Pancreatic Cancer APPG Inquiry

Further evidence form the research community – 7th July 2014

Eric Ollerenshaw: Thank you for coming along. My name's Eric Ollerenshaw and I'm chairing this inquiry.

On my left I've got Baroness Masham and Baroness Morgan. I will try and keep them under control, which is my job. We're sitting like a select committee so we can actually produce what we hope will be an evidence based report to go to the Secretary of State for Health. We have already done one and this one is specifically looking into the research of pancreatic cancer and so on. We're not a select committee in the sense of all the rules and regulations, so just to reassure you that whatever you say will be taken down in evidence and all the rest of it, but you can then have a say over what you've said.

What I've always said to people who come along, if there's something when you leave this place you think you should have said, then please put it in too, because we aim to produce a report by October we're aiming for, anything on those lines would be really grateful.

We've got apologies from Doctor Mukherjee, he's hurt his back and is unable to attend today.

We've had your written evidence which we have looked at and we have been really grateful, so what we intend to do is give you a few minutes just if you want to say anything beyond that and then we'll go straight to questions.

I'm going to have to leave here at twenty-past-four because I've got to be in the chamber to get a question in on M6 and exit routes for it, nothing to do with pancreatic cancer. Shall we start with Professor Evans first?

Professor Jeff Evans: Yes, well thank you very much. I work in Glasgow where I'm Director of the Institute of Cancer Sciences and Professor of Cancer Research at the University of Glasgow, and also I work in the CR UK Beatson Institute running a laboratory group on pancreas cancer. I am a Consultant Medical Oncologist there, running the Glasgow Experimental Medicine Cancer Centre.

I think since this is the third time this group has met I don't think we need to reiterate how difficult a problem pancreatic cancer is, I think we're all well aware of the statistics. For anybody who's not been to one of the meetings before, this is one of the hardest cancers to treat in all of oncology.

Not only is it increasing in prevalence and incidence in the developed world, but in addition to that the death rate has not improved at all over several decades and as a consequence, is predicted to be probably the second commonest cause of cancer deaths by the end of this current decade.

I think there are a number of challenges but also a number of opportunities. I think the way ahead is to go back and increase our understanding of the basic cancer biology; how this cancer develops and progresses; the molecular and cellular events that underpin that, because it is a genetic and a genomic disease; and how we can best exploit that, not only for better treatments but also better diagnostics and better detection, ultimately so that we can improve quality of life and also survival for patients.

I think now we have a very strong grouping of experts within the UK who are committed to researching this disease, and in addition to that we've had generous contribution from Cancer Research UK and other relevant charities, but I think that should really be the catalyst to lever more finance from other stakeholders, so that we can make further advances and make a real difference in this disease.

I think that we could be the international leaders in pancreatic cancer research and treatments in the future. We've got the right people and the right infrastructure; it now needs the right resource.

Eric Ollerenshaw: Well, that's a fantastic end; we'll come to that in a minute. Nick, do you want to say…

Nick Grant: Yes, thank you very much. My name's Nick Grant, I'm the Director of Strategy at Cancer Research UK. As many of you all know we're the largest fund raising charity in the UK, and the largest independent funder of cancer research in the world, actually second in overall scale to the US government.

We're phenomenally fortunate to receive all our funding from the generosity of the UK public through a range of different fundraising activities, and we support around £350 million worth of research per annum across some of the basic biology areas, that Jeff was talking about, through translational, clinical and population sciences, really well across, supporting about 4,000 scientists, doctors and nurses across the UK, clearly researching into all different types of cancer, so over 200 different types of cancer.

In my role at Cancer Research UK I work to support all the teams across the charity in terms of strategy development, so our long term approaches of how we make better progress against our ambitions.

A lot of my time over the last couple of years has been in the development of our new research strategy which we published in April this year, so working with my scientific colleagues, with experts from the scientific and clinical communities, and with our partner organisations, including Pancreatic Cancer UK, Pancreatic Cancer Research Fund.

I can talk in more detail about what's in our research strategy, but we've highlighted pancreatic cancer research as one of the very highest priorities because we're very keen to see an increased focus and a significant increase in the level of research that happens within the UK into pancreatic cancer, so this is a very timely and welcome enquiry for us in terms of how

we all work together in terms of making progress against what Jeff said is the most devastating form of the disease.

Lord Aberdare: I'm sorry I'm late.

Eric Ollerenshaw: Don't worry. Don't worry. Baroness Morgan, do you want to start us off?

Baroness Morgan: Yes, I would actually. Obviously, CR UK's new strategies are very important and particularly, as you say, as the largest independent funder of cancer research in the world, so very important for patients who are concerned about pancreatic cancer.

In really simple terms what will be different for pancreatic cancer research as a result of the new strategy?

Nr Nick Grant: I think the largest and most significant statement of intent that we've made in the strategy is to grow the overall level of activity, and therefore our research then in the area. We've stated an ambition to increase our spend in pancreatic cancer research by two to three fold over the next five years.
Coupled with that, clearly it's not just about volume; it is about the quality of research. As Jeff said already, we have already a number of absolutely leading experts internationally in pancreatic cancer research in a number of fields in the UK. What we would like to ensure over the coming years is that we build on that by attracting new people to work into the field.
That would both be established researchers who are currently potentially working in other cancer types who can adjust their focus to increase the focus on pancreatic cancer, but also attracting new generations of researchers into this field as we continue to build the breadth and depth of the research field.

Baroness Morgan: Doubling or trebling, so obviously people here today will be interested in the trebling, so how do you go from doubling to trebling? What will influence that?

Nick Grant: Yes, it's probably quite helpful to talk a little bit about how we fund research, and therefore what some of the barriers are to actually making that increase in funding happen in practice.

We broadly have two mechanisms by which we support research. We have our intramural research efforts which essentially are our own research institutes that sit within universities, and so, as Jeff was saying, he works within our Beatson Institute in Glasgow. That represents about a third of our funding.

Then the other two-thirds are through what we call response mode funding, so that's where a researcher in an academic location makes an application for funding by writing a grant proposal, we will send that out to the leading experts around the world in that area of science for peer review.
It will come back to one of our scientific committees for review, and we pull together a panel of, again, scientific experts and they will address whether that research is of suitable quality for us to fund it or not.

Now, one of the issues we've had historically is, and the reason why pancreatic cancer research hasn't got as much funding as we would have liked, is not that we haven't necessarily prioritised it against other cancers, applications that have come through, but we simply haven't seen the applications – as many application as we would like come through for funding in pancreatic cancer research.

In essence there's a lack of capacity in the UK community with an interest in working in this field. Where we have received applications, they've had the same success rate, if you like, at our committees as applications from other cancer types. A lot of the thinking over the last year or two has been how do we change that? How do we get more people interested in working in the area? How do we signal our intent and how do we ensure that the new generations who are coming into cancer research are starting to work in this field?

One of the important things that we have done within our new strategy and are working on with our funding committees is to say to them where you receive applications across a number of cancer types, we would like you to first of all make a clear decision on is this of acceptable funding quality or not?

Then, where we have a number of applications that are of acceptable quality but we don't have the funds to fund all of them, because typically we aren't able to fund everything that comes through, we would like you to prioritise applications that are in the four, what we call, cancers of unmet need, so lung, pancreatic, oesophageal and brain cancers, such that they will, if they're of an acceptable quality, receive preferential treatment in our committees.

We're confident that we'll make a difference but it also sends a signal of intent out to the UK community that this is an area that's very important to us.

Professor Jeff Evans: Perhaps if I could add to that as well. I obviously can't speak on behalf of Cancer Research UK, but I am a recipient of research funding from them, and I think that the emphasis that was made on the last strategy, of increasing awareness of pancreatic cancer and driving more research, has clearly had an impact, I think, on the existing infrastructure in the UK, which is far higher up the agenda now than it was more than five years ago.

I think several of us have been fortunate to have been researching into pancreatic cancer at the time those advances were made. It's not just about pancreatic cancer research itself, it's how we exploit what's happening in cancer research in general and apply that to pancreas cancer. I think that, I can only speak for our own institutes since some of us started working on pancreas cancer, the models that we've used in the laboratory to facilitate that research have been used by many other groups, where previously they might have used other tumour models.

So the amount of research that is coming out of pancreatic cancer is probably greater than perhaps the amount of money that is put into it because of this almost ripple effect on other people as well.

Baroness Masham: Professor Evans said that pancreatic cancer was the hardest cancer to treat. How do you treat it? Yesterday in the 'Sunday Times' there was a big spread which was very disturbing about new treatments not being used because NHS England wouldn't pay for them where Scotland pay for them. It must be terribly frustrating if there is a cure or a better way of treating something and you can't use it because of the money. What can be done about that?

Professor Jeff Evans: I think perhaps we're one step further back from that and before we come onto the issue about funding for new regimens, perhaps talk a bit about existing agents we use, how we might improve that in future and then how will that be resourced, which I think is a big question.

At the moment pancreatic cancer patients will present either with advanced disease or a spread outside their pancreas, about 50% of cases. They will present with disease that is localised to the pancreas but can't be removed which is probably another 35% of cases. Then there is about another 15% of patients that can be treated with an operation.

Now, although they can be treated with an operation, the results of surgery, even with post-operative chemotherapy, are still hugely disappointing. This is a disease that has probably either already spread or is primed to do so at the time of diagnosis and at the time the symptoms may develop, and therefore that is one of the challenges the disease presents us with.

For those where surgery is feasible and they have surgery, and this is a surgery associated with quite a bit of morbidity and sometimes mortality, and if the patients are fit enough that is followed by post-operative chemotherapy. The drugs that we use there, there is no issue about funding because the drugs have been approved for 15 to 20 years.

Then there are those with locally advanced disease where we treat them with chemotherapy, and there is some controversy about whether radiotherapy should be used as well, and then there's chemotherapy for those with advanced disease. Having highly effective new drugs that we campaign for would be probably an easy challenge; in some ways the real challenge is to find better treatments in the first place.

You're absolutely quite right; we're beginning to see the challenges of funding for cancer treatments that have been prevalent in other tumour types beginning to come into the pancreatic arena. How we develop better treatments in the future, I'm sure we'll come onto and I'm happy to discuss that.

Clearly we will need to have a strategy in place that if we do come up with better treatments, and it is not just about new drugs but also refining which patients get the existing drugs we use, so that we give the right drug to the right patient, because clearly some people are much more sensitive to existing chemotherapy than others, repurposing some drugs that we probably use in other tumour types that have been sometimes forgotten about, as well as the new entities we're trying to develop, and that will be

where the funding issue comes into play when we've got evidence that they work.

Baroness Marsham: Do you find you're getting the patients quick enough? Do GPs know enough about diagnosing?

Professor Jeff Evans: Yes, I think there are two questions there. Do we get patients with a diagnosis of invasive cancer quick enough, and can we diagnose a cancer quick enough? Can we go back and detect it before it's cancerous? We'll come back to that one, because I think that's a bigger challenge intellectually.

At the moment these patients are often quite unwell at first presentation. Their performance status, which is a guide that we in oncology use for how fit the patient is, often deteriorates quite rapidly. So there is sometimes when patients go through the diagnostic process they have considerable morbidity, weight loss, anorexia, muscle wasting, fatigue, probably more so in this cancer than many others, and also this often occurs over a rapid time scale.

Therefore this presents challenges to us in that a lot of patients aren't fit enough to go on to experimental treatment trials by the time that they come to us. If we could certainly increase the speed of the diagnostic journey, if you like, of patients when they initially become symptomatic and in primary care or when they're in secondary care undergoing investigations by the time they get to tertiary care and oncologists, I think that would make certainly a difference to those individual patients.

It would probably make a difference for us as well because we might capture more people when it's at an earlier stage of the disease, such as operable or locally advanced disease, and those who have advanced disease from, right from the start as we mentioned earlier, maybe then more fit to be able to undergo the existing treatments we have and then enter into clinical trials and better treatments in the future.

A second question though is that if this is a disease that is already spread or primed to be spread right from the time that the invasive cancer becomes symptomatic and diagnosed, can we diagnose pre-cancerous, what we call PanIN, pancreatic intraepithelial neoplasia, we call it PanIN 1, 2, and 3. We don't have a very well identified high risk group we can screen, we don't have a robust screening tool that we can use to identify those patients, or a very good treatment once we've identified it.

I think it is probably high risk but highly rewarding researching, diagnosing and developing screening tools and biomarkers, be it blood borne, tumour based, or imaging, of pre-cancerous lesions, and then going for a screening strategy as well as focusing on clearly the needs of patients with advanced disease and new drugs.

Baroness Masham: My last question: would the CyberKnife help with tumours?

Professor Jeff Evans: Well, I'm not a radiation oncologist, so I'm sorry someone else isn't here to answer that question. I guess the honest answer is we can't say that it will and we can't say that it won't, because we haven't done a trial comparing CyberKnife with other forms of radiation treatment for locally advanced disease.

Now, I know enough about radiotherapy, if not the technical aspects of it, to know where it fits into this disease. There have been some negative trials recently coming out of the French group, where the addition of induction chemotherapy and then continuing chemotherapy or radiation, hasn't improved overall survival.

Now, I would question the design of that trial because I don't think overall survival is the right question, it should be about local control with radiotherapy because it's a localised treatment. So I think radiation treatment does have a role to play, particularly in those that we call 'borderline resectable', - we've now defined a new entity in pancreas cancer, 'borderline resectable – not sure if we can operate it but if we shrank it down it might do. Probably about 7% of the patients present in that way.

With a borderline resectabletumour, I think there clearly is a role for radiation and optimising the local control. We have ideas about doing that by using drugs that might sensitise the radiation.Whether CyberKnife, or other forms of technical radiotherapy is superior to existing treatements, I don't think we've done the trials to find out.

Eric Ollerenshaw: Can I just say, for the benefit of everybody here, that Lawrence Dallaglio, which the article was about, is having a meeting from four o'clock today in the Jubilee Room. When you leave here it's just off Westminster Hall. I think anybody's welcome to go along. He's following up on what he was saying. He's been in the 'Sunday Times', which might be an interest, which I'm hoping to get along to myself later on.

Can I just ask a political question? You don't have to answer if you don't want. There has been some talk in the paper by the Secretary of State of having a kind of hit-list of GPs by their performance. What's your personal view on having such a list?

Professor Jeff Evans: Well I'm not a GP but I've many friends who are GPs. Quite honestly, in this disease I don't think that's going to be helpful. If I can make a political statement, I think it's easy to deflect the blame onto GPs for saying you don't pick this up early enough.

I obviously see the patients who come to me when they've been through primary care and secondary care, and it's quite easy to look at in retrospect could we have shortened the journey? But many of these patients present with fairly non-specific symptoms that are very difficult to distinguish from other benign causes.

I think until we facilitate GPs to have more rapid access perhaps to the sort of investigative tools like CT scanners that are available in secondary care,

or expand the capacity in diagnostic services, both pathology, radiology and secondary care to investigate red flag symptoms in a quicker way, I think we're probably diverting attention from the challenge of this disease onto blaming GPs when actually they should probably be blaming the cancer because by the time it's presented it's often inoperable and difficult to treat.

I think that's where research comes in, to try and improve that. Inevitably there are cases we can all encounter in our daily lives of friends and family where we think could the diagnosis have been made quicker or better? Retrospect's a wonderful thing. I really, if you ask me, is blaming GPs going to improve the survival in this disease in five years' time? I would say no.

Baroness Masham: Wouldn't it be better if GPs did some sessions with professors working in secondary care who can teach them.

Professor Jeff Evans: GPs tell me would it be better if professors did sessions in primary care? I'm not sure I want to do that, but I think you raise a very important point, that is raising awareness and education about this disease.

I think the difficulty is when you think there are 8,500 new patients in the UK in a year, how many will one individual practice see in a year? For pancreas cancer, I then do it for lung cancer, for breast cancer, cervical cancer, all the other non-malignant diseases, it's a very valid point and we could spend an awful lot of GP time up-skilling them on pancreas cancer for perhaps one patient every year or every other year in the practice.

I don't have a quick, easy answer to that. Clearly raising awareness of the disease and it's symptomology amongst primary care, but distinguishing it from other causes and having rapid access to the diagnostic tools to make that distinction, I think was the key question.

Baroness Morgan: Just picking up on some of the points that have been pointing to in the papers, not the 'Sunday Time' I mean in the papers that have been sent round, and thinking about that point about GPs, I mean it's an example, I would have thought, where if you had more research looking at how – what best education tools would work for GPs. In the other inquiry we did, we heard a bit about GPs and some work that Macmillan were doing looking at their tools for helping to identify the red flag kind of symptoms.

Professor Jeff Evans: I think we should perhaps go back a step now and say how does pancreatic cancer present? There are two broad groups. 75% of them will have a cancer on the head of the pancreas and they often present with obstructive jaundice. So they may have little in the way of symptom warning before they suddenly become yellow. With the benefit of hindsight they say, well yes, I've been a little bit tired and lost a bit of weight over the last couple of months."

That is quite different from the remaining 25% with the tumours in the body or the tail, where they don't have the obstructive jaundice, and they may have weight loss, intractable pain, and actually those are the ones where it does take quite a long time, because they present with non-specific weight

loss, anorexia, tiredness. They have an endoscopy, they have a barium meal ultrasound and eventually of course they get a CT scan and the diagnosis is made, that's the sort of clinical scenario we often see.
Those are the ones where perhaps the diagnosis has taken longer than it would be with the ones within the head, where they obviously develop obstructive jaundice and have a fairly rapid entrance to secondary care.

Baroness Masham: Does it show up on a blood test?

Professor Jeff Evans: No. You can detect abnormalities in a blood test that might make you investigate a patient in a certain way, with weight loss or belly pain for example, if a liver function test is normal. Is there a blood test that says, "Yes, this is pancreatic cancer?" No, that doesn't exist.
One of the things we touched on earlier, can we distinguish this PanIN-3 from cancer? Can we then look at the biology? Perhaps going back to our mouse models that are quite elegant in the way they recapitulate this disease, both going from pre-invasive through to invasive and advanced disease. Can we use that biological information in the laboratory and go back and develop perhaps blood-borne biomarkers of patients that might not be sufficiently sensitive and specific to be diagnostic, but sufficiently sensitive and specific to rule out those who don't have pancreas cancer?
And even if it's not that specific but sensitive enough to detect them, can we then rapidly escalate those patients through to further investigations? We're a number of years away from that and I think, research-wise, that's quite a challenge, high risk but high reward. Maybe not the sort of thing that would ever be funded in response-mode given the risk of it, but I think if there was a strategic initiative to do that, that would be very welcome.

Baroness Morgan: Sorry, I was going to ask about the capacity, building research capacity now, so with the CR UK strategy you've got the two arms, intramural and the response mode, so you must have two elements of the strategy for building capacity. I'd be interested to know in terms of the resource, the doubling and trebling of resource, how's that going to work?

Do you have a plan for increasing the resources going to the intramural institutions and what would that look like? You mentioned bringing in some big hitters but then there's also the potential to bring in young investigators and encourage them to own the field. How is that plan?

Nick Grant: We haven't explicitly set financial spend targets across all of those different fields. What we have had is a lot of success in terms of commitments already. Four out of our five institutes have plans in place to increase the volume of research in pancreatic cancer. Jeff could certainly speak to the Beatson, which is probably our leading location nationwide for that.

Five of the fifteen centres where we fund – a centre for us is essentially where the university and the hospital trust comes together in a major academic in a hospital location to work together around cancer research, and we fund fifteen of those around the country, five of those fifteen have made a commitment to growing the proportion or the focus on pancreatic cancer research in their locations.

What we're hoping is we'll see an increase across the board in all of those areas.

Professor Jeff Evans: If I could add to that as well, I don't think we should separate out the intramural from the response mode, because, as I explained, I work in one of the intramural institutes but I work also within the hospital and university as well, and the research that comes out of the intramural research could then facilitate applications of sufficient quality and depth and number from the response-mode route.

For example, if we look at, in our lab we look at tumour vulnerabilities in mouse models, looking at which particular genetic backgrounds may be more susceptible to existing drugs. That can then lead on to a clinical trial.
We're not going to do that as part of the intramural funding but we would then go to other branches of CR UK's funding, Experimental Cancer Network, New Agents Committee or CTAAC for the later phase studies, that we can then bring our ideas from the intramural research that then can increase the depth and quality and quantity of the applications that then go to the response-mode approach.

Baroness Morgan: One other quick one on capacity. Thinking about what kind of measures you could have for research capacity. I mean, I don't know, it should be evidence based, shouldn't it? The number of PhD students funded, the number of research fellows, the number of clinical research fellows, do you have ideas about that?

Nick Grant: We do. What we're interested in is the number of active people in all those different areas, so the number of clinicians, basic scientists and researchers at all the different stages of their carers who we are actively funding, or indeed working with the other funders who they are actively funding.

What we're also interested in doing is tracing that back through, and understanding why we're not funding as many new individuals as we would like to do, so what is the success rate of applications to our funding committees, and where in the pipeline are they falling down?

In addition, where in the career stages are people who have been successful in winning pancreatic research funding early in their careers but then don't go on to win the bigger grants, why is that? Is that because there's a structural gap in the funding, or is it because there was an issue with the research, or is it because ultimately they didn't meet the required quality.
Also we've got quite a holistic way of looking at, as you say, some of the quantitative measures but also some of the qualitative factors along the funding pipeline and along the career pathway.

Baroness Masham: Is pancreatic cancer going up? What I find really depressing is there are some excellent, like yourselves, excellent experts in this country but when we see the league in Europe we're right down near the bottom. What's gone wrong?

Professor Jeff Evans: I think the pancreatic league is reproducible across the world, in that the incidence is slowly rising in terms of how many new cases there are every year across the developed world. That graph is fairly reproducible. What is equally reproducible is the survival in this disease which hasn't, like other tumour types, plateaued or gone down and as a consequence the death rate continues to rise, and that's an international problem.

I really don't think the UK is any different from anywhere else in this disease. This is a global problem and I think it will need a cohesive effort across the globe to try and resolve it. It is encouraging for example that there's very good relationships between US investigators, UK and the EORTC in Europe.

CR UK have this thing called the International Rare Cancers Initiative, pancreas cancer doesn't fit into the Rare Cancers Initiative but that's already developed better working relationships with the NCRN, NCI, Canada, North America and Europe, that we can begin to tackle it.

In fact, on Friday of last week I had a conference call with the European group, pancreatic group who are interested in our multi-arm molecular stratified trial that we're putting together, myself and Juan Valle in Manchester, and that they are perhaps interested in joining in what we do and tackling on a Europe wide basis. I think with pancreas cancer, sadly the problem is fairly reproducible across the world.

Eric Ollerenshaw: You said earlier on that we're in a position in this country to take some leadership on this. What was the basis for that if we're just as bad as everywhere else?

Professor Jeff Evans: I think taking the leadership, not so much in terms of the frequency of the disease which is comparable to elsewhere in terms of population statistics, but in terms of a core group of expertise of investigators, like all the way from basic cancer biology through to pre-clinical testing, through to clinical trials.

With the infrastructure that we have to deliver clinical trials in the UK, which I think is probably superior to most organisations, and with a breadth of expertise that we've got all the way through from basic cancer biology through to clinical application, I think we've got world leaders in mouse models of pancreas cancer in genomic analysis, and international cancer genome leads are now relocated to Glasgow with us.

Also, in terms of clinical researchers and clinical trial design, I think we've got people who are internationally competitive and renowned in all of these key areas. We have the infrastructure and I think that's mainly been driven by a resource from CR UK and others. If we can expand and build on that core capacity, and leverage additional money, so that we don't rely entirely on the charity but other stakeholders as well, be it pharma, be it government and be it other sources, other charities, and welcome all research councils, the MRC, then I think we can make a really big impact that will have an effect internationally. That's good for UK science but it's even better for the patients.

Eric Ollerenshaw: We've had it mentioned before that in a sense because of the NHS we're in a particularly good position if we sort out all the different pieces of the bureaucracy. I think in Cancer Research UK's written submission there were problems again mentioned about the bureaucracy and interfering with applications for trials and so on. Is there anything specific?

Nick Grant: I think, as we said in the submission, one of the biggest concerns for us is around the speed at which we're able to recruit new clinical trials. As you say, it comes down to the bureaucracy. Now, there are clearly efforts underway in terms of addressing some of that. I know there's a process for developing a single approval process across all centres, so we don't have to go through individual approval.

I think we'd fully welcome that and just ensure a continued emphasis on ensuring the focus stays on that all the way through implementation to make sure that it's adopted as quickly as possible.

Baroness Masham: What do you think about discriminating against elder people, older people, having treatment?

Nick Grant: In terms of treatment or in terms of research?

Baroness Masham: Both.

Nick Grant: We very clearly in our new strategy called out the need for more research into treatment into more elderly patients, because as clearly as the population ages there is a significant burden of cancer in more elderly populations. We have seen instances where we've not seen as much research as we would like in those populations as opposed to other age groups, so it's an area that we're particularly looking to increase focus on.

Professor Jeff Evans: If I can add to that as a clinical researcher, it's not appropriate to write in a clinical trial protocol an upper age limit for patients who enter into clinical research. Ethics committees will make you take it out, and rightly so. As researchers we don't have an upper age limit, so it's usually over 18 or over 16, with no upper age limit. So those patients are not excluded from clinical trials.

We have to be sensible, however, as well in that for some, not so much to do with the miles on the clock, it's more the performance status that I mentioned earlier, how fit the patients are. Some of the more intensive chemotherapy regimens that have come along in the last year or two, or two to three years now, mainly came in again from the French groups, looking at four drug chemotherapy combinations, quite hard to deliver. There is significant toxicity, and therefore patients that are fit enough to tolerate this is paramount for that.

Now, that's not directly related to age because it's more to do with performance status, and you have some remarkably fit patients who are in their 80s, and you have some remarkably unfit people in their 40s and 50s. So I don't think it's as stark as that.

Baroness Masham: I've heard some people say, "I just can't face any more chemo," so it must be their choice really, mustn't it?

Professor Jeff Evans: Absolutely. I don't think any of us are going to dictate to patients how they should be treated, we can offer them options, we can advise them on the options but ultimately it's a decision they and their carers and us take together.

Eric Ollerenshaw: Is there anything in the regulations about clinical trials? I mean European Parliament passed one in April, is that helping or hindering? I know there's something going through this place (the Saatchi Bill), isn't there, about freeing up, giving people more, if you like, individual permission to say, "I'll sign up for it." Is there anything like that you can… I mean we're parliamentarians, if you want to suggest something we could be getting on with I'm sure we'd be – love to get on with something more, wouldn't we?

Professor Jeff Evans: I think the EU directive, when it came in however many years ago it is now, presented us some additional challenges. I think both in terms of the cost of trails actually, as well as the infrastructure needed to run it. We're fortunate in having a core-funded clinical trials unit in Glasgow from CR UK, which is an accredited one that can run national and international trials.

The number of people employed in that grouping has increased quite considerably as a consequence of the new directive, because we have to put in-house pharmacovigilance and put in in-house regulatory approvals. A certain amount of that is good because I think there were probably areas where corners might have been cut historically, but I think we have to be careful that the bureaucracy doesn't become the main reason for existence, and that we use the bureaucracy to enhance patient's journey to make clinical trials safer and to protect patients who are participating in clinical trials, but not to burden it so much that it actually slows down and hits the entire trial.
In terms of the Saatchi Bill, I've not read it in any great detail, but I think that's more about litigation for individual people who do things that are outside of a clinical trial or outside of ethics approval.

I don't think getting ethics approval for clinical trials is the problem, most ethics committees, and I've sat on one myself, and most patients groups are very keen to see trials in pancreas cancer and other forms of malignant disease, so getting ethics approval isn't the issue. It's then once we've got that, it's the regulatory burden of management approval, NHS resources, so I don't think that the Saatchi Bill is necessarily going to help us there.

Eric Ollerenshaw: How are we going to improve that NHS side of it?

Professor Jeff Evans: Well, I think there are two issues there. Nick has already mentioned the regulatory requirements. I think there's another challenge here as well, if I can perhaps go off the point slightly, in that if we are going to develop some more imaginative approaches to clinical trials, and as I mentioned we have a work in progress with CR UK with colleagues in Manchester and ourselves, whereby that we want to identify on the patients' biopsy the molecular phenotype that might give us an estimate of which tumour type

and which drug types they might be vulnerable to, and allocate them to treatment arms within a broad umbrella trial, call it multi-arm molecular stratified trial, which we're developing at the moment, a stratified medicine approach.

That requires for us to get adequate amount of tumour tissue and to be able to do all the molecular sequencing and analysis in a very robust but very quick way, and feed that information back to clinicians.

Now, we can have great researchers coming up with those ideas, but unless we get adequate amounts of tissue and adequately fund the access to tissue and our ability to use that in a quick way, and that really is dependent on both those involved in the diagnosis, invariably these days we do fine needle aspiration rather than biopsies, it's easier and nicer for patients, but if we get into the mind-set we need to do biopsies, that will be more costly, both in terms of time and the equipment.

Then actually being able to get biopsies for research rapidly through pathology, into the sequencing and into the genomic studies to inform the clinical trials is a big road block there in pathology services, because they are completely stretched in providing diagnostic services, and rightly so.
We need to put resource into enabling technologies that underpin the activities of the NHS to facilitate research. I think that's probably something we can influence more than the regulatory requirements.

Eric Ollerenshaw: What would that look like?

Professor Jeff Evans: A small example, so if we want to do this trial that we've alluded to, whereby we have about 25 centres in the UK where they have pancreatic diagnostic and treatment centres, that when they have their biopsy they would need to be perhaps down the endoscopic ultrasound, to have a biopsy needle and a fine needle aspirate, those needles cost several hundreds of pounds, my colleagues tell me, and you need to have people who can use that equipment.

Once the sample gets to pathology and it goes through the diagnostic process, can we have technical support that is not part of the NHS resource but is the NHS R&D, and is not people whose day job it is to do the diagnosis, but who are to deal with samples of tissue for research, to enable to get that quickly to the genomics teams, because as we've already said how quickly the people deteriorate.

If we're going to use that genetic and genomic information to inform entry into a clinical trial, we have to turn that around within about two weeks from the diagnostic sample to be taken, otherwise it'll fail.

Baroness Morgan: What you're talking about there is you're talking about people. You talk about technical support, you need trained people in the right places to do that work, it's not – you can't just buy a piece of kit that does that.

I think the point that people need to understand, what it seems to me that you're driving home is that yes, we've got pathology services that are fully engaged in diagnostics, as they should be, but in order to take the pathology service and the research to the next level we've got to have a parallel. Pathology research service is almost there that's supporting the collection and organising, and those are people, aren't they? They're trained people.

Professor Jeff Evans: We've done that on a smaller scale in some places, for example on a different tissue now is blood. Now, you think collecting blood is relatively easy, but in a different tumour type we were involved in looking at blood-borne biomarkers.

What it was that I had to consent the patients myself in the clinic, and then they came to the ward and if I was away in the lab or something and the blood sample didn't get taken, and we were finding we were missing a lot.

We've employed, through one of the CR UK's funding streams, Experimental Cancer Medicine Centre, a research nurse whose job it is to consent patients, collect all the blood samples and make sure they're all collected the right time and packed up the right way.

We've looked at recruitment curves on that clinical trial, since we appointed that post recruitment has gone up exponentially. Therefore we really have to have people who, this is not ground-breaking science that's going to get published in 'Nature', this is enabling technologies, enabling resources that can facilitate others to do the research so that we increase that bridge between diagnostic services, NHS treatment and NHS research capacity and driven by what has come out of academic laboratories.

I don't think biomedical science is something that's only in the domain of academics; this is something that everybody should be able to participate in, but we have to give them the resource to enable them to do so and to keep the whole thing running.

Eric Ollerenshaw: Very interesting point. Nick, have you got a comment on that?

Nick Grant: I think in addition to what Jeff's been saying there, there is a very specific skills gap that we've identified actually across the full set of cancers in molecular pathology, because the field of pathology has moved very quickly on with the advent of genomic technologies to be much more data and informatics based. In essence it's a new skillset that is highly specialised.

We're very interested in how we start to bring more people into that field, potentially bring some of the leading experts from overseas, because as Jeff said, in pancreatic cancer, in order to drive these new stratified trials, it's absolutely critical. Again, that applies across the full breadth of different cancer types.

Eric Ollerenshaw: Can I just ask to our administrators, have we got anybody from pathology coming in at some point? It might be an area we need to look at then. Yes, go on.

Baroness Morgan: Touching on the bioinformatics again. A lot of people have voiced concerns to me about how the NCIN is coping following the new NHS structures, it's lodged in, or part now of NHS England. A key part of all of this has got to be about collecting and releasing patient information. Do you have a view on how important that is to pancreatic cancer research?

Nick Grant: Very important and very important across all types of cancer, but both in terms of supporting research and in terms of understanding changes we might need to make to the care pathways and to the quality of care across the UK. A lot of the data that the NCIN collect is around care rather than research data.

Baroness Morgan: And outcomes.

Nick Grant: And outcomes data.

Baroness Morgan: It's much easier if the patient is part of the team and they feel part of the team, and information is shared.

Nick Grant: Absolutely. We as an organisation work very closely with NCIN and are providing some co-funding there to essentially prop up some parts of that team to continue forward.

Baroness Masham The thing about the Saatchi Bill which slightly concerns me is doctors are freed up against litigation but I'm not sure that there's enough safety at the moment for the patients. Will you look at that if it comes to you?

Eric Ollerenshaw: We had talked about the "Dream Team", and it is the kind of what you are talking about we're trying to get to? Where you've got this interlinking and…

Professor Jeff Evans: We've had discussions with CR UK and others over the last probably 12, 18 months about what we've called the CR UK consortium. I think we're due to meet in London next month, and have a meeting tomorrow morning back at our place to try and finalise some of the paperwork of what we think this consortium would look like and what we plan to do.

There is undoubtedly, based around the intramural institutes that Nick mentioned earlier, some of the key CR UK centres where pancreatic cancer is at the height of their strategy, we have a number of, and we all know each other, we're a relatively small country so we all know each other, and we work together and we collaborate.

Eric Ollerenshaw: Yes, and that should be an advantage we've got.

Professor Jeff Evans: Absolutely. We've got a number of key areas, geographically, but we actually span all the key scientific areas as well, sometimes all in the same centre, but across the entire consortium.

I think we can build a strong consortium that will drive the ideas we want to take through, both in the laboratory and in the clinic, and then of course on top of that we've got the existing network through the National Cancer Research Networks and the ECMCs that can exploit those ideas as they come through to the clinic.

Clearly we can't deliver these clinical trials and these really ambitious types of trials we're talking about in six centres, they have to be around all the networks, but we have that existing infrastructure and we have good relationships between the people who sit on the various networks, ECMCs, along with those people from the consortiums, because they're quite often the same people.

Baroness Masham: Isn't something happening with the Cancer Network, aren't they changing it?

Professor Jeff Evans: Yes, well it's changing in England so I don't think I'm best placed to comment on that. There have been changes in Scotland as well, but actually it hasn't changed the way we do cancer research there.

Baroness Masham: Change sometimes isn't for the better; do you think it will be all right?

Professor Jeff Evans: Yes, I think so. I think provided that… I mean cancer's really led the way in establishing those networks and I think the other disease areas have actually copied what cancer does, so I think it probably isn't going to affect us greatly.

Nick Grant: I think the concern for us is that cancer slips down the agenda. Clearly as the networks are reorganised to be multi-disease, that cancer loses any kind of focus of attention as part of that, so that would be our concern.

Baroness Morgan: I don't want to dominate. In terms of surgical research I think, well, it seems to me that pancreatic cancer where for a lot of patients the best hope will come through surgery, how does that – how is that promoted? When we talk about clinical trials, presumably there are clinical trials looking at different surgical procedures.
You touched on the question of readiness for surgery or appropriateness for surgery, is that something that you've had to put particular attention into? How do you go about building capacity there?

Nick Grant: It's another area that we've highlighted in our new strategy. Both research into improved surgical procedures per se but also the important role that surgeons play in the broader research agenda, because increasingly we're seeing, for instance, window trials where a therapy is administered prior to surgery and therefore the surgeon is a very active part of a clinical trial even though it's not a trial of a new surgical procedure per se.

We're very interested in bringing the surgical community much closer to the research agenda for both those reasons.

Baroness Masham: Are you looking at radiology too?

Nick Grant: Radiology absolutely the same. In fact, one of the biggest successes for UK cancer research in the last five years has been the huge growth in radiotherapy research. We've seen a trebling in the number of radiotherapy trials we're supporting in the last five years.

Baroness Masham: That's where the concern is about pay, because it's terribly sad if patients can have benefit but they can't have it because nobody will pay.

Nick Grant: Absolutely.

Professor Jeff Evans: I think we should acknowledge that, like all tumours, the management of pancreas cancer is a multidisciplinary team effort. In fact, we also have to acknowledge that the pivotal trial of administering chemotherapy rather than observation after surgical intervention was delivered by a UK based surgical group.

We do have, we have in our own centre, as there are in other centres, surgeons for whom pancreatic cancer is their research focus.Academic surgeons, involved in genomic research with us, involved in trial design elsewhere, for example in Liverpool, so we have practising surgeons who are also research active in this disease.

I think it's not just about the techniques of surgery, it's about selecting the right combination of treatments, including surgical, pre-operative, post-operative treatment, and the right patients for that as well, because if we can better identify those we think are operable but in whom surgery is clearly futile, looking at the results of a very poor outcome after surgery so we can spare them a fairly large procedure with significant morbidity, that would be an advantage.

Also if we can identify better, earlier, the disease so that they're actually accessible to surgery in the first place. I think that's probably where the surgical research role comes in.

Baroness Masham: Do children get pancreatic cancer?

Professor Jeff Evans: I suppose there probably have been cases but I've never seen one. It is a disease that occurs increasingly with age. The sort of optimal age is about 60 or 70. It increases from the 40s, 50s, 60s, and 70s onwards, but I think the median age of development is in the 60s and 70s. You do get tumours in the pancreas in children but it's not pancreatic cancer as we mean it here.

Eric Ollerenshaw: I was just going to say, to bring the other people on, I saw somebody shaking their head earlier on about something. Go on, go on.

Celia Goodman: My daughter was 29. At the same time we heard of other, a 28 year old and much younger. There were also two other cases.

Professor Jeff Evans: Yes, sadly I've seen in my own practice patients in their 20s. In terms of childhood and people under 16 I think was the way that I interpreted the question. Obviously I'm not a paediatric oncologist so I wouldn't see them anyway, but you're absolutely right, it can occur at any age.

That's more difficult when at the younger age groups because people don't suspect pancreatic cancer when they develop really nonspecific symptoms when you're in your 20s, because it's such a relatively uncommon thing to happen in those age groups.

Doug Goodman: But most doctors think "Fit, young girls of 29 who've just run a marathon and climbed Mount Everest don't get pancreatic cancer."

Professor Jeff Evans: Sadly I've seen it in my own practice with people in their 20s.

Eric Ollerenshaw: Thank you. You were shaking your head… Go on.

Celia Goodman: You were saying about trebling, doubling, trebling the fund. What's the base of that, I'm mean what's the percentage of your funding going into pancreatic cancer to start with?

Nick Grant: There are some slightly different figures in terms of how we count our research, but broadly when we count the direct research efforts, so the groups who are purely focusing on pancreatic cancer or the clinical trials that are in pancreatic cancer, it's around £3.4 million.

If we then include an allocation of some of the shared resources in our institutes and centres, so the buildings, the equipment that are shared across all cancers and we allocate that – the total is nearer to £6 million. That in total is around 1 to 2% or our total funding.

Celia Goodman: So it's not reflecting the…

Nick Grant: So not enough, absolutely. We're very clear that this is not as high as it should be given the unmet level of clinical need.

Celia Goodman: Even including the nonspecific. it's still only 1 to 2%?

Nick Grant: Yes.

Celia Goodman: Okay.

Eric Ollerenshaw: Is that what you're doubling on?

Nick Grant: That's what we're doubling on, yes.

Eric Ollerenshaw: So it will be 4% by one of your calculations?

Nick Grant: Well, because we see our over… We have plans for our overall funding to increase, it may not go up to 4% as a proportion, but we hope that it would go from 6 to 12.

Eric Ollerenshaw: Yes. Anybody else want to… You were shaking your head earlier (Laughter).

Maggie Blanks: Surely not (Laughter).

Eric Ollerenshaw: I was going to stop then and… Go on.

Maggie Blanks: I wasn't aware of shaking my head; I did want to ask a question.

Eric Ollerenshaw: Go on, please.

Maggie Blanks: Just going back to the question made about the big challenge of early diagnosis and it may well be that the planned consortium approach is going to include a focus on doing some more stuff on early diagnosis, and you Jeff were talking about, you just did sort of say in passing in talking about that particular challenge it needs a – it's high risk for high reward, it needs perhaps a strategic effort behind it.

If that's the case and that sounds right, that we have to sort of say maybe put down a marker as this is a challenge that we as the country interested in pancreatic cancer and want to get behind. Yes, it is high risk therefore presumably high cost, but with potentially high rewards. Let's make it a particular challenge that we want to take on. What are we talking about in terms of money and the resources that can be channelled to pick up that challenge?

Professor Jeff Evans: I wouldn't do it in isolation; I would do it as part of the overall research effort, a discreet entity. For example one approach would be, can we develop – can we go back to our mouse models in the laboratory that are meant to recapitulate this disease and identify markers that might distinguish between late stage pre-invasive cancer and the invasive ones?

If so, can we then develop novel imaging tools? Can we develop nominal blood-borne biomarkers? That's quite a protracted process. Then the difficulty will be, in terms of screening the general population, there isn't so much a high risk group that is very easy to identify, there are groups which are high risk but they're a relatively small percentage of the total, less than 10%.

Maggie Blanks: Yes.

Professor Jeff Evans: It has to be sensitive and specific enough to make decisions based upon it, or at least put you through to the next step of the diagnostic algorithm. Then you have to have a positive outcome from that early detection. I'm pretty sure that would be the case. I think in terms of figure I can't dream up a figure now.

It's very dangerous to ask a clinical academic how much money you need because you get the personal inflation rate, but I think you probably would want to invest a discreet number of several millions to try and pump prime an effort in this as part of a broader effort.

Nick Grant: Yes, let me maybe pick up on this Maggie. Because actually the challenge around early detection is not purely in pancreatic cancer, it's probably the greatest opportunity we have across all cancers, to make a really marked difference to survival.

Maggie Blanks: I understand doing things in some of the other areas, but with pancreatic it is just such a, I think, I see it as a different scale of challenge in terms of the hardness, the essentialness of it, in terms of the repercussions when it isn't picked up early. I would argue that it's a special case, but then I wouldn't, wouldn't I?

Nick Grant: One of the things we talk about a lot in our new strategy is making a very significant investment in early detection across all cancers. It's a very challenging area where there's very little research in the UK currently, and actually very little research elsewhere in the world. It is an area where the UK can genuinely be world leading and make a huge difference.

The interesting nature of some of the challenges Jeff talked about, in terms of detecting markers in the blood, in terms of imaging, is they start to call on new scientific disciplines, such as engineering and physics, who sometimes haven't been as close to the cancer research problem.
Therefore, that's one of the reason why, as Jeff said, it needs quite a strategic approach. It's not going to be catalysed through a pure response mode mechanism to funding.

One of the things we're very interested in doing is seeing how we start to build a critical mass in research focus in early detection across the UK. Particularly in academic locations where they have a real strength in the physical sciences, engineering science, mathematics, as well as in the basic biology in the clinical community.

We're just starting to consult on how best we do that at the month but we've made a commitment to, or at least an ambition, to spend at least £20 million in this area within five years' time. It's going to be an enormous focus for us. As I say, across all cancers, but as you said…

Maggie Blanks: You're saying pancreatic gets addressed within that more general effort, looking at early diagnosis?

Nick Grant: Absolutely. I think as we've been saying already, given the expertise that exists in pancreatic cancer research across the UK, there's great potential there for work in early detection as well.

Baroness Masham: What are the causes, the causes of pancreatic cancer?

Professor Jeff Evans: Just to finish off the last question, I think then there's a responsibility on us to make a stronger case when we do put in for that, for pancreatic cancer to get a slice of about 20 million is, coming back to earlier, the sort of quality aspect and I think...

Baroness Masham: Well, you just quote best strategy.

Professor Jeff Evans: There's also the quality aspect, and we don't need to quote the strategy because I think the quality of what we can produce with the core strengths we have now I think could make a very robust case for that, I would like to think, and others.

To come back to your question of what causes pancreatic cancer.Well, if I knew what caused all cancers I would probably pick up the Nobel Prize and stop right now. We know a lot about the hallmarks that make up why normal cells become cancerous. What makes it in any one individual, and at the time that it does so, I don't think we'll know. I think it will take an awful long time to know.

I think we know some risk factors that are associated with pancreas cancers. There are some of those risk factors associated with all cancers. It becomes more prevalent as people age. There's a higher incidence in people who are smokers. There's a higher incidence in obesity. There are some lifestyle factors that are implicated. The press release came out from CR UK last week, for example, has highlighted that.

I think in many patients we can't identify what the causative mechanism is, and is likely to be multifactorial. A lot of things collaborate in at the same time.

Baroness Masham: The young ones, they won't have had such lifestyles when they're young.

Professor Jeff Evans: No, absolutely. Clearly there may be different risk factors.Cancer, pancreas or otherwise is a disease of genes, is an abnormality of DNA, either from genes have become abnormal and drive the process or loss of the suppressor genes that stop those mechanisms becoming abnormal, and what causes that more catastrophic damage to DNA in the younger groups compared to the older folk is probably a different mechanism.

The challenge for us in pancreas cancer, when we identify a diagnosis, is to look at which are the activating, actionable abnormalities in the particular molecules in that individual, and exploit that with the right treatment. Rather than say, "Well young people get treated with one treatment, old people get treated with another."

No, it's to say this is a cancer that's dependent on this particular pathway or another pathway, and then ask questions about the drugs that target that tumour vulnerabilities, and that's only something that comes out of laboratory science, through into clinical practice.

David Park: Just ask a question. Picking up on the word strategy, we've heard a lot of today. In the US we have had the Recalcitrant Cancer Research Act 2012, which has led to specific strategies being created. In the UK we've got CR UK's strategy which focuses on throwing more money at cancers of unmet need.

You both talked about the need for a more strategic approach, I assume that means beyond your own strategy, so who else needs to be also stepping up, taking that leadership position, producing the strategies as

well? Is it the government? Is it NIHR? Is it the academic community separately? What else do you need basically?

Nick Grant: I think there are a couple of aspects. I think firstly it's very important that we stay joined up with the other funders of pancreatic cancer research. We're very grateful to Pancreatic Cancer UK and Pancreatic Cancer Research Fund for participating with us in our strategy consultation.
In doing so ensure that the way that we're funding, and our funding streams, are joined up so that there are opportunities for a researcher to come to one organisation and leverage the funding they've got to then be able to apply for funding for another organisation, and that there aren't gaps and that there aren't overlaps.

In terms of some of the broader funders of UK biomedical research, so the Wellcome Trust, the Medical Research Council, NIHR etcetera, I think what's very important is that there's a solid strategy there to ensure that the infrastructure to support research, and particularly clinical research, as we've touched on already, is there across all cancers, because it will absolutely underpin the research efforts specifically in pancreatic cancer.

David Park: Sorry, who should then be producing that strategy?

Nick Grant: I think that's part of the strategy process for NHS England, in terms of the R&D strategy for the NHS and the NIHR, in terms of their own strategy.

Baroness Masham: Does NICE come into it?

Nick Grant: You can speak to this more from a research perspective.

Professor Jeff Evans: I wouldn't have thought so, to be honest, because they're more tasked with looking at results of trials and whether the cost effectiveness of the treatments that come out. I think the challenge we have now is actually to get some new treatments that we can then take to NICE.

Coming back to your strategy question, I guess as we develop this UK consortium, obviously it's in partnership with Cancer Research UK, but we've got funding to various strands of the research from Wellcome, from CR UK, from the other pancreatic specific charities, there's money from the MRC.

You highlighted one key point earlier that enabling infrastructure, based around pathology for example, the radiology which comes from NHS R&D, to get slightly political for the moment, is that you mentioned NHS England but let's all be joined up and make it across all the devolved nations as well, because clearly we're too small. We mentioned we're a small country but if we're fragmented in our research efforts…

Eric Ollerenshaw: Better together argument or…

Professor Jeff Evans: I'm staying completely neutral on that as I've been told to do.

Eric Ollerenshaw: That's the trouble you see.

Professor Jeff Evans: I think it's a plea that when we begin to discuss – if you discuss with NHS England, for example, about enabling technologies under this, that we don't forget that pancreatic cancers are a problem throughout the devolved nations and we have the same conversation with the others.

Sue Ballard: Sue Ballard. I've been working with patients for about 12 years. I've got a couple of questions, probably for Jeff. One is that I know the surgeons are doing a lot of work to see which surgical patients respond best to treatments and survive longest, is any work going on the inoperable patients who survive a long time and yet we still lose them because there is actually no treatments for them, or they're maybe not being given enough attention to actually prolong their lives?

Sadly we lost somebody yesterday from the community that survived three years, and he's been about two years without treatments. Could anything have been done to actually prevent that loss of life?

Professor Jeff Evans: Most of what we've done historically has been about clinical trials, and therefore trying to find better treatments and building up the evidence base that can allow us then to make treatment decisions. Historically as oncologists we've probably invested a lot of a time and energy on understanding why cancers are resistant, and trying to overcome resistance, but you highlight a good point, is that maybe we should begin to focus on the exceptional responders and those who do particularly well and try and say, "Actually, why did they do so well? Can we then exploit that in the future for treatment?

In fact, we had a review article in 'Nature Reviews Cancer' about a couple of months ago on the concept of exceptional responders in pancreas cancer, which came out of our own department. I think you're absolutely right that we have to learn as much as we can. We are looking at biomarkers that are predictive of treatments of both in locally advanced and in metastatic disease, and we usually build those into clinical trials because we can collect the robust clinical data.

I absolutely agree with you that we should begin to look again with fresh eyes at those exceptional responders to see if we can learn what distinguishes then from the others, and perhaps to try and develop research strategies on that basis.

Eric Ollerenshaw: You had another question.

Sue Ballard: Yes, it's to do with the discussion about the GPs and the symptoms. I have until recently been refer for suspected cancer guideline group. I've been looking at the research that's been done on the symptoms. Now, Jeff said that 75% of the cancers will be in the head of the pancreas and the symptom will be jaundice, 25% will be in the body and that will be weight loss and intractable pain.
What puzzles me is why is it that the GP databases aren't reflecting that? In the GP databases we're only seeing about 35% reported jaundice and the second most significant symptoms, about 35%, pain, but only 10% with

reported weight loss. Now, is this the GP's not recording the information or is it the patients not giving the information?

All the red flag symptoms for referral for cancer are built around weight loss, but why is it the GP databases are only showing 10% with weight loss? Jaundice is a slightly different one. The Scottish referral guidelines that have recently been updated, before that, it was saying that 70% of patients had jaundice, but why the GP databases only say 35%?

Is that partly why we're only getting 10% having surgery, because the most obvious symptom is jaundice? So do we really know how prevalent these symptoms are? Is it a problem with the recording? What's been done in the past is a lot was based on what the surgeons saw, and they would only see the jaundice ones.

I think there's still a lot we need to understand about the symptoms, especially symptoms of younger patients and if there's some way of distinguishing them for referral for cancer, unfortunately the evidence in the papers at the moment covers the 60 plus that have got jaundice.

Eric Ollerenshaw: Any comment?

Professor Jeff Evans: Well, I'm less familiar obviously with the general practice database so I don't have any answers specifically to your question. I think only to agree with you that we probably do need to have better research into the symptoms of presentation of this disease.

If we had better ways of distinguishing between relatively benign conditions and those we're suspicious of malignancy, in other tumour types as well as pancreas, then that would be a huge advance. Whether that's based on symptoms or whether it's based on specific markers that we can detect in blood or imaging, or probably more likely an algorithm consisting of all of those, then I think that would be a major achievement.

Eric Ollerenshaw: Can I throw in a political comment before your question? I wanted to come back on the doctor's thing because it reminds me the argument about public side and what doctors do, like the argument… I was a teacher, and I can remember, I mean it's now commonplace, but I can remember the argument you shouldn't publish exam results for schools, because then they might be targeted, so to speak.
Now they've been published for years and years and years and they are used as a successful audit of what's going on. That's how I see this attempt to get some publication of what GP's performance is like. I think it's similar.

Professor Jeff Evans: One activity that we've been having a lot of traction with is working with GP surgeries to share with them some of the data and statistics around the performance of their surgery and their area, but actually to work in a workshop environment with them, if you like, around what it is they can do to improve performance around.
That's across all cancers rather than pancreatic cancer especially, but I think that collaborative approach, using the data as a starting point but not the endpoint is a nice way of doing that.

Professor Jeff Evans: A word of caution there as well in how we use statistics because if we look at outcome data, I practice in one of the areas which have got a large amount of social deprivation in the UK, and that clearly affects outcome as well. I think we have to be careful.

Eric Ollerenshaw: That's the same argument in schools, isn't it?

Professor Jeff Evans: Yes.

John Lancaster: I'm still concerned we need a strategy that leads us to a step-by-step measurable outcomes. At the moment we're in the position we're not getting enough applications for research. We haven't got a screening tool for precancerous lesions, these are things we haven't got and we think we need, but how are we going to get to a position where we've got – where there are measurable steps. Maybe it's a long-term strategy, maybe it's 10, 15, 20…

Professor Jeff Evans: I think you're right.

Eric Ollerenshaw: We've got Cancer Research UK doubling its money, so we've got a start.

John Lancaster: Well, that's right, that's right, but we've got also NHS England with the outcome strategy, one which says avoiding unnecessary deaths, so NHS England has got a responsibility for outcomes so surely they should be almost setting the lead in.

I would suggest. What I think is still lacking, as far as I can see, is immeasurable outcome. Are we in the next, without putting words into your mouth, in the next ten years going to aim to see a method detecting precancerous lesions? How are we going to move forward in terms of early diagnosis?

I mean everybody agrees what we need, I still don't actually see a plan that takes us in that direction with the measurable – with measurable outcomes. I know I'm asking but that's what…

Baroness Masham: Is there a checklist for GPs so they could tick off the symptoms to help them? Would that be helpful, or do they have one?

Professor Jeff Evans: Well, I don't work in primary care so again I'm not sure I'm the best person to deal with that.

Baroness Masham: Cancer Research might be able to help them and make a checklist for them.

Professor Jeff Evans: I think we've heard before there's some work being done, isn't there?

Hollie Chandler: There is, there's a risk assessment tool.

Nick Grant: As we've said we're developing this consortium approach now in the UK. As we take that forward to CR UK and others to fund, clearly they will want to put milestones on achievement and what we deliver. Some of those will be scientific, some of them will be about delivery and development of clinical trials, but it's hoped that some of those will lead to positive outcomes as well.

We can't always guarantee that the result of all your trials and all your research is going to be positive but we very much hope so.

Baroness Morgan: Just picking up on the strategy point and the need for a roadmap or some clear milestones along the way to say, you know, we don't – things haven't changed enough, we've got to change for the future.

No one can say exactly well what is the early diagnosis breakthrough that's going to revolutionise things, but we know more capacity need, more funding needed, more voice for policy at the highest level and so on. Given that there's no, in the Department of Health, there's no cancer policy team anymore, cancer networks are radically changed, we've not NCIN in a different shape and so on.

In the new world, in the new NHS environment and UK wide, what, as an all-party group on pancreatic cancer, what should we be saying to all the agencies? What is the most important thing that they should be doing now? Should we be having a new strategy? Should we be saying we want milestones on early diagnosis?

We're in a new NHS environment, whether you're thinking about research as UK wide, Europe, Cancer Research UK is a UK organisation, we don't know what's going to happen with the referendum, but we've got all these different organisations, how do we rally this?

Professor Jeff Evans: Well I think like writing any research grant you've got several stands to your work, some of which you know we can deliver on, some of which are more speculative and blue-skykind of thinking.

Those where we know we can make fairly rapid gains now is in bringing together this group of people that we have working on the basic biology of cancer, and we've kind of done that. The new investment will help that, so we have better understanding of the genetic and genomic hallmarks that cause cancer, to develop and to progress.

The next step is then how we use that and use that resource to identify sub-groups of patients that will be susceptible to different types of treatments, and then evaluate that within one of these broad umbrella clinical trials.

I think that is something that has got definite achievable outcomes, and deliverables. Can we get enough patients to get next generation sequencing? Can we get them into clinical studies? Can we actually identify sub-groups that benefit from new treatments?

I think the challenges around detecting pre-cancerous lesions and detecting established cancer earlier in a symptoms pathway, I think would come as the next strand of that, because those are harder to do given the current research efforts, but I think would make a significant difference as well.

Baroness Morgan: Our chairman's had to go to his statement that's starting in the chamber shortly, in the Commons. I think we probably ought to be wrapping up now anyway. I mean obviously, Professor Evans, you've just given us a kind of statement there, I'm just wondering if you want to say anything further and then we'll… I don't know if anyone wants to… From the audience… No.

Baroness Masham: I just wanted to say one thing, which was last week our liver group, our hepatology group had a meeting with NHS England, I think they're overwhelmed, I really do. I think everything is so big.

I think it's very important to press forward with each speciality, to really push it forward because we were quite worried. We were worried about NHS England. We were more hopeful with Public Health England.

Nick Grant: Maybe two thoughts for me. One is in terms of a plan. What's written in our strategy is a sort of a very high level description, but clearly behind that we have quite a concrete plan with steps, and are committed to, at least on an annual basis, reviewing how we're doing against that with the other charities, and with the leading researchers, and adjusting our approach if we're not making the progress we want to.

In terms of the broader environment and the support for pancreatic cancer there, I think it's similar to across all the cancers and some of the issues we've talked about already, so a commitment to on-going support for medical research, to the right infrastructure, particularly for clinical research, the simplification of trial approval processes and the harmonisation of clinical trial processes across Europe.

Then I think one other issue that maybe we haven't touched on today is awareness of the opportunity to participate in clinical research among patients. We have a concern that not enough patients are currently asked about opportunities for them to take part in clinical trials, when we know that maybe 30% are asked and probably 80 to 90% would be willing to participate if asked, so continuing to move that agenda is very important.

Baroness Morgan: Well I think that's been really helpful. Obviously on behalf of our chairman I would like to thank speakers for coming and giving evidence. I think we've got one more session, I think.

David Park: 8th September.

Baroness Morgan: Yes, so we've got one more session and then we'll be compiling a report in October, which we'll then be sharing widely and hoping to keep the issue really high on the agenda. Thank you everyone for coming and participating in another successful meeting. Thank you.