HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: National Health Screening, HC 244

Wednesday 25 June 2014

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Written evidence from witnesses:

- Prostate Cancer UK
- Early Cancer Detection Consortium
- PHG Foundation
- PROMISE 2016
- Public Health England
- Public Health Wales

Watch the meeting

Members present: Andrew Miller (Chair); Jim Dowd; Stephen Metcalfe; David Morris; Stephen Mosley; Graham Stringer

Questions 153-236

Witnesses: **Owen Sharp**, Chief Executive, Prostate Cancer UK, **Professor Ian Cree**, Yvonne Carter Professor of Pathology, Warwick Medical School, representing the Early Cancer Detection Consortium, **Dr Hilary Burton**, Director, PHG Foundation, and **Professor Ian Jacobs**, Director, PROMISE 2016, gave evidence.

Q153 Chair: Good morning, and thank you very much for coming here this morning, on this glorious day. We were just discussing whether we could have an alfresco meeting it is so glorious out there.

It would be helpful if, for the record, you would kindly introduce yourselves.

Dr Burton: I am Hilary Burton. I am director of the PHG Foundation in Cambridge, an independent organisation that is a think-tank on how we can get innovation in genomics into policy.

Professor Cree: I am Ian Cree. I am professor of pathology at the University of Warwick. I lead the Early Cancer Detection Consortium.

Professor Jacobs: I am Ian Jacobs. I am vice-president of the University of Manchester and Dean of medicine and health; in this capacity I have a research programme in ovarian cancer research, which includes some big trials that we will talk about, and a Cancer Research UK programme. I should also mention that I am a trustee of the Eve Appeal and a non-executive board member of Abcodia, which is a screening and blood test development company.

Owen Sharp: Good morning. I am Owen Sharp. I am chief executive of Prostate Cancer UK. I am also co-chair of the prostate cancer advisory group, a national panel that advises the Department of Health and the chief medical officer on prostate cancer policy.

Q154 Chair: Thank you. First, I want to explore some of the issues around targeted screening programmes. Would you briefly explain how genomic information might be used to target cancer screening programmes to those most at risk?

Dr Burton: Shall I start off with that?

Chair: It seems to be right up your street.

Dr Burton: The first thing to remember is that a population is not totally homogeneous as to its risk. The risk is determined at least in part by genetic and environmental factors. If you are thinking about a preventive option, such as offering a screening programme, we have characteristically offered that to the population as a whole. Obviously, the people who are at lower risk have less chance of benefiting from it because they were not going to get the disease anyway, and more chance potentially of being harmed, or at least inconvenienced, whereas the people at higher risk have more chance of benefiting from the preventive option and, in proportion, less chance of being harmed.

If you take something like breast cancer, you can use known genetic susceptibilities, and there have been large studies lately that have looked at a number of variants that increase the risk of cancer. If you then look, for example, at the top 1% of the population with the most deleterious variants, they have about a three times risk of the average population. If you can then use that information to target, for example, a breast screening programme, you are able to optimise the benefit-harm ratio better, because you can screen fewer women and detect a similar number of cases.

Q155 Chair: In an ideal situation, you would presumably drive down overall costs because you would be targeting, and the benefit versus harm ratio would be better.

Dr Burton: You are optimising it. For example, with breast and prostate screening there is a major harm from what we call false positives. People whom the screening programme picks up as being potentially positive go forward perhaps to a biopsy, perhaps even unnecessary treatment, when in fact they were not at risk of serious disease. That is what we want to avoid by targeting towards the higher risk.

In future, we may be able to say that, for higher risk people who are more likely to get aggressive disease, we can focus that preventive intervention on those who are most likely to benefit, and reduce the risk of harm. It will potentially be possible, but evidence so far is modelled evidence, rather than empirical evidence.

Q156 Chair: For the other disciplines represented here, does that pattern reflect your own areas?

Professor Cree: It certainly plays into what we are trying to do in the Early Cancer Detection Consortium, in terms of developing blood tests for cancer—ideally, on a single sample. It is a multiple test, but done on a single sample, and who we would invite for that would certainly depend very heavily on risk. That can be judged in a number of ways, genomics being one. Environmental factors and the standard health factors that we all know about—smoking, obesity and that sort of thing—can all be factored into those equations. There are some very good groups around doing that sort of work at the moment.

Professor Jacobs: Similarly, with ovarian cancer, which is my area of work, the nirvana would be that you put together genetic predisposition, with demographic and social differences and epidemiological differences, into an algorithm that allows you accurately to define which women are at very low risk, which women are at intermediate risk and which women are at very high risk.

For women at very low risk, either you would simply reassure them that they are unlikely to get this cancer and they don't need to worry about it, or there would a screening intervention or something like that, which was suitable for the low-risk population. At the very high-risk end, there would be a whole bunch of strategies, from surgical prevention through to screening, and different intensities of screenings. Screening may start at a different age for women in the intermediate and high-risk categories and so on. That would be the objective, and it is within sight for ovarian cancer.

Owen Sharp: It is exactly the same for prostate cancer. Hilary has talked about it, but it is exactly the same nirvana that we are all working towards.

Q157 Chair: As we move towards more stratified screening processes, and, as you say, not just genomic processes, presumably there will be quite a complicated dilemma for the medical profession and, indeed, for the Government in carrying the public with you. Clearly, there are going to be people who do not fit that stratification who nevertheless end up with the condition. One can envisage all sorts of rows about the trust or the Government stopping this screening programme, and we have taken a step backwards. How is the medical profession planning this transformation, which is going to be quite important?

Dr Burton: We thought about that quite a lot in the context of the work that we did on breast and prostate screening. One of the problems is that in the past we have portrayed screening as being a good thing, that you really ought to take it up because it would be good for your health, as it were. We have not necessarily always given balanced messages about that. We have to rebalance that so that the public understand that there are risks and benefits to screening or prevention.

You brought up a little earlier the cost-effectiveness argument. It is slightly more difficult when you are balancing screening for what is most cost-effective, but when you can get across to people that we really do not want to inconvenience or harm them by offering unnecessary screening, one would hope that they would gradually start to accept it. However, I accept that it is a difficulty, when you have a programme that is already

running, such as the breast screening programme, if you appear to be withdrawing a service from people that you have ascertained, partly on a genetic basis, as being at low risk. That might be problematic, and we would have to think through that very carefully.

Owen Sharp: Following on from that, it is a challenge and we would have a job to do to explain it well. You have to compare it with the current situation, which I suggest is an awful lot worse. This is obviously specifically around prostate cancer, but you would be describing that against a backdrop that we have at the moment, where there is no screening programme nationally. We have a thing called the prostate cancer risk management plan, which leaves the ball entirely in the man's and the patient's court to do something.

The most common question I get asked as chief exec of Prostate Cancer UK is, "Why is there not a screening programme? Why can I not have a better job on understanding my risk and where I sit, potentially, in the disease pathway?" At the moment, we are completely fudging that. We do not have an answer that is very well articulated to the well-educated patient, let alone the general population. While there would be a job to explain it and be clear that screening programmes, of whatever shape or form, are not absolute, they give you a better sense of where your risks lie, and the public are probably a lot more open to that than we allow or consider them to be at the moment. To be honest, at the moment, it is a bit like the emperor's new clothes. We don't really talk about it. It is ignored and left as a debate among the well-educated middle-class population, and the rest of the world we slightly brush off.

Q158 Stephen Mosley: Professor Jacobs, in one of your answers to the Chair's questions you talked about an algorithm bringing together genetic and lifestyle information to produce almost a universal risk assessment. We have seen a bit of that in the evidence that we have been given. Do you think that the NHS should systematically collect lifestyle information in order to develop this algorithm—this universal risk assessment?

Professor Jacobs: As a note of caution, I shall be focusing most of my answers around the specific example of ovarian cancer. In that area, we have a big programme, a multicentre multi-national programme called PROMISE—Predicting Risk of Ovarian Malignancies and so on, which is what the acronym stands for—which is addressing those very questions. How do you put together algorithms that define a woman's risk of developing ovarian cancer accurately? Secondly, how do you put together algorithms that can use all the tests that we have for screening early detection optimally? Then, how do you put them together as one overarching algorithm that will tell a woman every year what her risk is, based on her prior risk and her screening risk?

That sort of work requires carefully designed research, which brings me to the direct answer to your question. Answering these challenging issues—how you devise these algorithms, and how you use them in practice; what does the population want to know, and with ovarian cancer it is women, and what is the best way to tell them and inform them; how do you provide really accurate information, and then how you use it and do the interventions work?—all that requires really careful research. You phrased your question, should the—

Q159 Stephen Mosley: Should this data be collected universally? I know that you are talking about ovarian cancer, but the lifestyle choices that people make affect all forms of cancer, do they not?

Professor Jacobs: It should be collected systematically, in the context of carefully designed research. If you ask whether it should be collected universally, then you get into some really challenging issues about confidentiality, consent and all those things. Putting that aside for the moment, the more of that sort of information that we can collect in a responsible way and use in well-designed research to answer these difficult questions, the better. Then society, politicians and the public would be able to make really well-informed decisions about how we use the fantastic opportunities that not only genetics and sophisticated statistics but new biomarker and test discoveries offer us at the moment. It is a very exciting area, but it needs to be addressed in a systematic and carefully designed way.

Dr Burton: I think, yes, lifestyle information is going to be useful for a whole host of chronic conditions—heart disease, cancers, diabetes, obesity and all the rest of it. The idea of systematically collecting it for the whole population for all time is rather difficult, because of questions of confidentiality; but lifestyle information obviously changes as people stop smoking, lose weight, take more exercise and whatever. Should you be trying to keep it up to date?

The complexities of doing that in a routine way are difficult, but I can quite see that people may in the future even self-access over the internet something that puts together information on lifestyle and family history, and possibly even send off biomarkers to get a risk for disease. They will find it useful working with their physicians to work out how to stay healthy.

Professor Cree: We would probably prefer to see something that is a bit more organised than that. In the UK, we have the National Health Service. We are lucky to have it, in that we are able to do things on a population basis that other countries find difficult. We can model what will happen within our own population if we take certain steps in terms of screening. We need to link it back to prevention. The lifestyle question links very closely back to prevention. If you are a smoker and you stop smoking, your risk diminishes quite quickly of certain diseases.

It is worth while looking at the whole thing in context. It is not just about screening. It is about screening, lifestyle and health care itself. The whole thing has to be joined up. That is something that health economic modelling is becoming extremely sophisticated at doing. We are moving in that direction quite quickly.

Q160 Stephen Mosley: The focus, from what the three of you have said, is very much on the modelling. You are looking at the health economy as a whole, and then creating models to predict what happens at the national scale. From an individual perspective, can it help people know whether they are at risk?

Professor Cree: Yes, I think it can. If you are invited for screening, then you can be fairly confident, knowing that that modelling has been done, that it is in your best interests to do so. The take-up of certain screening programmes is excellent.

Professor Jacobs: The end point of this would be that an individual would be given information about their risk, based on a whole range of different factors, including genetics and lifestyle. They would also be given options for interventions, depending on their risk, for them to decide where they went in terms of prevention, screening or other interventions. That would be the final end point.

Dr Burton: We are perhaps increasingly seeing a bundle of diseases at once. People may have an assessment using lifestyle for a range of common chronic diseases at certain points in their life.

Owen Sharp: The other thing is that we should not see screening in the future as an entirely passive thing. There is a point at which you want to get the patient involved, and that can be part of bringing in some of the lifestyle factors.

The other thing is that we do not have to jump to the full end, where you bring screening together with a completely big and sophisticated health-screening element. At the moment, we do not put any pieces of information together. We do not properly bring in age in prostate cancer cases, and we certainly do not bring in family history. We definitely do not bring ethnicity into it, yet prostate cancer for black men is a huge issue. No one is taking two or three of those basic factors and starting that, and, once you have done some level of screening, putting it together, potentially, with a patient involved in a fairly simple element of their own assessment of lifestyle, which you can do at the point of some screening interventions.

You do not need masses of information to make a big difference, to develop different risk trajectories, and then empowering the patient to be part of that—to understand the risk and the lifestyle factors—should not be that difficult to do. We do not necessarily need to have a huge database, where every element of our lifestyle is mapped, which channels you into which blood test you go for. You need some simple measures—they can be things like age, family history and ethnicity—and from that point you can start saying, "If that is your profile, and you can add to that some of these lifestyle factors beyond that, you then have a different screening profile that you can involve the patient in."

Q161 Graham Stringer: Professor Cree, you have already mentioned detecting multiple cancers from one blood test. What are the advantages for the patient of doing that?

Professor Cree: First, we are not detecting it from a single test; we are detecting it from a single sample, potentially. This is future stuff; at the moment, we are at the point where we are looking at the cancer testing that is being done, and at all the tests that have been discovered and tried out. To give you a flavour of the sort of thing that we are looking at, we are looking at about 88,000 papers in the scientific literature. There is a very large literature out there, where people have looked for biomarkers for cancers, and they have usually looked for specific cancers.

One of the realisations that have come to us in the last few years is that cancer has a large number of facets, which cancers of different types share. It may be possible—it is a "may"—to deliver a series of tests done on one blood sample that allow you to look for multiple cancers. Effectively, you get the benefits of combining screening programmes into one.

The other benefit you get is that you will be able to look for rare cancers, ones for which you will never be able to set up a screening programme on their own. From the patient's point of view, something like 20% to 25% of patients die of rare cancers—cancers that are outside the top 10 common ones, for which we might well devise screening methods. For many, it is in their best interests to detect those cancers early. Detecting cancers early usually means much easier treatment, much less invasive treatment, and much more successful treatment.

Across all the cancers that I look at, that is part of the scene. If we can devise blood tests that allow us to future-proof what we are doing, we will have something very special, and it is worth while doing the research to find out if it will work.

Q162 Graham Stringer: It has become clear to the Committee since the start of this inquiry that in all screening programmes there is a problem of possible overdiagnosis and false positives. In taking one blood sample and doing a number of tests, are you increasing the risk of overdiagnosis and false positives?

Professor Cree: No; you are decreasing it, because you will be taking a single test that has a high sensitivity. I have to explain this to some extent, but I mean a test that has a high degree of sensitivity for detecting most of the people who might have cancer, but it will detect a lot of people who do not. On that same sample, you do further tests that allow you to throw out the false positives. The false positive cases that would otherwise be sent up to a hospital, perhaps, for further investigation would probably never get that far, because we are able to do further tests on the same sample which rule them out.

Rather than looking for a single, specific test that does everything for you, you are able to use tests on the blood sample, but they are more general in a way that just would not be possible if you were looking for a single cancer. There are potential advantages in making sure that you do not do that. Once you get to the point where you have a population of cases that have a high risk of having a cancer, you then refer them on for further testing. The way that we do that at the moment for colorectal cancer, for instance, is that we have a test that is pretty sensitive, which probably detects 90% or so of the colorectal cancers out there. The tests are changing at the moment, so that figure is not so accurate, but 50% of those who have a colonoscopy on the basis of that test do not have anything wrong with their colon. There is no cancer there.

If we can triage our patients so that we do not investigate those who do not have cancer, we are clearly doing less harm, and we are answering your question about false positives.

Q163 Graham Stringer: Have you discussed this with the NHS and the National Screening Committee?

Professor Cree: I am running a research programme. We have Julietta Patnick and a number of other people on the consortium who are involved in just that. We are at the point where we are doing the systematic reviews and Delphi exercise to see whether this sort of approach is feasible and whether it is logical to pursue it. This is very much from the research angle. It is not something that is going into practice tomorrow.

Q164 Graham Stringer: I was interested to hear whether there had been any response from the screening committee.

Professor Cree: We have certainly talked to SPED, the committee within the National Cancer Research Institute. We have not talked to the National Screening Committee directly, no.

Professor Jacobs: I wonder if this might be a good moment to introduce ovarian cancer as an example of the way that this works in the current system.

I direct a large trial called the UK Collaborative Trial of Ovarian Cancer Screening, or UKCTOCS, which came out with 30 years of research in 2000, based on research to that point. It involved 202,000 women, and it was funded by the Medical Research Council, Cancer Research UK and the Department of Health, now the NIHR, to make sure that the questions about the potential of ovarian cancer screening were answered in a systematic way, and then could flow through into the NHS if positive. Those discussions have been going on from that point until now. That trial will report mortality data—how many lives ovarian cancer screening can save—in early 2015. Throughout the trial, we have been linked in to NHS screening, and those discussions are more intense now as we get close to having the answer. The NHS screening committee will commission a health economics study ready to plug in the results of the research.

In the UK, connectivity is really impressive, at least in the field of ovarian cancer. It is fair to say that to do a trial on that scale, with 202,000 women participating in a randomised trial over 15 years, would be pretty hard to do in many other countries around the world. It requires connectivity between research councils and charities and the NHS, in a truly impressive way.

Q165 Stephen Metcalfe: Obviously, there is research going on into the possibility of new screening programmes and improving the techniques that are currently used. Who is funding that? Who are the main funders? Are they individual projects, or is there a standard model?

Owen Sharp: I would suggest that they are not collectively funded. There is no co-ordination of it. I would say that the funders are the main sources—the people funding the rest of the research, such as drug development and so on. In my world of prostate cancer, the biggest single group of people funding prostate research are charities, along with the medical research community and the like. These things tend to get considered as part of the broader call that you would make for other research.

Professor Cree: There is a joined-up system for medical research in the UK. The MRC and the National Institute for Health Research are the two main Government-funding bodies in that area. They are in constant contact, and their research is co-ordinated. I am well aware of that, as I was director of one of the programmes for some time.

There is certainly a large charitable component, and Cancer Research UK is obviously funding our work, but it is also involved in a large number of other studies, and it has made early detection and prevention one of its major aims over the next few years.

Q166 Stephen Metcalfe: The funding can come from various sources, but the MRC is the one that is co-ordinating.

Professor Cree: No. The MRC's remit is research in the pre-clinical space. The National Institute for Health Research funds the UKCTOCS study, which was originally an MRC study. That is probably a good example.

Professor Jacobs: In the case of UKCTOCS, the funding agencies came together. This was 15 years ago, and it is impressive that they were working together at the time. The application went to the MRC, which reviewed it with Cancer Research UK, the NHS and the Department of Health; it is now the NIHR providing the support for the clinical implications of the screening programme. The Eve Appeal charity filled in a lot of the gaps. It was an impressive confederation of funding agencies all agreeing that this particular issue was really important, and then coming together to fund it.

Other things will be funded in different ways. For biomarker discovery, for instance, Cancer Research UK will take applications from scientists and researchers who think that they have a technology or a new approach, and then peer review it. The Medical Research Council will do the same. NIHR will do the same in a different part of the research spectrum, between basic science and translation and clinical application.

Dr Burton: Quite a bit has been EU-funded. The work that we did with prostate, breast and ovarian cancer was EU-funded, and I know that the upcoming Horizon 2020 EU funding will have a focus on personalised prevention.

Q167 Stephen Metcalfe: The usual processes are in place to ensure that there is no crossover—lots of different groups are not working on the same issue. I see some shaking and nodding of heads.

Professor Cree: Inevitably, there is going to be some crossover. That is probably a good thing, in that you want to make sure that science is corroborated by other studies in the same area. That is very important. One of the things that we are keen on in our consortium is having multi-centre studies, because if you do something in one centre you do not necessarily know whether it is going to work in others.

Multi-centre funding is important, and some overlap is helpful rather than no overlap. But, yes, in terms of making sure that we are not funding a large study—let's say a clinical trial of ovarian cancer—and someone else is funding the same trial in a different setting, that perhaps is not as useful.

Q168 Stephen Metcalfe: At what point does the National Screening Committee get involved to evaluate the usefulness or usability of an improvement in screening technique or a new programme altogether?

Professor Jacobs: I assume that you are getting evidence from the National Screening Committee itself. I would not want to speak for that committee, but in my experience that committee is working on an evidence base, so it strives to ensure that the evidence coming through from trials in the UK or anywhere else in the world is fed in and that it can consider it.

I turn to the specific example of ovarian cancer. I am sorry to keep coming back to it, but it is relevant because it is going to come to the National Screening Committee at the beginning of next year. We already have a dialogue. I have met the committee and people in the NHS such as Julietta Patnick, who would be implementing screening if the National Screening Committee thought it was a good idea. That dialogue is ongoing, but they need to wait for definitive data that they can act upon.

Dr Burton: Sometimes they can fast-track a health technology assessment process. They can also support pilot programmes—for example, the recent pilot on the expansion of newborn screening. Again, it was because the National Screening Committee supported that pilot, although I think it was funded through the NIHR. Because they supported it, it happened. Am I wrong on that?

Professor Cree: You are right. It was funded by the NIHR's EME programme.

Q169 Stephen Metcalfe: As to how it works, does the National Screening Committee tend to be a pull model or a push model? Are you pushing stuff towards it, or it is out there trying to pull things in?

Dr Burton: On the whole, the communities are pushing towards the National Screening Committee rather than the other way around.

Owen Sharp: Can I be slightly less polite?

Stephen Metcalfe: Yes, please do.

Owen Sharp: This is anecdotal, and I am sure that there are a lot of preconceptions in it, but in the world of prostate cancer the screening committee is historically seen as a barrier. It is seen as the guardian of a barrier that you have to get over. Its job is to have a measurement of threshold where you have to get a screening programme that has this level of efficiency and effectiveness, and you have to do lots of things to prove that you have come up with an answer that gets over that barrier.

It is starting to shift, although I think there is more to be done. I would like to see a place where the screening committee's broadest objective is to come up with a national screening programme for prostate cancer that is its No. 1 objective, and that it works with us to achieve it—that things are the other way around and that it helps us, so that we work together to design calls for research, because we have a big part to play, as other funders do.

The simple objective should be, "We have done our job when we have a really good screening programme for prostate cancer," as opposed to, "We have decided whether the ones out there are right or not at the moment." We are always working on evidence bases that by definition are retrospective, so they have to look at big cohorts of patients. They go back.

You get into the concept that we heard in the previous question about overdiagnosis and overtreatment, which are treated as if they are absolute terms—and they are not. Diagnosis is about the day when you have a definitive decision, when a patient is told that he has prostate cancer. That does not happen through a screening programme; it happens through

a series of things. Overtreatment will change, based on the development of treatments and the impact of overtreatment, so it should not be overtreatment as an absolute term. You have to consider the impact of treatment and the impact of diagnosis, right or wrong.

We are not in a place where that relationship is proactive enough, and we are all trying to work to the same objective. At the moment, it often feels a little bit as if it is something that you have to get past, and that is how the prostate cancer community would historically describe it.

Q170 Stephen Metcalfe: Would anyone else echo that?

Professor Cree: I take a slightly different slant on it. I think there is a need for regulation of any health care intervention, whether you are looking at introducing a new drug to practice or introducing a new diagnostic to practice. Essentially, in the screening sphere we are dealing with diagnostics, which is my business as a pathologist.

There is a need for regulation, and there clearly is a limit to how much the regulator should be talking to those who are producing the goods. so I take a slightly different perspective on things. That said, NICE, which is one of the regulators that I know well, talks to companies that are producing diagnostics, and talks to groups that are producing evidence for diagnostics, and it does so on a regular basis.

Dr Burton: The National Screening Committee is very much about public health programmes, and it is important that it is a guardian of public health. If you are going to be proactive in offering screening, you have to be careful not to harm. The committee was set up when we were thinking about the big common conditions such as breast cancer and cervical cancer and so on, and the criteria were developed and were suitable for those sorts of programmes. I think that genomics takes us into a new era, and we are talking about the possibility of diagnosing a rare disease, a variable disease; they may be very rare and, even within that, there may be lots of different sub-types of disease. We are talking about potentially being able to prevent a range of diseases by knowing the risk a long time in advance. Some of the ways in which the National Screening Committee makes those judgments may need to be rethought to take into account some of the new capabilities that we have.

Professor Jacobs: I have been thinking about the role of the National Screening Committee, and that brings us to the thorny issue of the overall public good, and decisions for the NHS, as opposed to what a specific individual might decide based on the evidence and information if they had it. They can be rather different things.

The National Screening Committee quite legitimately is looking at whether it is safe and does it work, and then whether it is cost-effective. That decision in the context of the NHS may be rather different from the decision that an individual person may make, based on the same evidence. For instance, six months of extra life at a cost of x thousand pounds may be worth it to an individual, but it may not be worth it in the whole population context, especially if there are downsides. The National Screening Committee does that pretty well in the context of the NHS.

Q171 Stephen Metcalfe: Going forward, as new techniques are developed, there is more targeting and more stratified screening. Is the current model the correct model for programmes into the future that will deliver those aims?

Owen Sharp: I do not think so. There can be some work around that. As I said, we work to different objectives. They have an incredibly difficult job to do, and, if they are doing the job as it is set up, I think we can shift the way that is emphasised.

There could almost be a broader assessment of disease type, where you get to the simple answer—and it is a simple one—that we have a disease profile and an impact on the population that, were we able to detect this early or able to do this around it, it would therefore be a good thing; and, then, how can we all work towards meeting that challenge? That would be a shift in the dark. That is not their fault as individuals, because they work to what they are asked to do. I think we would have to come up with a new way—

Q172 Chair: Would it not always be the case that that will be individual disease-dependent—that you could not simply have a single set of rules that applied to every condition? It has to be a judgment based upon the broad benefit that could emerge from a screening programme, using whatever today's technologies are, in the context of that narrow group of people. There is not going to be a one-size-fits-all answer.

Owen Sharp: No. At the moment, we broadly define it by the disease as opposed to the person. That may change over time, once we get into the wider world with biomarkers and genetics.

Chair: We are going to come on to that.

Owen Sharp: Once again, I speak for prostate cancer, which will be the biggest cancer in men in this country in the next 15 years. I don't feel that we are all working towards a common objective saying, "What on earth can we do to pull all our efforts together, across every aspect of the community?" in order to come up with the answer that we are diagnosing this disease accurately and early. If we were all working on that, and we shifted the dial to that, we would be in a different place.

Q173 David Morris: Good morning, gentlemen and lady. What steps have been taken to investigate whether risk-stratified approaches to screening that involve providing a DNA sample would be acceptable to the public?

Dr Burton: We did quite a bit of thinking about that in the context of the work we did with breast and prostate cancers. A lot depends on what you are going to do with the DNA sample. If you are going to store it, it may then be available for other people to access it; if you are going to do it as a mere patient thing, where you run the test and then throw it out, all you will have is a risk score. Particularly in the former case, if you are potentially going to be storing the genetic information, people need to know and to have consented to the fact that part of the risk assessment will involve DNA testing.

People also need to be clear how that information will be managed—for the sake of argument, whether family members will have access to it, or insurers and others, and whether it will be available for them to look at later. At the moment, it is similar to the

concerns that people have about really any DNA testing. These are the concerns they have about how that information and those samples will be stored and managed.

Professor Jacobs: We need to be careful not to make assumptions about what individuals or society generally wants. We also need to realise that this is a quickly shifting area. Perhaps society is getting much more comfortable with the idea of genetic testing and other sorts of testing being available.

The key is to study it carefully and really understand it. We have begun that in a preliminary way. Susie Meisel in our group led a set of focus groups with people in the general population, both men and women, and the preliminary response seems be that people really do want to know what their risks are. They then want to know what they can do about their risks. The thing that makes them anxious is if they get a diagnosis of cancer. They do not seem to feel anxious about understanding what their risk is and understanding what the possible interventions are.

This is preliminary, but there does seem to be a thirst for information. It is not that people are averse to knowing it. Of course, one then has to study whether, given that information, it causes unwarranted anxiety and other unwanted consequences, but the initial evidence seems to be that people want the information. As a profession, we have perhaps been rather paternalistic, trying to protect people from information that they actually want to have.

Q174 Chair: You are not very good as a profession at explaining to people in lay terms what risk is about, are you?

Professor Jacobs: That is the other side of it. If you have this really powerful information, how do you present it to people? What is the best way? There are all sorts of technologies and ways that can make it more efficient and get it across more effectively. We have a lot of work going on in that area as well. As you say, some of it is quite complex so it needs to be explained in a comprehensible way that provides the key bits of information.

One also has to acknowledge that no one individual, whether medical or among the lay public, will be able to master all the mass of information. The question then becomes what level of information people want, and different people will want different amounts of information. We should make sure that whatever they want is available. That in itself is a challenge.

Q175 David Morris: May I ask what safeguards are put in place to protect this information from being abused? To give an example, an insurance company is using macros to work out what life expectancy could be if it runs through families, and whether it is genetic. For purposes of that nature, how could you safeguard that information?

Dr Burton: It is already safeguarded to a large extent through the current moratorium, but that is really about highly penetrant genetic disorders. Those are the sorts of things about which people have been more worried, in a sense, that the insurance companies may get information.

With respect to susceptibility to chronic disease, we had a workshop about this in Canada that involved some insurers. In fact, they were not that interested. It did not tell them a lot more than what family history would have told them about susceptibility to chronic diseases. Although people will be concerned about it, it has to be worked through with the insurance industry.

The other thing about genetic information that people need to understand when they are talking about chronic diseases is that, just because they have an underlying genetic risk, it does not mean that they cannot do anything personally to stop themselves getting the disease. It is still important not to smoke, nor to drink or become overweight, because you will still reduce your risk even though you have a high genetic risk. When we are communicating, it is important to get across that it is not, therefore, a deterministic risk that you cannot do anything about, so you might as well take a fatalistic approach to it. There is still a lot that you can do to stay healthy.

Professor Jacobs: It is fair to say that there are certainly lots of safeguards within the NHS in terms of how data are handled. If you have a biopsy in my hospital, I would not be allowed to look at it if I was in any way related to you, or anything like that. Equally, you would not be able to gain that data yourself very easily. You can—it is your data—but you would have to request it and go through the hoops, prove you are who you say you are and that sort of thing.

Data are held, and they are held properly. We have the Data Protection Act, and we have a lot of safeguards in place. Most of us are used to providing a lot of personal data online all the time, and most of us have e-mail addresses. Anyone that you Google these days will generally come up with something, and you will find information that you could use in a health care setting if you really wanted to. If insurance companies started doing that, there is very little to stop them.

Q176 Stephen Metcalfe: May I pick up on some of those points? You said that by screening you could identify where people are at higher risk. Presumably, the reverse works as well, and you can tell people that they have no propensity to this particular condition.

Dr Burton: Probably not, no, but certainly you could find people who were at a lot lower risk, and you might well advise them that they did not need, for example, to have mammography testing. Again, you would still have to tell them that they still needed to do the sensible things to reduce the risk, such as with alcohol, BMI and so on. It is important to reassure those people that, although it is not worth having mammography, they would still need to adopt a healthy lifestyle. It is not that they are no risk.

Professor Jacobs: That perhaps is one of the biggest benefits of risk stratification. A bunch of people are reassured that they are low risk, which is welcome; they avoid having tests that they would otherwise have to have, and there are the health economic benefits of not screening a bunch of people in the population who are at low risk.

Q177 Stephen Metcalfe: When you ran the focus groups that you spoke about, you said that you were talking to groups who wanted to know what their risk was. Were you laying out to them, as an aside, that the downside of knowing what their risk was may be heightened

anxiety, and that they might struggle to get insurance if that information became available? Were those points made clear?

Professor Jacobs: This was a focus group qualitative study, not a quantitative study, and all of these issues were discussed. There is a publication about those focus groups, which I can provide to the Committee. Fundamentally, people wanted to understand all that and hear about it, rather than being averse to hearing about it at all.

Q178 Stephen Metcalfe: At that point, of course, it was not specific to them. For instance, if it was stratified screening for breast cancer and you suddenly found that you were in the much higher risk group, would you not then have heightened anxiety?

Professor Jacobs: That is what needs to be tested. Once we have the algorithms and we start to use them, the last year of the programme—and it is a five-year programme—is all about putting those algorithms into a first-based clinical trial. When we have these wonderful algorithms that take us to nirvana, which can tell us accurately who is at risk and help them to decide what they should do, what does it actually do when you start putting that into use in the population?

Q179 Stephen Metcalfe: So using some of your social scientists in this.

Professor Jacobs: We have a quite a lot of experience in the UKCTOCS trial, which was of 202,000 women. Half of them have been screened every year for eight years, and they are getting a lot of information. One of the biggest psychological quality of life studies ever conducted, led by Lesley Fallowfield, has been part of that big trial. A lot of data is going to come out from there. Quality of life, anxiety and the psychological issues in all of this are absolutely fundamental.

Dr Burton: There has been some work done with respect to lung cancer and genetic risk, and whether people might be encouraged to stop smoking. They found that people with the higher genetic risk were more anxious for a small time but that it did not last long, and their resolve, although initially definitely to quit smoking, did not last over a long period. Probably those anxieties and even the determination to do something different on the basic genetic risk may be short.

Q180 Stephen Metcalfe: I am conscious of the time, so I want to move on, going back, Dr Burton, to points that you raised earlier about whether, as we change the way that we do screening, the National Screening Committee is fit for purpose. Would you set out your concerns in a little more detail?

Dr Burton: I can give a few examples. The National Screening Committee sticks firmly to its 21 or 22 criteria against which it judges programmes. I may have said that there is often a need to trade off against those and that it is often difficult to make the judgments, and that genomic conditions make it even more difficult.

Taking a couple of examples, the criteria are that the condition should be an important public health problem and that the natural history should be well understood. Thinking about that in the context of newborn screening and the recent expansion of the

programmes, we are talking about very rare conditions with a prevalence of perhaps one in 200,000, so we may get four such births in a year.

It is impossible to argue on the basis of rarity that these are themselves major public health problems. They are heterogeneous diseases, and we do not know their natural history; in a sense, the sub-types are fairly recently discovered. It is impossible to know what screening might do. Set against that, with newborn screening you have a relatively cheap and easy test, which is highly sensitive and specific, and they are very treatable. You are setting impossible criteria if you say that it has to be a major public health problem and that we have to understand the natural history. Already we have to trade those off.

If you go back to the public health problem and take all the inherited metabolic conditions together, if you went into any children's hospice, children's ward or special needs school, you would find a large proportion who had inherited metabolic diseases, but not any one of the rare disorders. We need to move towards thinking of bundles of conditions for the National Screening Committee. We need to be thinking, perhaps, about inherited metabolic diseases or a range of rare diseases as a bundle. With multiplex technologies, they can test for all of them at once, so their insistence on taking them one at a time makes it difficult to make judgments.

Q181 Stephen Metcalfe: How would you change the committee to adapt to this changing world?

Dr Burton: It is not for me to say how to change the committee.

Q182 Stephen Metcalfe: Someone has to make suggestions.

Dr Burton: We have to think through how the criteria are judged. There are other areas where we are not clear how to value the information that may be given. In the genomic condition that we are doing in our antenatal testing, there is a potential for pre-conception carrier testing. Again, it is hard to argue in terms of mortality or morbidity.

Q183 Stephen Metcalfe: Does the membership of the committee need to change to reflect that change?

Dr Burton: It is partly the membership; but we also need to rethink the criteria, the methods for judgment, the sorts of evidence and the ways in which conditions will be considered, so that we can rethink the different demands of the new technologies and perhaps set a more structured process for decision making.

Q184 Stephen Metcalfe: What if the committee membership were to change, depending on what discipline or field was being examined?

Dr Burton: They need to be able to get expert advice, possibly with different panels to consider specific areas. If you went to newborn screening, or other aspects of genomic screening, it would not be unreasonable to have a specialist sub-panel to consider those. I might suggest that the National Screening Committee takes a decision in principle, for

example, for newborn screening, carrier testing or any of those, but that it puts the working out of the details into more of a programme group. That group might then consider what conditions would be included, what variants would be tested, how it would be monitored and perhaps how we should make adjustments, as we see the outcomes and effects over the years.

Q185 Stephen Metcalfe: Does anyone else want to comment?

Professor Cree: There is a model that one could look at; that would be the one used by NICE—for instance, the Diagnostics Advisory Committee on which I sit—where we have a standing committee and, for each topic that we consider, a specialist committee. That includes experts who we can grill in the way that you are grilling us, perhaps, to get the sort of detail that we require to make a decision. The recommendations that we come up with are very much along those lines, and it may be worth talking to them about what they do and looking at other models. We have used similar models in the National Institute for Health Research, where invited experts come in to help us with our deliberations.

Professor Jacobs: I was going to go along the same lines; you could look at the relationship between the National Screening Committee and NICE. It is fair to say that NICE started out very much looking at therapeutics, but it now begins to look much more at population and public health and will begin to get into this area. Some of the expertise in NICE may be useful. I am not sure precisely how it would work, but there could be something at that interface that could be valuable.

Owen Sharp: I go back mainly to the point that I made before. In some ways, we should avoid the temptation to try and redesign the detail of the committee. It is a little bit more about its objectives, and then looking at some broader ways about how it could work. In itself, is the committee the right approach to do some of this stuff? There are things that could happen in other slightly more interactive ways.

I would also be looking a bit more at the objectives of the committee and about it being a bit more proactive, and very much with it leading and being part of a partnership with the wider stakeholders in all this. We are all broadly working to the same objectives. Let us be a bit clearer about that, and see whether we can all work to achieve the same goals.

Q186 Jim Dowd: First, I apologise for being delayed elsewhere and for missing the first few minutes of your presentation. I want to look at randomised control trials. We have heard that the earlier ones, or certainly those of a couple of decades ago, did not pay much attention to the associated harms but rather to the benefits. Is it your belief that the bulk of RCTs now address harms as well as benefits?

Professor Cree: The answer is yes; they do. That is why you do randomised control trials. No randomised control trial would be funded by the National Institute for Health Research unless it involved assessments of toxicity and harms. It just would not happen.

Q187 Jim Dowd: Does the screening committee, for example, provide a template for guidance on how trials should be constructed?

Professor Cree: In screening?

Jim Dowd: Yes.

Professor Cree: That is not my area of expertise.

Professor Jacobs: May I comment on that? UKCTOCS is a good example. It is a big randomised trial, definitely focused not only on benefits in terms of survival and mortality but on minimising morbidity, unnecessary interventions and false positives, and measuring them. Right from the outset of that programme, those key things were written into the protocol. It is extremely unlikely that that randomised control trial would have been funded if it did not have those things as part of it. They will be key aspects when the full data are produced.

There may have been some historic issues, but everyone is very aware of the potential downside of screening in all sorts of ways, whether it is physical morbidity or psychological consequences.

Q188 Jim Dowd: Forgive me if I haven't understood you correctly. There are no formal guidelines per se, but there is a broadly understood standard.

Professor Jacobs: Any randomised trial would have to go through peer review to get funded by any of the agencies that we have talked about. As part of the peer review process, they would be looking at that. It would be a key thing for them. The trials would also have to go through careful ethics scrutiny, and those sorts of issues would come up at that point.

Q189 Jim Dowd: That is clear. Finally, do you report the outcomes of your trials using absolute numbers, according to reductions in all-cause mortality? If you don't know now—

Professor Cree: The short answer, I think, is yes. If the trial is about mortality—not all screening is about mortality; some is and some is not—then, yes, you would certainly look at it. However, the outcome measures that you use are defined in the trial, and the trial is powered statistically to look for differences on that primary outcome measure. If the primary outcome measure is mortality, then, yes, you would look at mortality as your outcome...

Professor Jacobs: All of that data would be available. In UKCTOCS, it is powered to have 80% power to a 30% reduction in mortality from ovarian cancer. That is not the same as saying a reduction in mortality in the entire population. It is a reduction from one disease—a reduction in mortality from ovarian cancer. The absolute data would also be available and would be reported. So the answer is both.

Owen Sharp: I am no scientist, so you won't get a very scientific answer from me, but there is a shift towards random control trials, and there has previously been criticism that the approaches have not really picked up or have understated the element of overtreatment. The counterargument to that is that, in some ways, some trials overstate it because the world in the background is ever moving.

One of the things that we have to find a way to do in all of this is to do it quite quickly and on a decent scale. For example, in the world of prostate cancer, if you are doing a random control trial where you ask what the impact is on people who don't go through the process, what is happening to them may be changing quite quickly. With prostate cancer, we have had a series of NICE guidance that changed the way in which clinicians should be approaching biopsies, and the big one is around doing an MRI scan before you have a biopsy to locate the tumour.

That practice is going to evolve and develop very quickly. There are issues around access to MRI machines, and around the expertise of people reporting on that, but, if you assume that that is going to be changing over the next couple of years and happening, you are measuring something where we are changing the number of people having biopsies, the accuracy of those biopsies and their impact.

The danger in this, if we try to achieve one fix and spend ages looking at it, is that the minute you have the results from it you are saying that it is already out of date. Because we now do MRIs, the impact of overtreatment is different from what we thought it was when we started. It is incredibly important to do RCTs, but we need to find a way to do them that has responsiveness and is fairly quick, and that looks at the wider environment and not just the narrowness of the individual test.

Chair: I thank you all very much for your time this morning. It has been very illuminating.

Examination of Witnesses

Witnesses: **Dr Anne Mackie**, Director of Programmes, UK National Screening Committee, **Dr Kevin Dunbar**, Director, National Chlamydia Screening Programme, **Jamie Waterall**, NHS Health Check National Lead, Public Health England, and **Dr Sharon Hillier**, Deputy Director of Screening Division, Public Health Wales, gave evidence.

Q190 Chair: Good morning. I welcome you to the session this morning. It would be helpful if you started off by introducing yourselves.

Dr Mackie: My name is Dr Anne Mackie. I am the director of the UK National Screening Committee.

Dr Dunbar: I am Dr Kevin Dunbar. I am the director of the National Chlamydia Screening Programme.

Dr Hillier: I am Dr Sharon Hillier. I am deputy director of Screening Division, Public Health Wales.

Jamie Waterall: Good morning. I am Jamie Waterall. I am the national lead for the NHS Health Check programme at Public Health England.

Q191 Chair: May I start by asking you, Dr Mackie, to clarify whether the members of the UK National Screening Programme are independent or are employed by Public Health England?

Dr Mackie: The members are independent of Public Health England. Shall I expand on that?

Chair: Yes, please.

Dr Mackie: Public Health England hosts me and my team, and the purpose of my team is to bring together the best international evidence and expert opinion, following consultation and a synthesis of the peer review literature, to the committee and to present it. The committee is the one that makes a recommendation to the four UK Governments. The committee is chaired by a CMO on behalf of the other three; in this instance it is David Walker, who is deputy to Sally Davies, the English CMO. The remainder of the members are experts, lay people, consumer representation, user reps, health economists, ethicists and researchers.

Q192 Chair: It is not on the Government Office for Science list of science advisory committees. Is there a reason for that?

Dr Mackie: I do not know about the list, but we looked at this not long ago when talking about the NHS constitution. The advice was that we were a standing ministerial advisory committee in terms of governance.

Q193 Chair: Let me go a little further. There is a code of practice that the Government Office for Science has adopted for scientific advisory committees. Do you work within that code of practice?

Dr Mackie: We work within the code of practice relating to public bodies, for consultation, the getting of expert witnesses—

Q194 Chair: But not within the GO-Science code of practice.

Dr Mackie: I do not know that, no.

Q195 Chair: There is no logical explanation for that.

Dr Mackie: I would have to come back to you. I would need to talk to the Department to understand which code of practice we work within.

Chair: Okay. Can we move straight on to Stephen Metcalfe?

Q196 Stephen Metcalfe: I want to examine the evidence base on which decisions are made. You spoke in a previous answer about taking evidence from the UK and abroad. How do you check that the quality of the evidence that you take from abroad is the same as the quality of evidence that you might use in the UK.

Dr Mackie: The evidence that we use is brought together by a variety of external organisations. Some of that is done in a systematic reviewing way, and some in a literature synthesis way. The reviewers are expert at saying what the quality of the evidence is. We

therefore only bring together good quality, peer-reviewed evidence. However, in quite a lot of the cases where we are asked to consider screening programmes, people say that Italy do it, or the Americans do it, or "They do it in the south of France. Why aren't we doing it here?" We have therefore tried to find out as much as we can about that. It is often grey literature, by which I mean that it is not published. We would take that into account.

Q197 Stephen Metcalfe: Did you say grey literature?

Dr Mackie: Yes; that is the word for not peer-reviewed literature.

Q198 Stephen Metcalfe: Where it is grey, how do you decide? Do you then conduct your own inquiries? You gave an example of another country using it, but based on grey evidence. How would you decide whether there was any value in what it was doing?

Dr Mackie: We try to look only at the peer-reviewed literature, so the literature synthesis brings together what is done. If the Americans have done some work on group B strep screening, for instance, we would look at that. We would have wished that to be in the peer-reviewed literature, and we would only take that into account when we came to a conclusion about what is the evidence base for making a recommendation to Ministers.

The Minister, or the public, will often want to know why they do it in America and not here, or why they do it in Italy and not here. Quite often, the answer will be that they do not, or it is not like that here, but where the evidence is published—say, the Italians have published some information on sudden cardiac death—the peer reviewers here have said, "Well, we don't think that is of very high quality," and have gone through why that is the case. Quite often in the case of the American examples, the arrangements are so different from those that pertain here that it is difficult for us to say, "Let's move that lock, stock and barrel."

Q199 Stephen Metcalfe: Where another country is conducting a programme that we do not, even if you don't think very much of the evidence that has been published on sudden cardiac death in Italy, would that be enough to get you to conduct your own inquiry and seek evidence here in the UK? It must cost them money, so there must be a reason why they are doing it, even if the evidence is relatively poor by our standards. Would that instigate a possible inquiry into a programme?

Dr Mackie: We would look to ask why they were doing it and to understand, but very often the answers are cultural rather than scientific.

Q200 Stephen Metcalfe: Thank you. If I can, I would like to move on to the NHS Health Check programme, which I believe was implemented without conclusive evidence of its effectiveness. Is that a fair charge?

Jamie Waterall: When the policy was introduced, strong economic modelling was undertaken by the Department of Health to look at the impact. However, it is fair to say that, with regard to the evidence of the impact of the programme that is being introduced and rolled out currently, we do not currently have it for the entirety of the programme.

It is important, first, to recognise, if we look at the evidence in terms of what we are trying to achieve, that there is strong evidence that we know behavioural and physiological risk factors are leading to people dying prematurely, and developing long-term conditions. The global burden of disease study, which was published last year, makes a strong case that the concept of risk factors—smoking, obesity, lack of physical activity, alcohol, cholesterol or blood pressure—are common causes of long-term conditions and mortality.

We know that there is strong evidence that we have to do something. In terms of how we manage those individual risk factors, there is strong evidence of individual management of the risk factors, and we have clear NICE guidance for those. For example, there is clear evidence in the NICE recommendation that people should have their blood pressure checked every five years, and then how those individuals should be managed, along with advice and guidance from NICE on physical activity, smoking and the variety of risk factors that we have in the health check programme. There is strong evidence that there is a problem. There is strong evidence for the individual risk factors, and how they are managed. Where the debate comes, and where there is controversy, is over the totality of the evidence. If you put these into a total programme, and try to manage them at the population level, what is the impact?

Public Health England published a report back in July last year, which we included in our written evidence. It was called "Our approach to the evidence." In it, we set out firmly and clearly that we feel there is need for action, and that we must be addressing these risk factors. We know that there is strong evidence for individual risk factor management, but what we need to glean and gain is better evidence around treating them as a collective.

We have done a few things. One is that we have established an expert clinical and scientific advisory panel to the programme, which has both external and internal academics and clinicians. They are now overseeing the content of the programme and also ensuring that we get that focus on research and evaluation of the programme across England. We made a commitment recently that we will publish a research and evaluation strategy for the programme, and we held a symposium only a month ago where we brought 100 academics and a variety of colleagues together. By the autumn, we will be publishing a document to focus on how we can bring stronger scientific rigour and evidence to the programme.

It is also important to note that two national evaluations are currently under way commissioned by the Department of Health. Some of the early findings that we are getting from the English programme are reassuring. Stoke-on-Trent colleagues published results on their programme recently. It showed a significant impact on reduction of cardiovascular risk on the individuals that they were interacting with, and some publications came out of Queen Mary University, which had been doing an evaluation.

One of the criticisms has been that the uptake will only be high in the affluent communities—the "worried well." Again, the evidence coming from Queen Mary University is that there is equitable uptake in the deprived communities, and high uptake in the BME communities. However, it is important that we continue to monitor the outcomes and get a greater sense of what the programme is achieving.

Q201 Graham Stringer: The independent review of the National Screening Committee says that you bring your judgment to bear on policy recommendations. If you just bring your judgment to bear, how do you stop it being subjective and leading to inconsistencies?

Dr Mackie: We start with a review of the peer-reviewed literature, as I said, and we put it out to consultation. Each time we do a piece of work, we put it out to consultation. Sometimes we do it directly with stakeholders; we might work with the national clinical director for cardiovascular disease, for instance, or the dementia tsar, as he was known, to make sure that what we write is sensible, and we then put that out for three months' consultation.

Often, we have a lot of correspondence and responses to those consultations. We then bring that lot back together and come to a decision, and we try hard to make sure that those decisions are consistent. If you look at the criteria that we use, some of those are about acceptability to the public and to professionals, and, in the end, the committee needs to bring judgment to bear in order to decide whether to implement these screening programmes.

Q202 Graham Stringer: I suppose this is asking a similar question in a different way. The independent review also says that you do not rigidly score and combine the criteria. If you are not using a scoring process, what is the purpose? Again, you are back to subjective assessments, are you not?

Dr Mackie: Inevitably, some bits of it will be so, and that is why we need to involve as many people as possible. So the recent decision on screening women under 25 had several hundred responses. But the core of the evidence relates to whether we are likely to do more good than harm at reasonable cost, and the majority of that can be done by the synthesis of the peer-review literature.

Q203 Graham Stringer: In 1998, in your committee's first annual report, there was a recommended format for systematic reviews that outlined the evidential requirements. Is it the case that that guidance is no longer available? If that is the case, why is it no longer available?

Dr Mackie: Well, 1998 is an awfully long time ago, and things move on. We have done quite a bit of work in relation to the current NSC review, but ever since I started, in around 2006, we have been looking at how we can best bring evidence together to help guide the service. Over that period, there has been international consensus on systematic reviewing, on evidence synthesis, on rapid reviewing and on updating. The Americans and Canadians, for instance, have a lot of experience in doing this, so these things move on. NICE has been invented, too, and it does a lot of reviewing of evidence in literature. We should not stand still but should use best current practice to review and synthesise knowledge.

Q204 Graham Stringer: I am sure that that is the case. It is a long time—16 years ago—but there was a case then for making publicly available a format for systematic review. You can

improve on that and get better at it. Why have you not just improved that process and made publicly available what the new system of scoring is?

Dr Mackie: You are right that we do not score. Therefore, we would not be publishing a report about scoring. We have a methods process in development, and we describe fairly carefully how we go about our process, about deciding to do a review and identifying stakeholders, and we do some scoping about the question. We then take a view on in how much detail we need to do the piece of work. Those things are clear and open to public inspection.

A review was done recently by Warwick University, comparing how the UK NSC goes about its business, in terms of gathering evidence and making recommendations. We bear favourable comparison with the other groups that do it, with other countries looking to us regularly for the evidence reviews that we use, and quoting them in the literature, as well as coming to us to ask about how we go about delivering or setting standards for individual programmes. We have good reason to think that we are doing it well, but we also need to keep going and make sure that we continue to improve how we do it.

Q205 Jim Dowd: I want to look at measuring outcomes. Obviously, the purpose of screening programmes is to benefit somebody identifiable at some stage. What processes are in place to capture the published data on whether a programme is reducing morbidity and mortality?

Dr Mackie: They vary hugely across the screening programmes. The cancer screening programmes have got very good ways of doing that. They publish details about the processes within the programmes; how many people are invited, and what proportion of the people invited come; how accurate the tests are; how many people screen positive, and how many have a disease; and then how many people are treated. They publish regularly on the outcomes of those.

Some of the non-cancer screening programmes are newer, and the monitoring is much more difficult and new, but we are able to say with some confidence that we find a thousand or so babies with metabolic conditions and other conditions on the blood spot. The evidence suggests that we are saving lives, and brains and limbs, doing that. We know through work with the Institute of Child Health that we have the lowest rate of maternal to HIV transmission in the world, and we published on that recently.

We do our very best to make sure that we publish regularly. We produce an annual report on how the screening programmes are delivering, and that contains as much outcome data as we can possibly lay our hands on.

Q206 Jim Dowd: Have you ever come across a programme that clearly was not performing?

Dr Mackie: Yes, actually. We are currently—

Q207 Jim Dowd: What action did you suggest in the light of it?

Dr Mackie: It was slightly before my time, but the screening of young children for dental disease was looked at, and the evidence seemed to suggest that the money would be better spent helping children from deprived and poorer backgrounds to use fluoride toothpaste and to brush their teeth better. The decision to stop the whole systematic population screening programme was made, and the resources should have been put into primary dental prevention.

We are currently talking about screening pregnant women for rubella susceptibility—German measles susceptibility. It seems that it is probably the worst time to be finding out that someone is susceptible to German measles, since you cannot do anything about it then. We are therefore in conversation with our PHE colleagues in the vaccine department to see whether, between us, we can organise to bolster the prevention of German measles by MMR before women become pregnant, so that we do not continue to do it in pregnancy, which does not seem to be a particularly effective way of going about it.

Q208 Jim Dowd: In order to save one life with breast cancer screening, we have seen evidence that the number that you have to test varies by a factor of two and a half. I have seen a figure as low as 84 and a figure as high as 200. How do you deal with such uncertainty, such anomalies, and how do you explain that to the wider population?

Dr Mackie: How we deal with it is that we do our very best to try and get an answer, but, inevitably, with the technology that we have, we all think that it is benign. The development of ultrasound and MMR are all good, but they find lots more things than they originally did, so the advent of smaller breast cancers and ductile carcinoma in situ has happened, and we are less clear about how that develops. Because we cannot do a randomised control trial and say, "Let's leave these women and see what happens, and let's treat these," we have to make assumptions. Therefore, we need to make assumptions about how many women we are helping and harming.

There is lots of discussion in the literature about how you go about doing that for the best, but inevitably you end up with one end of the world saying, "We get this much benefit," and another saying, "We get that much benefit." We need to be open about that and say, "Our best estimate is 1,300 lives that we save," and we try very hard to make the best brains help us in coming to those conclusions, but we have to be honest and say that it might be a bit more or a bit less.

We need to make sure that we let the public know that, so we try hard to take any opportunity to put a message out about screening. We try to grab that opportunity so that people can see it is not completely accurate.

Q209 Jim Dowd: The main reason for that uncertainty is in fact the absence of the randomised control trial, because you cannot deny people treatment simply to benefit your evidence.

Dr Mackie: Exactly. We do not understand fully how DCIS develops, and we therefore cannot say reliably to that lady, "You're okay; let it be," and to another lady, "You really need it treating." Prostate cancer is very similar.

Q210 Jim Dowd: I turn to you, Dr Dunbar. I was astonished when I read the briefing papers at the number of Chlamydia tests that are carried out every year. My initial instinct on seeing such a huge database was that you must be able to make some fairly accurate and precise assertions, but your website says: "Opportunistic screening" for Chlamydia "will probably have resulted in reductions in prevalence…" How come you don't know for sure?

Dr Dunbar: First, it is hard to measure prevalence. Prevalence is a specific epidemiological term; it means the number of people currently infected, and we can only know that when we test them. To determine the total population prevalence, we would have to test everybody in our target age group. As you can imagine, it is hard to test large groups that would give us a sufficient sample.

When we do attempt to gather survey data on prevalence, we find that only a small number of people apply, so we have been unable to make that kind of monitoring programme work. We are in the process of evaluating and validating seroepidemiological studies. Seroepidemiology is evaluating markers in the blood of prior infection, and we hope to use this to review serology samples from patients who have not come forward for any particular reason, to find out what the prevalence of Chlamydia antibodies is within the population.

Q211 Jim Dowd: You say that you test only a proportion of your target group, but your target group is not everybody who is sexually active; it is those who indulge in risky behaviour, is it not?

Dr Dunbar: No; it is all sexually active people between the ages of 15 and 24.

Q212 Jim Dowd: It is the total population.

Dr Dunbar: The total sexually active population, but you can find that quite a lot of people will not have started having sex until later in their teens and even early 20s.

Dr Mackie: May I answer your first question about the code of practice?

Q213 Chair: We have been looking it up as well.

Dr Mackie: Shall I see if you say what we say? It is not classed as a scientific advisory committee or a public body, so it is not statutory and not subject to the recent Cabinet Office review of scientific committees and public bodies. It is not required to comply with the code of practice for scientific advisory committees, but there is an agreement between the four countries that sets out a set of process and procedural rules and governance. As part of the UK NSC, a code of practice is being developed that draws on CoPSAC.

Q214 Chair: Presumably, when you say "draws on," it will be tested by asking the opinion of the Government chief scientist or the chief medical officer on whether it fits.

Dr Mackie: Absolutely. The review has been stimulated to some extent by David Walker's arrival as the new chair, taking over from Harry, and he has said that we are slightly overdue our three-yearly update of how we go about our business and whether we are doing it properly. The recommendations will clearly go to all four Governments to make sure that they are happy.

Q215 Graham Stringer: I go back to Dr Dunbar, and his inability to get the prevalence of Chlamydia in the population. I realise that there may be a complicated statistical answer, but why can't you just sample an adjusted population to get the prevalence?

Dr Dunbar: You are exactly right. There is a complicated statistical answer to that.

Q216 Graham Stringer: Will you tell us?

Dr Dunbar: Essentially, in order to sample a sufficient amount of the population to get down to the confidence intervals required to give you the accuracy to measure the change that we are looking for, you have to sample phenomenally large numbers of people, and they have to respond in an unbiased way.

For example, if you send invites to people in the mail, and ask whether they would like to submit a sample for a national survey, for anything, there is always a degree of bias in the response. If you were asked about heart disease in a survey and you had had heart disease, you might be more inclined to respond because you have had personal experience and it is something that is of interest to you, and if you had not you might not be. Getting those sampling surveys is challenging. We have attempted to do them, but we have simply not been able to get people to respond in the numbers that are required to give us the accuracy to measure the differences in prevalence that we would like to see.

Q217 Stephen Mosley: I want to ask about the difference in screening programmes between the four nations within the UK. I shall start with Dr Hillier. We have some evidence from the Save Babies Through Screening Foundation, and Children Living with Inherited Metabolic Diseases—CLIMB. They have noted how the test for MCADD was introduced in England in 2009 but it was not introduced in Wales until 2012. We have also seen evidence on cervical cancer screening that, in England, the changes were made in 2003-04, but they were not updated in Wales until 2012. Why was Wales behind the curve?

Dr Hillier: In terms of process and the decision making policy in Wales, that is made by the Welsh Government. The Welsh Government established a Wales screening committee to advise the Minister for Health and Social Care. There is a good process in that the committee receives recommendations from the UK NSC, and two members from Wales sit on the UK NSC. The director of the screening division, Dr Rosemary Fox, and Dr Heather Payne, from the Welsh Government, have seats on the UK NSC. Wales has a good structure on the policy side.

The Wales screening committee receives the recommendation, and it is looking at the programme as a whole. Generally, the issues about the screening programme are about the criteria of 19, where you have to establish a programme on that pathway. You have to

ensure that you have adequate staff, and facilities for testing, diagnosis, treatment and programme management. Unless you have that in place, you are potentially going to cause more harm. That is probably the bit in Wales where we have had issues, in terms of MCADD.

In terms of newborn bloodspot screening in Wales, this was not a nationally managed programme; it was not managed under the governance of anyone in Wales. It happened, and it happened as well as it possibly could in Wales, but no one had the overall governance of it. The Welsh Government asked us to look at that, so we established a project, and there were three bits to that project. One was to establish a safe and sustainable newborn bloodspot screening programme. Another was to establish policies and standards, and to introduce the screening tests that were recommended by the UK NSC, of which one was for MCADD. The third one was to review Duchenne muscular dystrophy screening, because that has happened in Wales but it was not a UK NSC recommendation. That was started as a pilot 20 years ago, and it kind of happened.

We established a project, and we brought that into a programme rather than a test. As part of that programme, we established MCADD screening; we implemented that in 2012. We had to have a governance structure in before we could implement that test.

With the change in age range in cervical screening, that was a significant policy change for us, and that was something that we wanted the UK NSC to consider. Once it had considered it, it reviewed the evidence, undertook a public consultation and made a recommendation. That recommendation then went to our screening committee, and we implemented that change. That was in terms of policy being discussed at that level.

Q218 Stephen Mosley: Would Public Health Wales implement, amend or withdraw programmes at a moment, without it first having a recommendation from the national screening committee?

Dr Hillier: No.

Q219 Stephen Mosley: How does that work elsewhere? In England, the change to cervical cancer testing was nine years ahead of Wales; with MCADD, it was three or four years. Why is England so far ahead?

Dr Hillier: In terms of the other countries, I think we were the last to introduce MCADD in Wales in terms of the other countries. As I said, it was the practical bits of information given in that whole programme approach. I could not answer why England was ahead.

Dr Mackie: On governance relating to the cancer screening programme in England, I did not say at the beginning but I have two jobs. One is to help the NSC consider really high-quality evidence and make a judgment on it, but the other is to oversee the non-cancer screening programmes in England.

The cancer screening programmes in England are overseen by a different set of structures, and they have got together some expert advisory committees that have been looking at and continue to look at how they can best improve the programmes. The English committee looked at changing the starting age of cervix screening to 25 quite a long time ago, based

on evidence relating to the English population. The Welsh officers of the committee asked us if we, in the UK NSC, would look to see whether that was something that should be applied across the piece. We undertook that in 2011-12.

Q220 Stephen Mosley: There is no automatic trigger. If one of the nations changes its policy, there is no automatic trigger to UK NSC.

Dr Mackie: We have sorted that out. Now, any big change in one of the existing cancer screening programmes or in other programmes—the Sickle programme wants to change itself quite significantly, as does the Down's programme—we would look to bring to the UK NSC. The cervix at 25 was an example of that. Flexi-sigmoidoscopy as part of the bowel screening programme was brought to the NSC, and that is a UK recommendation. Now, we are also looking regularly at updating existing cancer screening programmes.

Q221 Chair: Are there examples of screening programmes starting in one of the other three countries, ahead of England?

Dr Mackie: Not that I am aware of. People will set off doing screening for all sorts of good reasons, but I am not aware that there are whole-nation or even big screening programmes in the other UK countries that we do not do across the piece.

Q222 Stephen Metcalfe: I want to go back to an area that we covered with the previous panel, which was on the current research and the new technologies that are emerging, and how they are going to be adopted. How well equipped do you think the NSC is to adapt to changing technology, when it comes to including it in its future work programme?

Dr Mackie: Pretty well, I think. Each of our existing screening programmes—this is pretty much about existing screening programmes—has a large advisory committee. They are full of clinicians, often patients or people with relatives who have the conditions, and some public health people. They have a whole range of roles, but one in particular is horizon scanning. They will say, "What about non-invasive prenatal diagnosis for Down's? Free foetal DNA from the baby circulates in the maternal circulation, and somebody has invented a clever machine to measure it. Can we get on and do that?"

Either we do evaluative work within the NSC, funded and sponsored by the NSC, or we ask outfits like the health technology assessment agency or the MRC to undertake pieces of research for us. We have lots of good examples of that. The breast screening programme is currently running the largest randomised control trial in the world on whether we should screen women slightly younger and slightly older. We are sponsors and supporters of research work going on at University College London, looking at whether we should implement non-invasive tests for the Down's programme, on the basis of changing newborn screening technology and the tandem mass spectrometer. We have said that we should implement these for new bloodspot tests.

Q223 Stephen Metcalfe: Where there are gaps in the evidence base, you are funding some of it yourself to see whether you can fill the gaps.

Dr Mackie: I do not have a research fund, but I have some evaluation money and I can get people to do the literature synthesis. If we need new primary research, that would need to be done by research bodies. For instance, there is a proposal in at the moment to see whether we should do a trial of screening for a severe combined immune deficiency—babies in bubbles—and that is currently with the MRC and the HTA.

Q224 Stephen Metcalfe: Specifically where genomic information offers the potential for changes to screening programmes, how are you adapting to that?

Dr Mackie: Non-invasive prenatal diagnosis is a perfect example. Clearly there are claims being made for this in the literature. The far east has adopted this in one way or another. It is being used in the private sector. Can we, as quickly as possible, work out whether, with good faith, we can offer that to all 750,000 pregnant women in the UK and say, "This is better than, or as good as, the thing that we currently offer"?

Q225 Stephen Metcalfe: What do you do in terms of evaluating the social and ethical impact that a programme like that might have?

Dr Mackie: We take that into account when we do the piece of work within the NSC, tucked away in things like whether it is acceptable and whether we do more harm than good; some of those issues are taken into account. In the case of things like pre-conception genetic carrier screening, something where it is completely new, we might go out to another organisation. In that particular case, we asked the Human Genetics Commission if it would have a look. Much as we might ask, "Would you do us a cost-economic model of prostate screening?", we have people who are expert in that. We would do a specific piece of work—and we have done a specific piece of work.

Q226 Stephen Metcalfe: If your committee is accused of not being fit for purpose to adapt to the changes, you do not recognise that criticism.

Dr Mackie: I do not think that we are not fit for purpose.

Q227 Stephen Metcalfe: I meant in terms of the future.

Dr Mackie: We can always do these things better, and part of the current UK NSC consultation is to say explicitly, "Is there something new in the genomics world that would make us look at these things in a different and new way?", and is there an argument for having an external body with ongoing experience of the special things about screening which means that we could put ethical, legal and social questions to them with some confidence that they would represent a range of views? That is actively being considered right now.

Q228 Stephen Mosley: There was some mention of cost-effectiveness in those last answers. I ask the panel what methods your organisations use to evaluate whether a screening programme offers value for money.

Dr Mackie: The UK NSC uses the Treasury Green Book process when it looks at cost-effectiveness. We try to examine the benefits to the individual, but also at costs and benefits wider than that. We often have to rely on information such as the QALY, or NHS cost, because that is what is in the peer-reviewed literature. If we commission a piece of work, and prostate cancer is a good example, we would ask them to do as broad a piece of work as possible.

Dr Hillier: In terms of the screening programmes, again the UK NSC by that process gives us information on the cost-effectiveness and implementation of screening programmes.

Again, it is that balance of benefit versus harm at reasonable cost.

In terms of Public Health Wales, we are configured a little differently from Public Health England, in that Public Health Wales governs and manages the screening programmes. For the cancer programmes it is to the point of diagnosis; that whole pathway is within our governance. In terms of benchmarking, we are looking to see what our delivery looks like compared with other countries, but that is a little difficult because it is not comparing the same issues. Again, we get a lot of attention, from both the Welsh Government and our board, to ensure that we are delivering the programmes as effectively as possible.

We found recently that, because we govern and manage the whole screening programme, we have reconfigured it slightly so that we are actually managing it by dovetailing into each other's programmes, and our admin staff provide functions for different programmes. On how we deliver value for money, we are quite comfortable.

Dr Dunbar: As Anne said, we use the NHS costs for cost-effective analysis by using QALYs, the standard for cost-effectiveness analysis. In terms of the actual value of programming, because the Chlamydia screening is delivered by local authorities, we provide guidance to local authorities to ensure that they are targeting their resources in the most efficient way possible. We are currently undertaking an evaluation of the costs and the cost-effectiveness of the programme as well, to review and update the data, as the last bit of work on that is several years out of date.

Jamie Waterall: Prior to the introduction of the health check programme, the Department of Health undertook an economic impact assessment. Based on the fact that it had not been done before—it was based on modelling—it concluded that the health check programme would be cost-effective, potentially saving £3.6 billion a year at full rollout. Again, using the QALY model, it demonstrated that the programme would be very cost-effective. Because of what Public Health England said, based on the fact that it was modelled data because it had not been done before, we are going to refresh that modelling now that we have results coming out from local programmes to re-evaluate the cost-effectiveness.

Q229 Stephen Mosley: NICE indicates that health intervention should cost less than about £20,000 to £30,000 per quality adjusted life year to be considered cost-effective. Should screening programmes be subject to the same threshold?

Dr Mackie: The really interesting thing about screening programmes is how long and complex they are. They start with an offer to the public and, therefore, they are part of

public health programmes. They then move into the NHS, and you might say that they should be judged by NHS cost-effectiveness thresholds, such as those of NICE. There is then the piece in the middle; screening programmes are incredibly reliant on accurate tests, so NICE also has a set of diagnostic cost-effectiveness criteria.

We are currently working with a DH piece of work on how we should go about doing a cost-effectiveness piece, but if we are suggesting a screening programme we need to be able to say that we think it is possible to be done at reasonable cost. The latest one, which is the bloodspot screening programme extension—a piece of work done by Sheffield health economics—showed that it would be cost saving. You do not get many of those.

Dr Hillier: The new model of bloodspot screening is a good example, in terms of the programme acting at day 5 and getting that sample. You are identifying cases of MCADD and congenital hypothyroidism, for which the treatment is thyroxin, so it is a very small cost in terms of the treatment, and you are saving that whole lifetime of morbidity for that child. Although they are relatively rare, the benefit for that child from the point of birth onwards is quite considerable.

Dr Dunbar: In short, yes, it should be bound by the cost-effectiveness returns, but the challenge is how to measure that over lifetimes of benefits.

Jamie Waterall: I agree. QALYs were looked at in terms of the health check programme, and they all worked out at about £3,000 per QALY, coming well under the NICE threshold.

Q230 Chair: Several of our witnesses have questioned the quality, accuracy and currency of some of the literature that is available advising people about screening. Where does the buck stop with the literature?

Dr Mackie: The buck stops with the national screening programmes, for non-cancer and cancer screening programmes. We need to be sure that we are giving people the right information. The way we go about that is that both the cancer and the non-cancer programmes use the advisory groups that I have talked about. There is a huge amount of engagement with lay experts—so users and patients are on those groups—and certainly in the case of the recent breast cancer leaflets, focus groups include people beyond those who are affected directly by breast cancer.

We need to be on our toes and keep responding to comments, and make sure that the information is as good as it can be, recognising some of the uncertainties that we have discussed.

Q231 Chair: How do you do that? One of our witnesses said that she was not sure whether information leaflets were regularly evaluated to see that they were effective in enabling people to make an informed choice about participating in a screening programme. How do you evaluate the content of the leaflets, and with what kind of frequency?

Dr Mackie: At the moment, almost all of the leaflets are being updated in one way or another. "Screening tests for you and your baby" is just about to come out in its brand new colours. The breast screening programme leaflet has just come out. In the last six months

or so, the aortic aneurism screening programme has issued a decision aid. We look to the responses online to some extent, but also to the advisory committees, to make sure that they are current.

Q232 Chair: Finally, in the context of information given to people in private settings, do you have any oversight of that? Is there any different practice in Wales, for example?

Dr Mackie: We certainly do not have oversight of that. There have been quite a lot of discussions about whether the information given is sufficiently balanced in the private sector.

Q233 Chair: Would you support there being a regulatory function governing that?

Dr Mackie: I do not know whether regulation is the right answer. It is morally right, if anybody is being offered a test or a product, that they understand the pros and cons, and we go to huge lengths within the screening programmes to do that, however difficult it is. The private sector, or anybody offering tests or screening programmes, should do the same, but how we effect that is a matter for others.

Q234 Chair: Is that consistent across the panel?

Dr Hillier: In terms of leaflet production in Wales, we produce our own leaflets on the screening programmes. The breast screening leaflet is changing soon in line with work being done in England on informed choice, so we are consistent with that. In terms of information in the leaflet, we have a virtual reading panel. Our screen engagement team has established a reading panel, which is very diverse. We use that to feed it all the information that goes to the public, to get some feedback.

Q235 Chair: Do you engage with the private sector at all?

Dr Hillier: No, not in the private sector. We do not have any links in—certainly not on their information.

Q236 Chair: There seem to be missing bits right across the piece.

Dr Hillier: Yes.

Chair: Thank you very much for your time this morning. It has been very helpful.