Pancreatic Cancer Research Funding: Too little for too long.

A report by Pancreatic Cancer Action.

Introduction

Pancreatic cancer is the UK’s fifth biggest cancer killer, which accounted for 8320 deaths in 2011 - an increase of 399 on 2010. Incidence for the same year was 8,773 up by 318 from the previous year. 

While pancreatic cancer is only the 9th commonest cancer in the UK, it is by no means a rare disease and the average-size GP practice is likely to see at least one case every year. The median survival from the time of diagnosis to death ranges from 3 to 6 months after conventional therapy for locally advanced and metastatic disease. Relative survival in the UK is 3-4 per cent to 5 years and less than 17 per cent to one year. Despite much improvement for other cancers, the five-year survival rate for pancreatic cancer has remained at around three per cent with only moderate improvement in over forty years. European one-year survival rates average at ~21 per cent with the highest at 28.3 per cent. Poor one-year survival rates are generally taken to be an indicator of more advanced disease at diagnosis and if the UK matched up to the best in Europe, there is the potential for many more lives to be saved.

The poor prognosis for pancreatic cancer patients can be attributable to the fact that pancreatic cancer is often diagnosed at a late stage where the cancer has progressed to a point where surgical removal is impossible. However, patients who are diagnosed in time for surgery do considerably better and have a ~ 30% chance of surviving beyond five years after diagnosis.

Mortality is increasing:

Studies by Cancer Research UK suggest that pancreatic cancer could become the UK’s 4th biggest cancer killer by 2030 - the same report showing evidence of continuing decline in mortality for most common cancers – with one main exception: pancreatic cancer.

Predictions for 2014 show that in Europe, pancreatic cancer is the only cancer that, in both men and women, is to show an increase in mortality. 

Comparing predicted cancer deaths for 2014 with figures for 2009, the researchers predicted that overall rates of cancer death will fall in 2014 for men by 7% and for women by 5%.

It has been predicted that death rates in women will fall by 9% for breast cancer, 7% for colorectal cancer but will increase by 8% for lung cancer. In men, lung cancer deaths are predicted to fall by 8%, colorectal by 4% and prostate by 10%.

Pancreatic cancer is the only cancer where increased death rates are predicted for both men and women.

The same study showed that pancreatic cancer has been showing a small but steady increase in mortality rates since the beginning of this century. In 2014 they predict that 41,300 men and 41,000 women will die from pancreatic cancer in Europe – giving an age standardised rate of 8 and 5.6 deaths respectively per 100,000 of the population. Between 2000-2004, death rates from the disease were 7.6 per 100,000 men and five per 100,000 women.
Survival Rates for pancreatic cancer are not improving:

The following graph illustrates the little improvement in pancreatic cancer survival since the 1970’s:


This is not the case in other cancers where most have seen significant improvements in 5-year survival since the 1970’s:

![Figure 2 Comparison of 5-year relative survival across cancer sites (CRUK)](image)
In fact, a recent report by the London School of Hygiene and Tropical Medicine, funded by Cancer Research UK gave us the good news that for those in the UK who are diagnosed with a cancer in 2014, half of them are likely to survive more than 10 years. Sadly, this is not the case for pancreatic cancer patients – those diagnosed in 2014 can expect only a 1% chance of surviving 10 years or more – no change since the 1970’s.

There is a direct correlation between the lack of progress in survival for pancreatic cancer and the lack of research funding:

Figure 3 Ten year survival comparisons by cancer site (CRUK)

Figure 4 NCRI site-specific spend by cancer type 2002-2013
Funding of pancreatic cancer research in the UK

Currently, pancreatic cancer receives only 1 per cent of overall cancer research funding in the UK and has been chronically underfunded for decades. The graph in figure 4 shows the trend in survival since 1971 to 2009 for major tumour sites, including pancreatic cancer. It is clear that in some cases vast improvement in survival has been achieved for these tumour sites. The notable exception is pancreatic cancer where change has amounted to a fraction of a per cent.

By comparing the two graphs in both figure 4 and figure 5, it is easy to see that there is a clear correlation between increased research funding and improvements in survival for the majority of cancers over the past 40 years. The exception again is pancreatic cancer.

The majority of cancer research funding in the UK comes from the National Cancer Research Institute partners (NCRI) which is made up of 22 organisations, including the Department of Health, although the majority are very large cancer charities including Cancer Research UK, Macmillan, Marie Curie, Breakthrough Breast Cancer, Breast Cancer Campaign, Children with Cancer, Prostate Cancer UK, Roy Castle Lung Cancer Foundation.

Of the £503 million spent by the National Cancer Research Institute partners (NCRI) in 2013, only £5 million was spent on pancreatic cancer. In contrast, breast cancer received £40 million, bowel cancer, £25 million, leukaemia £34 million, and Prostate £22 million.

The criteria to become a member of the NCRI includes an annual research spend of over £1 million per annum and for these research funds to be allocated by independent competitive peer review. No pancreatic cancer charity currently fulfills this and the pancreatic cancer-specific charities do not have the ability to plug the funding gap for the disease, as they just do not have enough income dedicated to research in any one year.

As can be seen by figure 4, cancer research funding in the UK is very unevenly distributed and funding for pancreatic cancer is very low when compared with other cancer types. This is illustrated not only by the comparative cancer survival rates but also by the paucity of pancreatic cancer clinical trials currently open in the UK (see figure 6 below). At the time of writing, there
are only 9 clinical trials recruiting patients in the UK\textsuperscript{viii} whereas there are currently 76 for breast cancer.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>No. of recruiting clinical trials</th>
<th>5-year relative survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>76</td>
<td>85%</td>
</tr>
<tr>
<td>Lung</td>
<td>62</td>
<td>10%</td>
</tr>
<tr>
<td>Bowel</td>
<td>47</td>
<td>59%</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>40</td>
<td>52%</td>
</tr>
<tr>
<td>Prostate</td>
<td>38</td>
<td>81%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>34</td>
<td>46%</td>
</tr>
<tr>
<td>Oesophageal</td>
<td>26</td>
<td>15%</td>
</tr>
<tr>
<td>Melanoma</td>
<td>21</td>
<td>90%</td>
</tr>
<tr>
<td>Brain</td>
<td>20</td>
<td>19%</td>
</tr>
<tr>
<td>Myeloma</td>
<td>19</td>
<td>47%</td>
</tr>
<tr>
<td>Stomach</td>
<td>18</td>
<td>19%</td>
</tr>
<tr>
<td>Testicular</td>
<td>11</td>
<td>97%</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>9</td>
<td>3%</td>
</tr>
</tbody>
</table>

Figure 6 Cancer clinical trials by cancer site currently recruiting in the UK May 2014

Is incidence the main criteria for funding decisions?

Why there is such an inequality of cancer research funding is not altogether understood but assumptions can be made regarding the structure of the funding mechanisms and the lack of focus on cancers that have shown little or no improvement in survival over the past 40 years.

It is a logical argument that the greater the incidence, the greater amount of funding that is required to tackle the disease and to a large degree this is true. But when we look closely at the NCRI figures compared with incidence, mortality and survival by cancer type, we can see that there are some cancers that have a lower incidence, much better survival and lower disease burden (< % cancer death) than pancreatic cancer but per head receive a disproportionate amount of NCRI funding (see figure 7). For example, ovarian cancer has an incidence level 1657 lower than pancreatic, the 5-year survival rate is 40 per cent higher, it has half the disease burden and receives nearly 3 times as much NCRI cancer research funding. We need to understand why this is.

It may be time for funders to look at the disease burden as the main criteria for funding – to direct funds where they are needed most.

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>2011 Incidence</th>
<th>2011 Mortality</th>
<th>5-year relative survival (%)</th>
<th>2012 research spend £Millions</th>
<th>Spend per patient (£)</th>
<th>% of cancer deaths</th>
<th>% NCRI site-specific spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukaemia</td>
<td>8616</td>
<td>4603</td>
<td>44</td>
<td>32</td>
<td>£3,714.00</td>
<td>3</td>
<td>6.2</td>
</tr>
<tr>
<td>Ovarian</td>
<td>7116</td>
<td>4272</td>
<td>43</td>
<td>12.2</td>
<td>£1,727.00</td>
<td>2.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Cervical</td>
<td>3064</td>
<td>972</td>
<td>67</td>
<td>3.8</td>
<td>£1,240.00</td>
<td>0.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Myeloma</td>
<td>4792</td>
<td>2693</td>
<td>37</td>
<td>5.3</td>
<td>£1,109.00</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Breast</td>
<td>50000</td>
<td>11700</td>
<td>85</td>
<td>41</td>
<td>£820.00</td>
<td>7.3</td>
<td>8</td>
</tr>
<tr>
<td>Oesophageal</td>
<td>8332</td>
<td>7603</td>
<td>13</td>
<td>6</td>
<td>£714.00</td>
<td>5</td>
<td>1.2</td>
</tr>
<tr>
<td>NHL</td>
<td>12783</td>
<td>4646</td>
<td>64</td>
<td>7.3</td>
<td>£573.00</td>
<td>3</td>
<td>1.4</td>
</tr>
<tr>
<td>Brain</td>
<td>9365</td>
<td>4975</td>
<td>15</td>
<td>5</td>
<td>£526.00</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>8773</td>
<td>8320</td>
<td>3</td>
<td>4.5</td>
<td>£512.00</td>
<td>5</td>
<td>0.9</td>
</tr>
<tr>
<td>Prostate</td>
<td>42000</td>
<td>10700</td>
<td>81</td>
<td>21</td>
<td>£500.00</td>
<td>7</td>
<td>4.1</td>
</tr>
</tbody>
</table>
Pancreatic cancer is underfunded across the globe:

Sadly, the issues surrounding lack of pancreatic cancer research funding are emulated across the globe although the USA is making strides to adjust the balance, mainly through the Recalcitrant Cancer Research Act of 2012 and the National Cancer Institute has now a Scientific Framework developed specifically for pancreatic cancer.\textsuperscript{xv}

Pancreatic cancer attracts around 3% per cent of National Cancer Institutes (NCI) funding in the USA. While this is still small in percentage terms, spend has been increasing substantially. In 2000, NCI spent only $20million on pancreatic cancer research. In 2012, that figure was $105million – a rise of over 500%. Correspondingly, there has been a significant increase in the number of principle investigators having at least one grant relevant to pancreatic cancer from 37 in 2000 to 118 in 2012\textsuperscript{xx}

The NCI spend per head for pancreatic cancer is $2333.33 (or £1383.24) – equates to nearly 3x as much than is spent per head in the UK (NCRI).

Unlike the UK, federal government predominantly pays for cancer funding whereas the UK is hugely dependent on the charity sector. In Canada, pancreatic cancer amounts to around 0.5% of research funding\textsuperscript{xxi} and in Australia equates to about 0.8% of a $350 million budget.\textsuperscript{xxii}

What is similar across the globe is the proportion of funds for cancer research budgets allocated to pancreatic cancer is much lower than for other cancers and is illustrated by the following charts:\textsuperscript{xxiii}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Canadian_Cancer_Alliance.png}
\caption{Distribution of cancer research spend by cancer site Canadian Cancer Alliance 2008}
\end{figure}
Figure 8: Distribution of cancer research funding by cancer site Institut National du Cancer (France) 2008

Figure 9: Distribution of cancer research spend by cancer site NCRI (UK) 2008
Figure 10 Distribution of cancer research spend by cancer site American Cancer Society 2008

Figure 11 Distribution of cancer research spend by cancer site American Institute for Cancer Research 2008
**Figure 12** Distribution of cancer research spend by cancer site Congressionally Directed Medical Research Programme 2008

**Figure 13** Distribution of cancer research spend by cancer site National Institutes for Health (USA) 2008
UK Government Cancer Research Funding

With the UK having some of the worst cancer survival rates across the world, perhaps it is time that government funding bodies should identify shortfalls in research funding in areas not covered by private-sector/charitable investment - such as pancreatic cancer.

However, in April 2014, MP Luciana Berger asked the Secretary of State for Health what estimate he had made of the proportion of total funding for cancer research carried out in the UK that came from government in 2010-11, 2011-12, 2012-13 and 2013-14.

The answer was disappointing – funding from government sources reduced by nearly £20million between 2012 and 2013.

Pancreatic Cancer Action had to step in to continue funding for the pancreatic cancer arm of the SYMPTOM Study as recruitment was difficult (due to the nature of the disease) and National Institute for Health Research funding had run out. Without our intervention, the pancreatic cancer arm of this important study may have had to be scrapped.

Barriers to funding

Pancreatic cancer is not an obscure cancer but perceptions of it as a difficult challenge is preventing its progress. The recent success in the treatment of other difficult cancers such as melanoma shows that it is possible to make great gains and to challenge dogmas. Somehow we must change the nihilistic attitudes surrounding pancreatic cancer and to prevent funding not being directed to the disease because of this.

Where to direct funding

International funding for pancreatic cancer is currently proportioned to the following areas:

![ICRP Partners Pancreatic Cancer Areas of Spend 2008](image-url)
It is the view of Pancreatic Cancer Action that a greater proportion of pancreatic cancer research funding should be directed towards improving early diagnosis of pancreatic cancer as this is the area where we are most likely improve long-term survival for patients. Currently the global spend on treatments is more than double that for early diagnosis. In comparison, breast cancer spend on early diagnosis is only 1/3 less than the research spend on developing new treatments and is possibly why survival has increased substantially in the past 40 years for this disease.

If patients are diagnosed in time for surgery, their chance of surviving 5 years or more increases ten-fold. By focusing research spend on early diagnosis we have the potential to increase the number of patients eligible for surgery from 10-20 per cent to 30-50% if we can catch those who are diagnosed with locally advanced or borderline resectable disease (currently around 30% of all patients).

• Early diagnosis spend should urgently be increased in the hunt for a diagnostic biomarker for pancreatic cancer. Work is going on in this area globally but progress is still slow. International collaboration and sharing of ideas is essential for this area.

• Early diagnosis spend should be spent on areas to identify risk and management of patients with pre-cursor lesions such as Intraductal papillary mucinous neoplasms of the pancreas (IPMNs).

• Early diagnosis research spend should look at our primary care system and why it is currently failing to refer patients to the correct specialists in time.

The UK needs a strategy for pancreatic cancer research

There is currently an uncoordinated approach to pancreatic cancer research funding in the UK. It is difficult to understand who is doing what and where.

There is an urgent need to develop a pancreatic cancer research strategy perhaps through the development of a coalition or group. All stakeholders need to be involved including government, charities, researchers, clinicians and pharmaceutical companies to develop a long and short-term strategic plan in order to increase the levels of funding and decide on the priority areas of spend. This is imperative for the UK but we would argue that global collaboration is also formalised.

There are questions that need asking:

1. What is the criteria for funding specific cancers – incidence?
2. Who decides how much funding is given to pancreatic cancer?
3. With the NCRI dominated by large breast (x2), prostate and lung cancer charities – how is it possible to influence this group to increase the level of funding for pancreatic cancer?
4. How can we influence government to increase levels of cancer research funding rather than reduce it?
5. What is the role of pharmaceutical companies – what are they funding now and how can we influence them to increase funding for the future?

Conclusion

Pancreatic cancer has the lowest survival rate of all 22 common cancers and this has not improved in over 40 years. It has been a neglected disease and has been chronically underfunded for decades. This underfunding is directly related to the lack of improvement in survival. In comparison, those cancers that have seen increased investment in research funding
have seen corresponding improvements in survival, in some cases significant uplift in survival rates in excess of 100%.

Lack of research funding is demonstrated by the paucity of clinical research trials for pancreatic cancer in the UK.

Proportions of pancreatic cancer research funds in the USA, Canada, Australia and parts of Europe are similar to those in the UK relative to total cancer research funding although the amount of funds in terms of dollars spent are significantly greater.

Pancreatic Cancer Action is calling for:

- An inquiry into how cancer research funds are distributed between cancer types and why pancreatic cancer receives such a low proportion
- Develop a Pancreatic Cancer Research Strategy in the UK to involve all stakeholders
- Increased levels of government funding to plug the gap for pancreatic cancer
- Invest a greater proportion of research funding into early diagnosis – in particular in the search for a diagnostic biomarker
- Ensure that global collaboration is formalised to prevent duplication of effort (and wasted funds)
- Encourage large cancer research funders such as Cancer Research UK to commit a firm monetary value on their proposed commitment to increase funding where there is identified unmet need (such as pancreatic cancer)
- Encourage greater pharmaceutical/industry research investment in pancreatic cancer
- Change some nihilistic attitudes among funders that pancreatic cancer is not a lost cause.
Pancreatic Cancer Action. Registered Charity No. 1137689.
APPG Inquiry Pancreatic Cancer Research Funding May 2014


v ONS Cancer Statistics Registrations England (Series MB1 – No 41 2010) Released 13 June 2012

vi CRUK the 20 most common cancers in the UK 2009 data are available to download online http://info.cancerresearchuk.org/cancerstats/incidence/commoncancers/uk-cancer-incidence-statistics-for-common-cancers


xv CRUK: 1971-1990


1991-1995


1996-2003


2005-2009


xvi http://www.cancerresearchuk.org/cancer-info/cancerstats/survival/common-cancers/#One


xviii http://www.cancerresearchuk.org/cancer-help/trials/

xix National Cancer Institute, Scientific Framework for Pancreatic Ductal Adenocarcinoma (PDAC) February 2014

xx National Cancer Institute, Scientific Framework for Pancreatic Ductal Adenocarcinoma (PDAC) February 2014 Addenda

xoi International Cancer Research Partnership, Cancer Research Funding from an International Perspective 2012

xox National Health and Medical Research Council, Australia

xiii International Cancer Research Partnership, Cancer Research Funding from an International Perspective 2012

xiv http://www.theyworkforyou.com/wrans/?id=2014-03-31b.193693h