Pancreatic cancer incidence and survival and the role of specialist centres in resection rates in England, 2000 to 2014: a population-based study

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ABSTRACT

Background

The aim was to compare population-based survival for exocrine pancreatic cancer in England in the 23 regions covered by specialist centres. The centres were initiated in 2001, covering populations of 2-4 million.

Methods

We examined incidence for adults diagnosed with a pancreatic exocrine cancer during 1995-2014 and age-standardised net survival up to five years after diagnosis for patients diagnosed during 2000-2013. We examined variation in regional resection rates and survival for patients diagnosed during 2010-2013. The data were extracted from the National Cancer Registration and Analysis Service.

Results

Age-standardised annual incidence rates of exocrine pancreatic cancer increased from 17.1 per 10^5 during 1995-1999 to 18.7 during 2010-2014. Age-standardised one-year and five-year net survival increased from 17.9% and 3.6%, respectively, for 2000-2009, to 21.6% and 4.2% during 2010-2013. There were 2,086 (8.9%) resections among 23,415 patients in 2010-2013. The proportion ranged from 5.1% to 19.6% between centres. Among resected patients, survival was 73.0% at one year and 20.2% at five years. Of the 2,118 resected patients, 18 (0.9%) were at stage 1; 34 (1.6%) at stage 2; 791 (37.3%) at stage 3 and 140 (6.6%) at stage 4, although 53.6% of stage information was missing. Five-year survival was 2.1% for those who were not resected. The number of resections performed in each centre was not correlated with one-year survival.

Conclusions

Despite improvements in the management of pancreatic cancer in England with the introduction of specialist centres, resection rates remain relatively low, and survival remains lower than in comparably wealthy countries.

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INTRODUCTION

Pancreatic cancer is one of the most lethal cancers in adults. It is estimated that almost 460,000 cases occurred world-wide in 2018, with 430,000 deaths. (1) In England, survival is the lowest among the 10 most common cancers. (2) Unfortunately, there is currently no viable screening test for pancreatic cancer, (3) but there has been some improvement in outcome in recent years, especially among the 15-20% of patients who can have removal of the cancer by surgery, followed by adjuvant chemotherapy. (4-6) Trials have shown a small to modest improvement in the 30% of patients with locally advanced disease, and for patients with metastatic disease who have good performance status. (7, 8)

Cancer incidence and mortality rates vary widely, (9) but five-year survival from cancer in Europe has improved over the past 20 years.(10) Disparities in cancer survival persist, even between high-income countries. (11) Stage of disease at diagnosis, timely access to effective treatment, and the extent of comorbidity are probably the main determinants of patient outcomes. (12)

In the UK, wide disparities in surgical outcomes for pancreatic cancer between District General Hospitals and specialist tertiary centres led to the introduction of centralised pancreatic centres between 2001 and 2006. (13-15) Each centre covers a population of 2 to 4 million people, either as a stand-alone pancreas-specific centre or as part of a Hepato-Pancreato-Biliary (HPB) centre. (16) Patients referred to a pancreatic centre are given a diagnosis, and the specialist Multidisciplinary Team (sMDT) decides the best management. Surgical resection is carried out in the specialist centre, but oncological medical therapy and palliative care are undertaken either centrally or at the referring unit.

This is the first study to evaluate national incidence and survival trends for pancreatic cancer, and to assess variation in survival between areas covered by the 23 pancreatic cancer specialist centres for all patients in England, both for all patients and for those who had a resection.

DATA AND METHODS

Study Design

We calculated age-standardised annual incidence rates for all adults (15-99 years) diagnosed with a primary, invasive, malignant neoplasm of the pancreas in England between 1 January 1995 and 31 December 2014. We also estimated age-standardised net survival up to five years after diagnosis. The cohort approach was used for patients diagnosed between 1 January 2000 and 31 December 2009, all of whom were followed up for at least five years by 31 December 2014. The period approach was used to obtain short-term predictions of five-year survival for patients diagnosed between 1 January 2010 and 31 December 2013. (17)

This study is part of the Cancer Survival Programme, approved by the Ethics Committee of the London School of Hygiene and Tropical Medicine (#11984, updated 6 April 2018).

Data

The main source of information was the National Cancer Registry database, which was maintained by the Office for National Statistics (ONS) at the time of data acquisition. Cancer records were linked to Hospital Episode Statistics (HES) records and the Cancer Analysis System (CAS) to derive data on treatment and stage. These databases are now maintained by the National Cancer Registration and Analysis Service (NCRAS) in Public Health England (PHE).

Extensive quality control of the data was performed. Details of the eligibility and exclusion criteria have been described. (18) Patients for whom a death certificate or autopsy report was the only information available, were excluded from survival analysis because their duration of survival was unknown, but these patients were included in the calculation of incidence rates for the year of their death. Patients whose vital status was unknown, those aged 100 years or over at diagnosis and those whose records contained invalid dates or date sequences were also excluded from survival analysis.

Tumour morphology was coded according to the World Health Organisation's International Classification of Diseases for Oncology (revision 3.1).(19) Tumours were grouped into three broad morphologic categories for analysis: exocrine carcinomas, pancreatic neuroendocrine tumours (PNET), and other malignant cancers of the pancreas.

Pancreatic cancer specialist centres

For survival analysis, patients were allocated to one of the 23 areas covered by each pancreatic centre, by mapping all National Health Service (NHS) Trust hospitals, hospices and Primary Care Units, using treatment information from Hospital Episode Statistics. Each region represents one of the 23 pancreatic centres and its local providers. Patients were allocated to the hospital where they received surgery, or if not, chemotherapy or radiotherapy. If no treatment had been recorded, they were allocated to the hospital where they were diagnosed. Specialists in each centre agreed the mapping of hospitals to pancreatic centres, with the exception of Cambridge, Blackburn, Hull and North West London. This was a population-based analysis for residents of England, so patients resident in other UK nations (Wales, Northern Ireland, Scotland), or Ireland, but who were treated in a pancreatic centre in England, were not included in the analyses.

Treatment and Stage

Information on surgical treatment was obtained from Hospital Episode Statistics data. We used codes for 17 major surgical procedures from the Office for Population Censuses and Surveys' Classification of Interventions and Procedures (fourth version) (OPCS-4). (20) These procedures include all types of partial and total pancreatectomy (OPCS-4 codes J55.1-2, J55.8-9, J56.1-4, 8 and 9, and J57.1-5, 8 and 9) (S1 Table), which were designated as of curative intent by pancreatic cancer specialists. Patients who received major surgery between one month before and six months after diagnosis – regardless of any additional treatment – were assigned to the "resected" group, and patients who either received only minor surgery, chemotherapy, radiotherapy or no standard oncological treatment were assigned to the "non-resected" group.

Composite stage at diagnosis was derived from an algorithm that was designed to combine data on stage from various sources, prioritising information in the clinical audit data, then data from the Cancer Analysis System (CAS) and the National Cancer Registry database. (21) In this study, however, the only source of information on stage was the CAS database, because there is currently no clinical audit database for pancreatic cancer. Data on the individual tumour (T), nodes (N) and metastasis (M) components of stage were combined to derive a summary stage variable with four categories, with stage 1 representing localised cancer, stages 2 and 3 representing larger tumours, with nearby tissue or lymph nodes involved, and stage 4 indicating metastatic cancer. (22)

Statistical Analysis

Annual incidence rates per 100,000 persons were calculated for each year between 1995 and 2014, age-standardised to adjust for changes in the age profile of the population over time. We used the European Standard Population weights, modified to reflect only the adult population (15-99 years). (23)

We estimated net survival up to five years after diagnosis. Net survival is the probability of survival derived solely from the risk of death from cancer, correcting for the risk of death from other causes (background mortality).(24) To enable comparison of survival estimates for all ages combined between geographical areas and over time, survival estimates were age-standardised with the International Cancer Survival Standard (ICSS) weights. (25)

Variation in age-standardised net survival between the regions served by each pancreatic centre around the pooled estimate for England for patients diagnosed during 2010-2013 is shown in funnel plots, (26) in which the survival estimates for each region are plotted on the y-axis against their precision (the inverse of the variance) on the x-axis. The control limits, in the shape of a funnel, represent the theoretical distribution of survival around the overall mean value for England across the observed range of precision of the regional survival estimates, at 95% and 99.8% significance. Survival estimates outside the control limits represent regional variation that is wider than would be expected from simple random variation, after controlling for differences in the precision of the estimates. Linear regression was used to determine the association between the number of resections performed in each pancreatic centre during 2010-2013 and one-year net survival for patients who were resected. We used the number of patients who were resected, rather than the proportion of those referred who were resected, because some HPBs receive a larger number of patients whose tumours are not resected.

RESULTS

Pancreatic cancer was diagnosed in 133,325 patients in the 20 years covered by the study (1995-2014 inclusive). Based on the study eligibility criteria, 132,693 (99.5%) patients were included in the incidence analyses, and 121,359 (91.0%) in the national survival analyses (S2 Table). For 81,610 (61%) patients, the morphology of the pancreatic cancer was registered as 'not otherwise specified', either because of poor tissue availability or based only on co-axial imaging. These tumours were included among the exocrine tumours, since the vast majority of tumours with known morphology were exocrine carcinomas.

For the regional survival analyses (patients diagnosed during 2010-2013), 1,632 (6.2%) of 26,091 patients were excluded because of missing information on the hospital of treatment, including a small proportion of patients who were treated in private hospitals or cared for in hospices or nursing homes. In all, 24,459 patients were included in the survival comparisons between the 23 pancreatic cancer centre regions (Table 1).

National Incidence and Survival

Exocrine pancreatic tumours

Exocrine carcinomas comprised 97.6% of all pancreatic tumours diagnosed during 1995-2014 (S2 Table). Age-standardised incidence rates for exocrine tumours rose slightly but steadily from 17.1 per 10^5 per year during 1995-1999 to 17.3 during 2000-2004, 18.3 during 2005-2009 and 18.7 during 2010-2014 (Figure 1).

Age-standardised one-year net survival for pancreatic exocrine cancers increased from 17.9% for patients diagnosed during 2000-2009 to 21.6% in 2010-2013. Five-year net survival increased slightly from 3.6% during 2000-2009 to 4.2% in 2010-2013 (S1 Figure).

Pancreatic neuroendocrine tumours

Pancreatic neuroendocrine tumours (PNET) comprised only 2.3% of all pancreatic tumours diagnosed during 1995-2014 (S2 Table). Age-standardised incidence rates also rose, but remained below 1.0 per 10^5 per year throughout the 20-year period 1995-2014 (data not shown).

For patients diagnosed with a PNET during 2000-2009, one-year net survival was 62.0%, rising to 71.3% for patients diagnosed during 2010-2013. Five-year net survival for patients diagnosed during 2000-2009 was 36.5%, rising to 42.9% during 2010-2013 (S1 Figure).

Variation of Survival by Pancreatic cancer Centre region (exocrine tumours)

For exocrine tumours, age-standardised one-year net survival varied between centres from 16.1% to 36.4%, while 5-year survival ranged from 1.7% to 7.6% (Figures 2a & 2b).

One-year net survival was within the control limits for 19 of the 23 regions (Figure 2a). Survival estimates for Manchester and South West London were high outliers, whilst those for Leicester and North East London were low outliers. Five-year net survival was also within the control limits for 19 of the 23 regions (Figure 2b). The estimates for Oxford, South West London, Liverpool and Manchester were above the 95% control limit but within the 99.8% limit. The estimates for Cambridge, Birmingham, Nottingham and Stoke-on-Trent were low outliers, outside the 99.8% limit.

Variation in Stage, Resection rates and Survival after resection (exocrine tumours)

For all 24,769 pancreatic exocrine patients diagnosed in 2010-2013, including those treated in private hospitals, hospices or nursing homes, stage 1 was reported for 110 (0.4%), stage 2 in 288 (1.2%), stage 3 in 1,838 (7.4%) and stage 4 in 7,315 (29.5%), but information was missing for 15,218 patients (61.4%) (Table 2). Among 2,118 resected patients, tumour stage 1 was returned in 18 (0.9%), stage 2 in 34 (1.6%), stage 3 in 791 (37.3%) and stage 4 in 140 (6.6%), while information was missing for 1,135 (53.6%) (Table 2). Among the 398 patients with stage 1 or 2 exocrine cancer, 52 (13.2%) were resected. South West England (Plymouth and Bristol) and West Midlands (Birmingham, Coventry and Stoke-on-Trent) had the highest proportion of stage 4 tumours (data not shown).

Nationally, only 2,086 (8.9%) of 23,415 patients with an exocrine tumour underwent resection (Table 3) in 2010-2013, 13,827 (59.1%) received minor surgery, 977 (4.2%) received only chemotherapy and 6,173 (26.4%) underwent only a diagnostic procedure (results not shown). A small proportion of patients (1.5%) received other or unrelated procedures. Among resected

patients, net survival was 73.0% at one year and 20.2% at five years (Figure 3a). One- and five-year net survival was higher among resected patients than non-resected patients (Figure 3a).

One-year survival for patients who were resected for an exocrine tumour diagnosed during 2010-2013 was within the 99.8% control limits for all 23 regions (Figure 3b). Survival in South West London and Guildford territories was above the 95% control limit, and in Plymouth, below the 95% control limit. Five-year survival ranged between 6.6% and 29.9% for those who were resected and between 0.2% and 5.4% for those who were not, but most of these estimates were not statistically robust due to the sparseness of data (flagged in S3 Table). The proportion of resections for pancreatic exocrine cancers ranged from 5.1% in Nottingham to 19.6% in Oxford (Table 1), but the number of resections performed in each centre was not significantly correlated with one-year survival among resected patients (r^2 = -1.2%).

DISCUSSION

The incidence of pancreatic cancer in England has increased slightly over the 20 years between 1995 and 2014. Similar increases have been reported in the USA and globally, (27-29) suggesting change in the prevalence of risk factors. Whereas smoking has decreased, other risk factors, notably obesity and diabetes mellitus, have been increasing. (30) It has been estimated that lifestyle and environmental factors accounted for 31.5% of all pancreatic cancers in the UK in 2015. (31)

Despite small improvements in one-year and five-year survival between 2000 and 2013, pancreatic cancer patients continue to experience poor survival. Exocrine carcinomas, which comprise the vast majority of pancreatic tumours, have a particularly poor prognosis. Survival for patients who underwent resection was much higher than for those who did not. Short-term (one-year) survival varied between the regions served by the 23 specialist centres, but the number of resections performed at each centre did not explain this variation. At one year after diagnosis, net survival for patients diagnosed during 2010-2013 in South West London (36.4%) was much higher than in North East London (16.1%). At five years after diagnosis, net survival ranged from 7.6% in Oxford to 1.7% in Stoke-on-Trent. For most regions, geographic variation around the national average in one-year and five-year net survival was not wider than would be expected from chance. Only Leicester and North East London were low outliers in one-year survival, while Cambridge, Birmingham,

Nottingham and Stoke-on-Trent were low outliers in five-year survival. Regional variation in short-term survival was smaller among patients who were resected.

Major obstacles in managing exocrine tumours include the lack of specific early symptoms, advanced stage at diagnosis, and rapid progression. Emergency presentation is still the most common route of diagnosis, and it is linked to lower one-year survival. (32) Patients diagnosed following urgent referral by their primary care physician under the "two-week wait" rule may have a better prognosis, but only 11% of patients with pancreatic cancer were diagnosed through this route, whilst 50% were diagnosed with an emergency presentation in 2006-2008. (33) This has not changed much over the last 10 years, such that in 2016, emergency presentation still accounted for 46% of diagnoses. (32) In some regions, a large proportion of patients are diagnosed with advanced disease. In Birmingham and Stoke-on-Trent, 60% of patients were diagnosed with stage 3 or 4 cancers. These regions were also among the 20 most deprived Local Authority districts in England on the Index of Multiple Deprivation 2015. (34) In 2016, emergency presentation was the route of diagnosis for 49% of patients living in the most deprived areas, compared with 40% in affluent areas. (32) At the same time, Liverpool, Knowsley (part of the Liverpool region) and Manchester Local Authorities are amongst the top five with the highest proportions of the most deprived neighbourhoods in England, (34) yet Liverpool and Manchester have relatively good survival outcomes, so deprivation alone is unlikely to account for the generally poor outcome data.

This study shows that under-treatment of pancreatic cancer is an important barrier to improving outcomes. In the four-year period 2010-2013, only 8.9% of all patients with an exocrine cancer received a resection. The National Cancer Registration and Analysis Service reported 23,741 patients with an exocrine carcinoma between 2013 and 2015, of whom only 1,917 (8.1%) received surgery: 1,189 (62.0%) of these patients received both surgery and chemotherapy.(35) A study of 147,700 patients diagnosed with pancreatic cancer in the USA, the Netherlands, Belgium, Norway, Slovenia, Denmark and Estonia over different periods during 2003-2016, reported that 23,683 (16.0%) patients underwent a resection. (36) Resection rates varied from 13.1% in Norway and the Netherlands to 21.7% in Belgium, whilst adjuvant chemotherapy ranged from 12.0% in Estonia, 19.2% in Norway, 28.6% in Slovenia, 39.6% in the Netherlands, 55.0% in Belgium, and 55.7% in Denmark, whilst 29.5% had chemo-radiotherapy in the USA. (36)

In this study from England, resection was only undertaken in 52 (13.2%) of 398 patients known to have been diagnosed in stages 1-2 during the four years 2010-2013. The National Cancer Registration and Analysis Service reported that 1,252 (39.3%) of 3,186 patients with stage 1-2 tumours diagnosed during the three years 2013-2015 had a resection, of whom 847 (67.6%) also had chemotherapy. (35) These discrepancies are mostly due to a high proportion of missing data on stage in the Cancer Analysis System database (more than 60% during 2010-2013) that was used to extract the summary stage variable.

Recording a valid cancer stage at diagnosis is vital for treatment, as well as for actionable research, but a major limitation of the NHS data for evaluating outcomes has been the substantial proportion of missing information on stage at diagnosis. Data on stage at diagnosis are often missing in the clinical record. Since 2012, NHS Digital of Public Heath England has routinely published the percentage of all cancer patients for whom a valid stage was recorded, both at national level and by Clinical Commissioning Group (CCG), as part of the CCG Outcomes Indicator set. (37) Under this system, the validity of stage is assessed according to rules set by the UK and Ireland Association of Cancer Registries.

The completeness of stage data for all cancers diagnosed in England increased from 59.4% in 2012 to 81.4% in 2017. (37) A similar increase was seen for pancreatic cancer, from 56% in 2013 to 80% in 2017. (35) The improvements can be attributed to more complete pre-operative staging, better hospital recording of stage and better registration practice (38), but we have not yet been able to access those data. The lack of readily accessible data on stage at diagnosis continues to hamper accurate assessment of treatment outcomes at regional and national level.

In an international study, the proportion of stage 1-2 cancers resected varied from 34% in Norway, 43% in the USA, and 47% in the Netherlands, to 55.7% in Denmark, 61% in Slovenia, and 63% in Belgium. (39) The relatively high proportion of patients receiving adjuvant chemotherapy in England compared to Europe and the USA is related to the longstanding leadership taken in England with the development of adjuvant chemotherapy through large randomised multicentre clinical trials. (5, 40, 41)

For 2009-2011, the 12-month unadjusted survival for resected stage 1-2 exocrine cancers varied from 60% (95% CI: 50–68%) in Slovenia, 68% (65–71%) in Belgium, 69% (65–72%) in the

Netherlands, 70% (68–71%) in the USA, and 77 (70–83%) in Norway. (39) Comparable data for survival by treatment and stage in England are not available, either at a national level or by specialist centre. (35, 42)

Other factors that may have contributed to the differences in survival between pancreatic specialist centre regions include the quality of medical oncological regimens delivered in the palliative and adjuvant settings, the number of specialised surgeons or clinical nurses, and referral patterns between local or specialist hospitals, but we have not been able to access these data yet.

This study showed that one-year and five-year net survival was 21.6% and 4.2%, respectively, for patients diagnosed with an exocrine pancreatic cancer in England during the four years 2010-2013. Comparable data from the US Surveillance, Epidemiology and End Results (SEER) programme show one-year and five year relative survival of 33.5% and 9.3%, respectively, for patients diagnosed during 2009-2015. (43) The European Cancer Registry (EUROCARE) programme showed that the European average in age-standardised one- and five-year relative survival was 26% and 6.9%, respectively, for adults diagnosed with a pancreatic cancer during 1999-2007. (10, 44)

Centralisation of cancer care in high-volume providers has been a gradual but beneficial process in England, as it has led to lower post-operative mortality and morbidity for cancer (45-48) and other non-communicable diseases. (49) A study in Finland showed that the proportion of radical surgery for pancreatic cancer was higher in healthcare districts with a high level of experience compared to regions with a medium or low level of experience, even after adjusting for demographics and stage.(50)

In England, despite the introduction of pancreatic cancer specialist centres more than 10 years ago, survival remains lower than in comparably wealthy countries, and this is reflected in low resection rates, as well as in the high proportion of patients for whom data on stage and morphology are missing. Taken together, these observations reflect an inability to provide timely access to full investigation and effective treatment, reflecting systematic issues of health care funding and organisation. (12)

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CONFLICTS OF INTEREST

John P Neoptolemos is a member of the Medical Advisory Board of Pancreatic Cancer UK. Georgia Papacleovoulou is employed by Pancreatic Cancer UK.

AUTHORS' CONTRIBUTIONS

MPC, AE, BRa, JN, GP and WM designed the study. GP, WM and AE did the mapping of NHS Trust hospitals, hospices and Primary Care Units to the areas covered by the 23 Hepato-Pancreato-Biliary centres in England. AE, GP, WM and JN did the literature search. BRo and MPC created the morphologic groups. AE and WM did the data analysis. AE, JN and MPC drafted the manuscript, tables and figures. GP was involved in the analysis and provided advice. All authors contributed to the interpretation of the results, revised and critically reviewed the manuscript. JN contributed clinical insight. MPC supervised the study.

LEGENDS to FIGURES

Figure 1. Trends in the age-standardised annual incidence rate for pancreatic exocrine tumours in England, 1995-2014.

Figure 2. Funnel plot of age-standardised net survival at (a) one year and (b) five years, in the 23 pancreatic cancer centre regions*, for patients diagnosed with a pancreatic exocrine tumour in England during 2010-2013.

Figure 3. (a) Age-standardised one- and five-year net survival (%) for exocrine pancreatic cancer by resection status in England during 2010-2013. (b) Funnel plot of age-standardised one-year net survival for resected patients with a pancreatic exocrine tumour in the 23 pancreatic cancer centre regions* in England during 2010-2013.

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Table 1. Proportion of resected and non-resected pancreatic tumours in the 23 pancreas regions in England, 2010-2013 inclusive.

HPB territory	Pancreatic Exocrine carcinomas					Pancreatic neuro-endocrine tumours					All Tumours*
	Resected		Not resected		Total	Resected		Not resected		Total	
	No.	%	No.	%		No.	%	No.	%		
London South East	149	**10.7**	1,249	**89.3**	1,398	20	**37.7**	33	**62.3**	53	1,452
London South West	58	**10.5**	492	**89.5**	550	9	**28.1**	23	**71.9**	32	584
London North East	66	**6.7**	912	**93.3**	978	18	**42.9**	24	**57.1**	42	1,020
London North West	76	**14.0**	465	**86.0**	541	10	**30.3**	23	**69.7**	33	574
London North	117	**8.1**	1,330	**91.9**	1,447	30	**40.0**	45	**60.0**	75	1,525
Cambridge	139	**8.2**	1,559	**91.8**	1,698	32	**38.1**	52	**61.9**	84	1,784
Leicester	50	**7.1**	651	**92.9**	701	10	**47.6**	11	**52.4**	21	722
Nottingham	54	**5.1**	1,008	**94.9**	1,062	9	**28.1**	23	**71.9**	32	1,095
Guildford	73	**7.3**	923	**92.7**	996	6	**23.1**	20	**76.9**	26	1,022
Oxford	132	**19.6**	542	**80.4**	674	15	**50.0**	15	**50.0**	30	704
Southampton	123	**7.8**	1,454	**92.2**	1,577	15	**30.6**	34	**69.4**	49	1,628
Plymouth	110	**10.1**	982	**89.9**	1,092	7	**25.9**	20	**74.1**	27	1,119
Bristol	64	**8.9**	653	**91.1**	717	10	**26.3**	28	**73.7**	38	755
Birmingham	132	**7.4**	1,658	**92.6**	1,790	25	**25.5**	73	**74.5**	98	1,888
Coventry	45	**12.0**	329	**88.0**	374	8	**47.1**	9	**52.9**	17	392
Stoke-on-Trent	51	**8.8**	531	**91.2**	582	13	**52.0**	12	**48.0**	25	607
Hull	51	**8.4**	553	**91.6**	604	9	**32.1**	19	**67.9**	28	633
Leeds	94	**6.5**	1,363	**93.5**	1,457	23	**29.1**	56	**70.9**	79	1,538
Sheffield	79	**9.1**	789	**90.9**	868	14	**48.3**	15	**51.7**	29	897
Newcastle	96	**7.6**	1,165	**92.4**	1,261	27	**42.2**	37	**57.8**	64	1,325
Blackburn	61	**7.1**	800	**92.9**	861	6	**21.4**	22	**78.6**	28	890
Liverpool	121	**11.4**	940	**88.6**	1,061	22	**40.0**	33	**60.0**	55	1,117
Manchester	145	**12.9**	981	**87.1**	1,126	28	**45.9**	33	**54.1**	61	1,188
All centres	*2,086*	***8.9***	*21,329*	***91.1***	*23,415*	*366*	***35.7***	*660*	***64.3***	*1,026*	*24,459*
Private hospitals	4	**1.6**	242	**98.4**	246	*1*	***25.0***	*3*	***75.0***	*4*	*251*
Other	28	**2.5**	1080	**97.5**	1,108	*4*	***14.8***	*23*	***85.2***	*27*	*1,136*
Total	*2,118*	***8.6***	*22,651*	***91.4***	*24,769*	*371*	***35.1***	*686*	***64.9***	*1,057*	*25,846*

*Total number of patients, including patients diagnosed with pancreatic tumours of rare morphologies.

Table 2. Proportion of pancreatic exocrine tumours patients by stage and treatment: England, 2010-2013. Total = 24,679.

		No Resection		Resection		Total	
Age group	**Stage**	**No.**	**%**	**No.**	**%**	**No.**	**%**
15-44	**Stage 1**	-	0.0	-	0.0	-	0
	Stage 2	2	40.0	3	60.0	5	100
	Stage 3	12	44.4	15	55.6	27	100
	Stage 4	115	95.8	5	4.2	120	100
	Missing	178	80.5	43	19.5	221	100
45-54	**Stage 1**	3	37.5	5	62.5	8	100
	Stage 2	16	84.2	3	15.8	19	100
	Stage 3	73	44.8	90	55.2	163	100
	Stage 4	502	98.0	10	2.0	512	100
	Missing	718	85.5	122	14.5	840	100
55-64	**Stage 1**	10	76.9	3	23.1	13	100
	Stage 2	28	77.8	8	22.2	36	100
	Stage 3	186	48.6	197	51.4	383	100
	Stage 4	1,406	97.0	43	3.0	1,449	100
	Missing	2,158	87.4	312	12.6	2,470	100
65-74	**Stage 1**	20	71.4	8	28.6	28	100
	Stage 2	54	78.3	15	21.7	69	100
	Stage 3	342	49.9	344	50.1	686	100
	Stage 4	2,324	97.7	54	2.3	2,378	100
	Missing	3,832	90.0	426	10.0	4,258	100
75-99	**Stage 1**	59	96.7	2	3.3	61	100
	Stage 2	154	96.9	5	3.1	159	100
	Stage 3	434	75.0	145	25.0	579	100
	Stage 4	2,828	99.0	28	1.0	2,856	100
	Missing	7,197	96.9	232	3.1	7,429	100
All ages	**Stage 1**	92	83.6	18	16.4	110	100
	Stage 2	254	88.2	34	11.8	288	100
	Stage 3	1,047	57.0	791	43.0	1,838	100
	Stage 4	7,175	98.1	140	1.9	7,315	100
	Missing	14,083	92.5	1,135	7.5	15,218	100

Figure 1. Trends in the age-standardised annual incidence rate for pancreatic exocrine tumours in England, 1995-2014

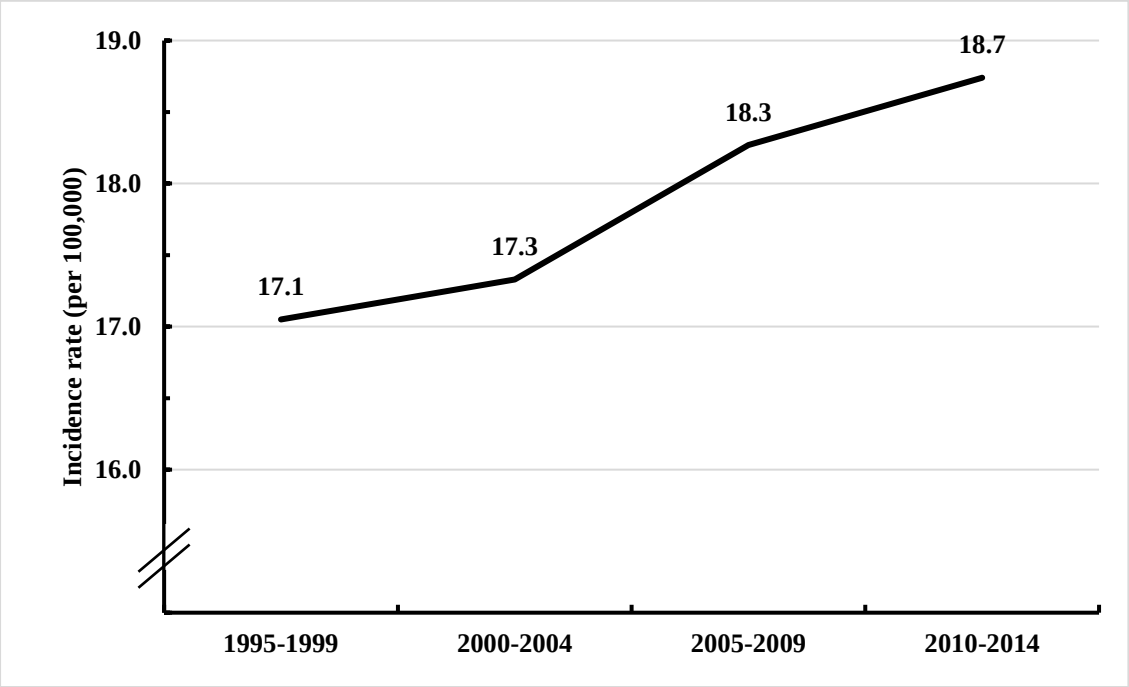
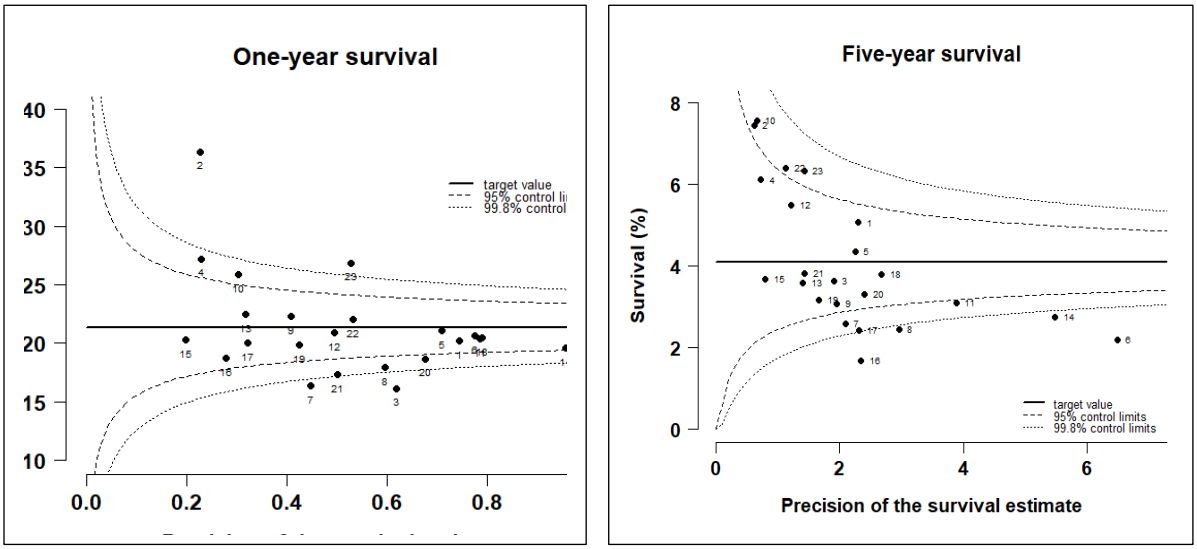


Figure 2. Funnel plot of age-standardised net survival at (a) one year and (b) five years, in the 23 pancreatic cancer centre regions*, for patients diagnosed with a pancreatic exocrine tumour in England during 2010-2013

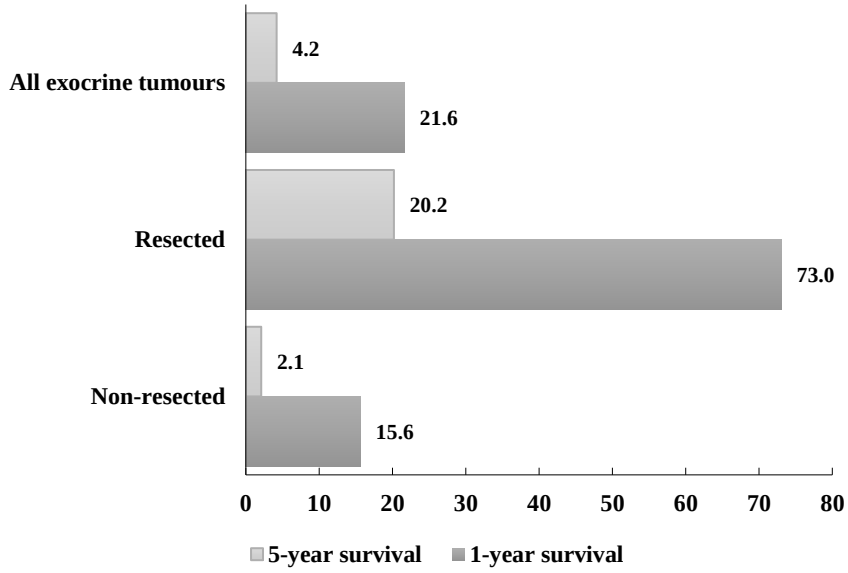
(a) **(b)**



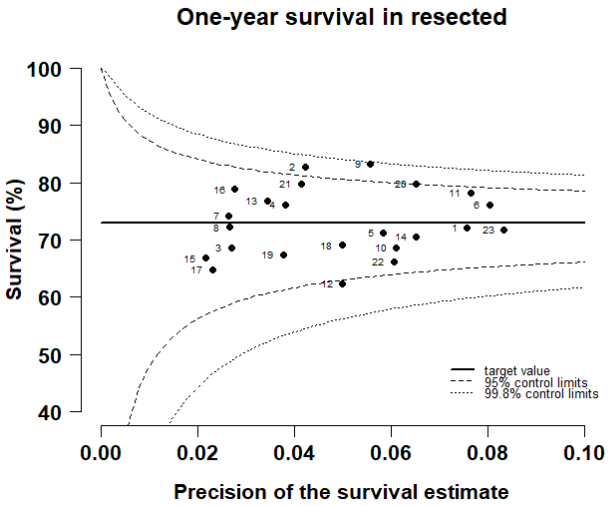
***1** - London South East, **2** - London South West, **3** - London North East, **4** - London North West, **5** - London North, **6** - Cambridge, **7** - Leicester, **8** - Nottingham, **9** - Guildford, **10** - Oxford, **11** - Southampton, **12** - Plymouth, **13** - Bristol, **14** - Birmingham, **15** - Coventry, **16** - Stoke-on-Trent, **17**- Hull, **18** - Leeds, **19** - Sheffield, **20** - Newcastle, **21** - Blackburn, **22** - Liverpool, **23** - Manchester.

Figure 3. (a)Age-standardised one- and five-year net survival (%) for exocrine pancreatic cancer by resection status in England during 2010-2013 (b) Funnel plot of age-standardised one-year net survival for resected patients with a pancreatic exocrine tumour in the 23 pancreatic cancer centre regions* in England during 2010-2013

(a)



(b)



*** 1** - London South East, **2** - London South West, **3** - London North East, **4** - London North West, **5** - London North, **6** - Cambridge, **7** - Leicester, **8** - Nottingham, **9** - Guildford, **10** - Oxford, **11** - Southampton, **12** - Plymouth, **13** - Bristol, **14** - Birmingham, **15** - Coventry, **16** - Stoke-on-Trent, **17** - Hull, **18** - Leeds, **19** - Sheffield, **20** - Newcastle, **21** - Blackburn, **22** - Liverpool, **23** - Manchester.

Supplementary data

Pancreatic cancer incidence and survival and the role of specialist centres in resection rates in England, 2000 to 2014: a population-based study

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S1 Table. Classification of Interventions and Procedures Version 4 (OPCS-4) codes of major resections for pancreatic cancer

OPCS-4 Codes for major resections for Pancreatic Cancer	
J55.1	Total pancreatectomy and excision of surrounding tissue
J55.2	Total pancreatectomy not elsewhere classified
J55.8	Other specified total excision of pancreas
J55.9	Unspecified specified excision of pancreas
J56.1	Pancreaticoduodenectomy and excision of surrounding tissue
J56.2	Pancreaticoduodenectomy and resection of antrum of stomach
J56.3	Pancreaticoduodenectomy not elsewhere classified
J56.4	Subtotal excision of head of pancreas with preservation of duodenum and
J56.8	Other specified excision of head of pancreas
J56.9	Unspecified excision of head of pancreas
J57.1	Subtotal pancreatectomy
J57.2	Left pancreatectomy and drainage of pancreatic duct
J57.3	Left pancreatectomy not elsewhere classified
J57.4	Excision of tail of pancreas and drainage of pancreatic duct
J57.5	Excision of tail of pancreas not elsewhere classified
J57.8	Other specified partial excision of pancreas
J57.9	Unspecified other partial excision of pancreas

S2 Table. Number of patients diagnosed with Pancreatic Exocrine Carcinomas, Pancreatic Neuroendocrine Tumours (PNET) and Other malignant tumours: England, 1995-2014.

Morphology code		Number of cases (1995-2014)	%
Pancreatic Exocrine Carcinomas			
8000	Neoplasm, malignant	22,003	16.6
8001	Tumour cells, malignant	45	0.0
8002	Malignant tumour, small cell type	1	0.0
8003	Malignant tumour, giant cell type	10	0.0
8004	Malignant tumour, fusiform cell type	4	0.0
8010	Carcinoma NOS	59,607	44.9
8011	Epithelioma, malignant	2	0.0
8012	Large cell carcinoma NOS	65	0.0
8020	Carcinoma, undifferentiated NOS	104	0.1
8021	Carcinoma, anaplastic NOS	101	0.1
8022	Pleomorphic carcinoma	24	0.0
8031	Giant cell carcinoma	13	0.0
8032	Spindle cell carcinoma	18	0.0
8033	Pseudosarcomatous carcinoma	6	0.0
8040	Tumorlet, NOS	3	0.0
8046	Non-small cell carcinoma	3	0.0
8050	Papillary carcinoma NOS	29	0.0
8070	Squamous cell carcinoma NOS	150	0.1
8071	Squamous cell carcinoma, keratinizing NOS	15	0.0
8072	Squamous cell carcinoma, large cell, nonkeratinizing	3	0.0
8140	Adenocarcinoma NOS	41,916	31.6
8141	Scirrhous adenocarcinoma	30	0.0
8143	Superficial spreading adenocarcinoma	2	0.0
8144	Adenocarcinoma, intestinal type	13	0.0
8145	Carcinoma, diffuse type	9	0.0
8160	Cholangiocarcinoma	16	0.0
8200	Adenoid cystic carcinoma	5	0.0
8201	Cribriform carcinoma	1	0.0
8210	Adenocarcinoma in adenomatous polyp	2	0.0
8211	Tubular adenocarcinoma	26	0.0
8230	Solid carcinoma NOS	1	0.0
8245	Adenocarcinoid tumour	2	0.0
8251	Alveolar adenocarcinoma	1	0.0
8260	Papillary adenocarcinoma NOS	126	0.1
8261	Adenocarcinoma in villous adenoma	5	0.0
8262	Villous adenocarcinoma	1	0.0
8263	Adenocarcinoma in tubulovillous adenoma	7	0.0
8290	Oxyphilic adenocarcinoma	7	0.0
8310	Clear cell adenocarcinoma NOS	46	0.0
8323	Mixed cell adenocarcinoma	1	0.0
8401	Apocrine adenoma	1	0.0

8430	Mucoepidermoid carcinoma	2	0.0
8440	Cystadenocarcinoma NOS	140	0.1
8441	Serous cystadenocarcinoma NOS	1	0.0
8450	Papillary cystadenocarcinoma NOS	5	0.0
8452	Solid pseudopapillary carcinoma	31	0.0
8470	Mucinous cystadenocarcinoma NOS	62	0.0
8471	Papillary mucinous cystadenocarcinoma	47	0.0
8480	Mucinous adenocarcinoma	984	0.7
8481	Mucin-producing adenocarcinoma	919	0.7
8490	Signet ring cell carcinoma	146	0.1
8500	Infiltrating duct carcinoma	2,226	1.7
8503	Intraductal papillary adenocarcinoma with invasion	11	0.0
8510	Medullary carcinoma NOS	1	0.0
8521	Infiltrating ductular carcinoma	1	0.0
8550	Acinar cell carcinoma	161	0.1
8560	Adenosquamous carcinoma	304	0.2
8570	Adenocarcinoma with squamous metaplasia	6	0.0
Total Exocrine		***129,471***	**97.6**
Pancreatic Neuroendocrine Tumours (PNET)			
8041	Small cell carcinoma NOS	127	0.1
8150	Islet cell carcinoma	154	0.1
8151	Insulinoma, malignant	90	0.1
8152	Glucagonoma, malignant	15	0.0
8153	Gastrinoma, malignant	41	0.0
8154	Mixed islet cell and exocrine adenocarcinoma	19	0.0
8155	Vipoma	7	0.0
8240	Carcinoid tumour NOS	764	0.6
8241	Enterochromaffin cell carcinoid	2	0.0
8243	Goblet cell carcinoid	1	0.0
8244	Composite carcinoid	5	0.0
8246	Neuroendocrine carcinoma	1,888	1.4
8248	Apudoma	1	0.0
8360	Multiple endocrine adenomas	1	0.0
Total PNET		***3,115***	**2.3**
Other			
8720	Malignant melanoma NOS	1	0.0
8800	Sarcoma NOS	26	0.0
8801	Spindle cell sarcoma	4	0.0
8802	Giant cell sarcoma	3	0.0
8803	Small cell sarcoma	2	0.0
8810	Fibrosarcoma NOS	1	0.0
8830	Fibrous histiocytoma, malignant	1	0.0
8850	Liposarcoma NOS	2	0.0
8858	Dedifferentiated liposarcoma	1	0.0
8890	Leiomyosarcoma NOS	24	0.0

8891	Epithelioid leiomyosarcoma	1	0.0
8900	Rhabdomyosarcoma NOS	1	0.0
8920	Alveolar rhabdomyosarcoma	1	0.0
8933	Adenosarcoma	7	0.0
8940	Mixed tumour, malignant NOS	3	0.0
8971	Pancreatoblastoma	6	0.0
8980	Carcinosarcoma NOS	8	0.0
8990	Mesenchymoma, malignant	4	0.0
9070	Embryonal carcinoma NOS	1	0.0
9080	Teratoma, malignant NOS	1	0.0
9120	Haemangiosarcoma	1	0.0
9130	Haemangioendothelioma, malignant	1	0.0
9363	Melanotic neuroectodermal tumor	2	0.0
9364	Peripheral neuroectodermal tumour	5	0.0
Total Other		***107***	**0.1**
All pancreatic tumours		132,693	**100.0**

***NOS= not otherwise specified**

S3 Table. Age-standardised net survival (%) at one and five years after diagnosis from pancreatic exocrine tumours in the 23 pancreas regions in England, 2010-2013 inclusive.

HPB territory	One-year						Five-year					
	No Resection			Resection			No Resection			Resection		
	Net survival	95% CI		Net survival	95% CI		Net survival	95% CI		Net survival	95% CI	
London South East	**13.4**	13.1	13.6	**72.1**	67.0	77.3	**2.8**	2.8	2.8	**21.9**	20.5	23.3
London South West	**31.0**	29.7	32.3	**82.7**	74.8	90.6	**5.4¬**	5.2	5.5	**22.6¬**	20.2	25.0
London North East	**12.5**	12.2	12.8	**68.6**	60.4	76.8	**1.8**	1.8	1.9	**29.9¬**	26.2	33.7
London North West	**19.5**	18.7	20.3	**76.1¬**	68.5	83.8	**4.5¬**	4.4	4.6	**20.2¬**	18.2	22.3
London North	**16.1**	15.7	16.4	**71.2**	65.5	77.0	**2.6**	2.5	2.6	**19.4**	18.0	20.9
Cambridge	**14.6**	14.3	14.9	**76.1**	70.8	81.3	**0.2¬**	0.2	0.2	**19.0**	17.8	20.2
Leicester	**11.2**	10.9	11.5	**74.1**	65.2	83.0	**1.2¬**	1.2	1.2	**16.2¬**	14.7	17.7
Nottingham	**14.6**	14.2	14.9	**72.2**	63.5	80.8	**1.7**	1.7	1.7	**16.1¬**	14.5	17.7
Guildford	**15.7**	15.2	16.1	**83.3**	76.4	90.2	**1.2¬**	1.1	1.2	**20.1**	18.2	22.0
Oxford	**13.5**	13.1	14.0	**68.6**	63.2	74.0	**1.9¬**	1.8	1.9	**24.1**	22.2	26.1
Southampton	**14.5**	14.2	14.8	**78.2**	72.7	83.7	**1.3¬**	1.2	1.3	**19.8**	18.4	21.2
Plymouth	**14.9**	14.5	15.3	**62.3**	56.9	67.8	**3.4¬**	3.4	3.5	**16.7¬**	15.5	17.9
Bristol	**16.3**	15.7	16.8	**76.8**	68.7	84.9	**2.1¬**	2.1	2.1	**12.6¬**	11.5	13.6
Birmingham	**14.7**	14.4	15.0	**70.5**	65.1	75.9	**1.4**	1.4	1.4	**15.7**	14.8	16.6
Coventry	**13.1**	12.6	13.6	**66.8¬**	57.9	75.7	**1.4***	0.0	2.8	**21.5¬**	19.1	23.9
Stoke-On-Trent	**13.0**	12.6	13.5	**78.8**	69.5	88.1	**0.7¬**	0.7	0.7	**6.6¬**	6.2	7.1
Hull	**15.4**	14.9	15.9	**64.8¬**	56.5	73.2	**1.0¬**	1.0	1.0	**21.4¬**	19.1	23.7
Leeds	**16.0**	15.7	16.3	**69.0**	63.0	75.1	**1.3¬**	1.3	1.3	**23.8**	22.0	25.6
Sheffield	**13.6**	13.2	14.0	**67.4**	60.6	74.2	**1.3¬**	1.3	1.3	**14.2¬**	13.2	15.2
Newcastle	**12.5**	12.3	12.8	**79.7**	73.6	85.8	**0.8¬**	0.8	0.8	**22.1¬**	20.3	23.9
Blackburn	**11.6**	11.4	11.9	**79.7**	72.1	87.4	**1.9¬**	1.9	1.9	**25.4¬**	22.5	28.2
Liverpool	**15.0**	14.6	15.4	**66.1**	60.9	71.4	**4.2¬**	4.1	4.2	**19.6**	18.2	21.0
Manchester	**18.8**	18.2	19.3	**71.7**	66.9	76.6	**2.6**	2.6	2.7	**22.7**	21.2	24.3

* unstandardised estimate; ¬ estimates based on sparse data

Supplementary Figure

Pancreatic cancer incidence and survival and the role of specialist centres in resection rates in England, 2000 to 2014: a population-based study

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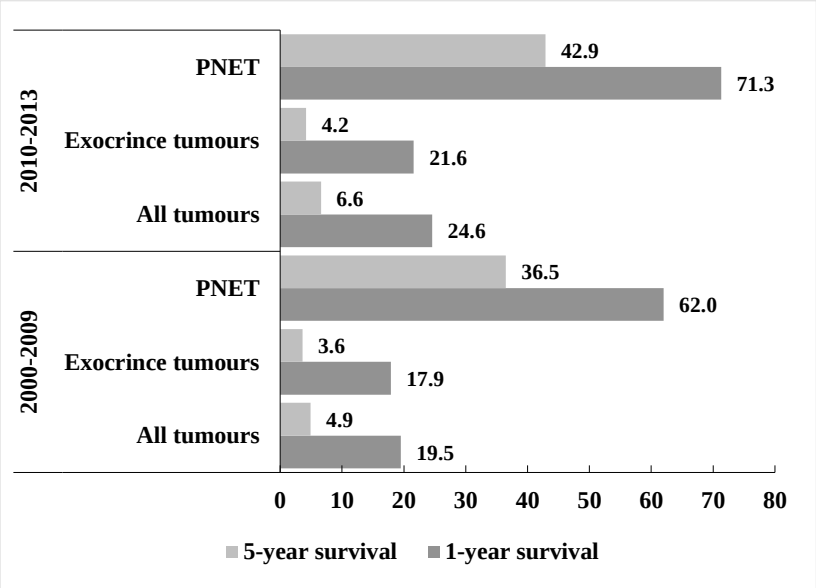
S1 Figure. Age-standardised one- and five-year net survival* (%) for pancreatic cancer by morphology group and calendar period of diagnosis in England, 2000-2013 inclusive.



* Survival in 2000-2009 was estimated with complete approach analysis and in 2010-2013 with period approach analysis.