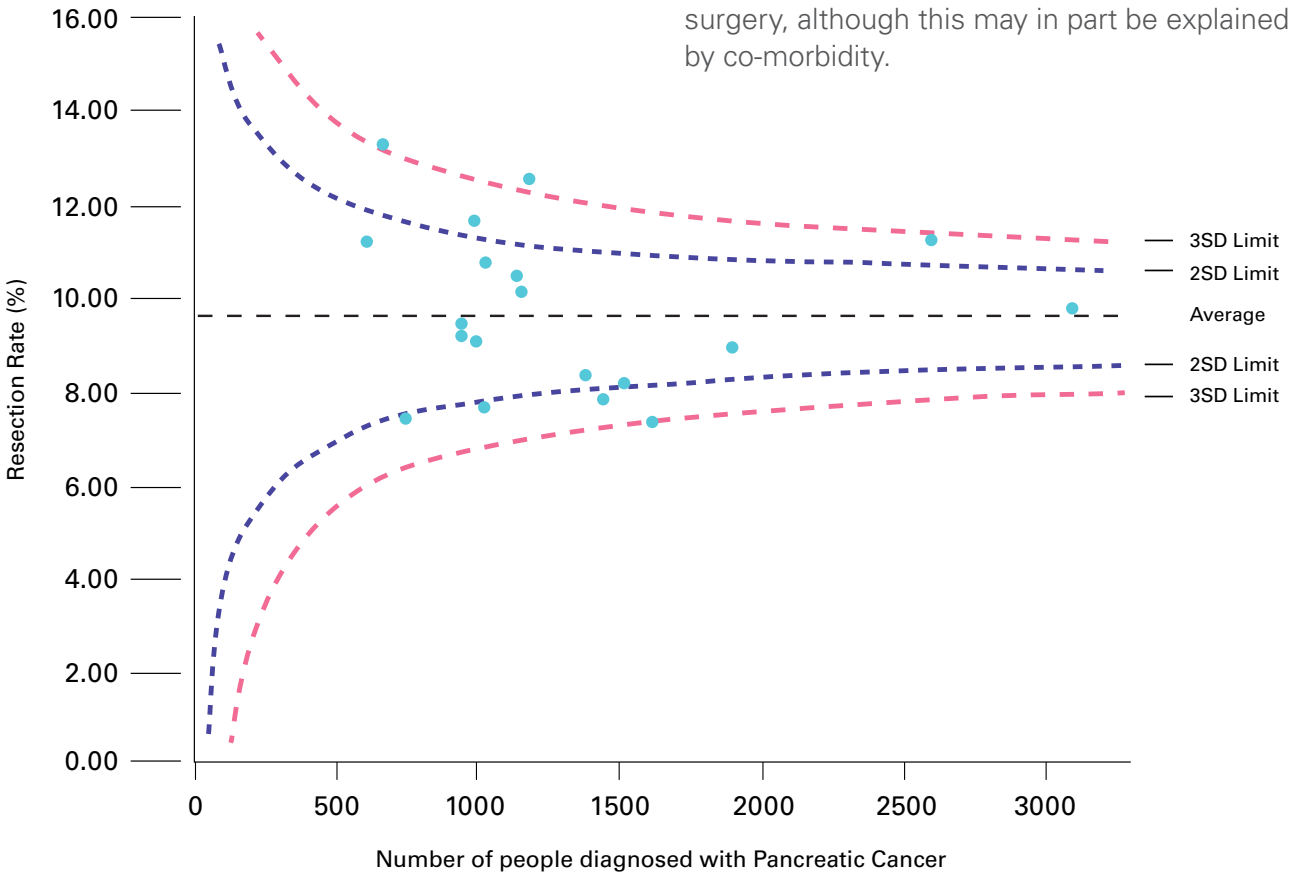


Figure 6: Funnel plot showing the variation in surgery rate for people with pancreatic cancer across the Cancer Alliances in England. Each point represents a Cancer Alliance. (2013-2015).

24 http://www.ncin.org.uk/view?rid=3682

25 https://www.sciencedirect.com/science/article/pii/S1424390320300302

Chemotherapy

Adjuvant chemotherapy

Adjuvant chemotherapy after surgery has been shown to provide significant survival benefit, with gemcitabine and capecitabine combination chemotherapy increasing median overall survival to 28 months and modified-FOLFIRINOX increasing median overall survival up to 54 months.[26, 27]

However, national data shows that only 50% of patients who have surgery undergo adjuvant chemotherapy, with variation between Cancer Alliances, ranging from 64.5% to 40.7% (2013 – 2015)[28]. While most variation in England is around the normal expected range, there are upper and lower outliers and anecdotally we know that some clinical centres have much higher rates of adjuvant chemotherapy delivery. Scotland also has higher adjuvant chemotherapy delivery with 83.3% of people who have surgery receiving adjuvant or neo-adjuvant chemotherapy (2018)[29]. England has higher adjuvant chemotherapy delivery than Europe and the USA[30], which could be due in part to the role of UK institutions in adjuvant chemotherapy clinical trials[31].

> "I have been offered poor information and advice, refused first line adjuvant chemotherapy - despite petitioning the oncologist to change his mind based on the NICE guidelines and research-based practice, resulting in me even involving PALS (Patient Advice and Liaison Service) and my local MP to fight for treatment for me. I have subsequently had to transfer my care which has delayed the start of my adjuvant therapy drastically and caused an insurmountable amount of anxiety, anguish and upset for myself and my whole family."

Palliative chemotherapy

Chemotherapy for patients with advanced and metastatic pancreatic cancer has been shown to improve survival, with 11 months median overall survival for the FOLFIRINOX regimen and 6.8 months median overall survival with gemcitabine first line therapy.[32] However, only 25% of people with metastatic pancreatic cancer (stage 4) receive chemotherapy. There is also variation across England in the provision of chemotherapy to inoperable patients, with chemotherapy delivery in people who do not have surgery ranging from 22% to 33% across Cancer Alliances in England (2013 – 2015).[33]

26 https://www.ncbi.nlm.nih.gov/pubmed/28129987
27 https://www.ncbi.nlm.nih.gov/pubmed/30575490
28 http://www.ncin.org.uk/view?rid=3682
29 https://www.shpbn.scot.nhs.uk/wpcontent/uploads/2020/01/Final_Published_HPB_Cancer_Clinical_Audit_Report_2018_Data_v1_0_06012020.pdf
30 https://www.ncbi.nlm.nih.gov/pubmed/29158237
31 https://www.sciencedirect.com/science/article/pii/S1424390320300302
32 https://www.nejm.org/doi/full/10.1056/NEJMoa1011923
33 NCRAS, Treatment 2013-2015

Access to PERT

Pancreatic Exocrine Insufficiency (PEI) is a common supportive care need in people with pancreatic cancer and Pancreatic Enzyme Replacement Therapy (PERT) should be prescribed to replace the enzymes that the pancreas would normally produce. PERT not only increases quality of life through managing digestive symptoms and reducing weight loss, it can also increase tolerance to treatment and significantly extend the life of pancreatic cancer patients.[34, 35]

NICE guidelines recommend PERT for all pancreatic cancer patients (patients with both operable and inoperable pancreatic cancer),[36] however, there is currently a failure to implement the guidelines, with only 54.5% of pancreatic cancer patients prescribed PERT.[37, 38] Furthermore, resectable patients are more likely to be prescribed PERT than unresectable patients. This variation in care also plays out between patients managed in specialist centres and tertiary care compared to those managed in secondary care, with patients more likely to receive PERT in specialist and tertiary care centres.[39]

The multidisciplinary team should consider diagnosis, treatment and holistic care, including nutritional assessment; however, multidisciplinary discussions are often under time constraint so nutritional care is not always a priority.

Unjustified variation in basic nutritional and supportive care for people with pancreatic is not only observed in the national data, but through the patient accounts and experience that we hear through our patient support services:

> "There appears little knowledge within GP practices and their support nursing staff of the usage and dosage of Creon [PERT Brand Name]. My dietician had to write to my GP in order for me to obtain the increased amount of Creon. This lack of knowledge led to many weeks of inability to tolerate food."

34 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5935964/
35 https://www.ncbi.nlm.nih.gov/pubmed/30385188
36 https://www.nice.org.uk/guidance/ng85
37 https://www.pancreaticcancer.org.uk/media/1891582/12-pert-prescribing-a-snapshot-of-current-practice-richard-wilkin.pdf
38 This may in part be due to the data collection being shortly after the publication of NICE guidelines
39 https://www.pancreaticcancer.org.uk/media/1891582/12-pert-prescribing-a-snapshot-of-current-practice-richard-wilkin.pdf

Discussion

The evidence outlined in this report makes clear that unwarranted variation is a real and substantial problem within pancreatic cancer treatment and care. Benchmarking the current available data for pancreatic cancer has highlighted variation in incidence, mortality, stage, treatment and survival for pancreatic cancer. It is clear that this variation is having a direct impact on the quality of care for many people with pancreatic cancer, and their chances of survival.

Many of these findings need further exploration. For example, this report has highlighted a consistent theme in the difference in the standard of care and variation observed between inoperable and operable patients. Less variation in one-year survival was observed when only looking at patients who received surgery among the 23 HPB regions, which suggests that more variation in survival may exist in the inoperable patient population. Additionally, operable patients have better access to nutritional care, with resectable patients being more likely to receive PERT compared to unresectable patients. A key difference in the management of those who have had surgery and those that have not is that surgery has been centralised to specialist centres, while chemotherapy and palliative care is often delivered in acute trusts, often by oncologists and palliative care teams that cover multiple cancer sites rather than HPB specialists. NICE guidelines for the management of pancreatic cancer recommend that, to help standardise care, a specialist pancreatic cancer multidisciplinary team should consider all patients.

One limitation of the data in this report is that the reporting period is before the publication of the pancreatic cancer NICE guidelines in 2018. As a result, this data will not capture any subsequent standardisation in treatment and care.

Health inequalities exist across many levels across the UK, influenced by geographical boundaries, as well as the impact of deprivation, socio-economic factors and ethnicity. The lack of available data on outcomes for pancreatic cancer for Black, Asian and Minority Ethnic (BAME) people and other disadvantaged and less represented groups, limits our understanding of the experience and outcomes of these patients, and is an area where further research and resource can be focused.

The national picture of variation is further clouded without consistent minimum data standards, incompleteness of staging data and lack of published granular regional data, which make it difficult to adjust for confounders, understand observed variation and compare regional outcomes. Nationally and locally, we need more detailed data published, stratified by tumour type, stage at diagnosis and detailed treatment approach so that we can better assess unwarranted variation and identify where issues persist across the country.

Analysing and publishing more and better data will start to improve data quality, highlight inconsistencies between data and clinical experience, allow more accurate comparisons between centres and drive up standards across the country.

Through working with national bodies and the clinical community to publish and feedback data, we can better understand variation and start to reduce unjustified variation in practice and outcomes. Better data can allow best practice to be identified and highlight areas of concern: a key step towards building consensus on optimal pancreatic cancer treatment and care, and ensuring that everyone with pancreatic cancer gets the best treatment and care possible.

Pancreatic
Cancer
UK

Pancreatic Cancer UK
Westminster Tower,
3 Albert Embankment, London SE1 7SP

020 3535 7090
pancreaticcancer.org.uk

Registered with FUNDRAISING REGULATOR

Registered charity number
1112708 (England and Wales),
and SC046392 (Scotland)