HOUSE OF LORDS

Science and Technology Committee

Uncorrected oral evidence: Commercial clinical trials in the UK

Tuesday 13 June 2023

10.10 am

Watch the meeting

Members present: Baroness Brown of Cambridge (The Chair); Lord Borwick; Viscount Hanworth; Lord Krebs; Baroness Neuberger; Baroness Neville-Jones; Baroness Northover; Lord Rees of Ludlow; Lord Sharkey; Viscount Stansgate; Lord Wei; Lord Winston.

Evidence Session No. 1 Heard in Public Questions 1 – 12

Witness

Lord O'Shaughnessy.

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Examination of witness

Lord O'Shaughnessy.

The Chair: I am very pleased to welcome Lord O'Shaughnessy to the committee's one-off evidence session on his recently published review of commercial clinical trials in the UK. For us, this is a follow-up of our letter, which covered the research culture in the NHS and, in particular, our concerns over the declining numbers of clinical academics in particular. Our questions will be our review in the context of your review. Our review is instigated by the members of our committee with strong medical interests. Lord Winston is one of the key ones, so I will hand over to him to ask the first question.

Q1 **Lord Winston**: Lord O'Shaughnessy, thank you very much for coming. It is a pleasure to be able to ask you some questions.

The metrics show that the environment for clinical trials in the UK has deteriorated somewhat, and there seemed to be a number of different reasons. Would you be kind enough to explain what you think has caused this decline and what we can do about it?

***Lord O'Shaughnessy*:** Thank you very much for the invitation. I was grateful for the briefing you gave me, Chair, in advance of my review, and indeed for the work you have done. I just wanted to say that at the beginning.

You are quite right, Lord Winston, but it is important to bifurcate the problem slightly. If you look at early stage trials, we continue to do very well, and we are ranked highly globally. I am sure there are changes that we could make that would improve that situation, but it continues to be an area of strength.

Unfortunately, the closer you get to both the NHS and industry, our performance has dropped. As you would have seen in the review's final report, there are a number of different ways in which you could measure that—the number of trials, the number of trials recruited, attractiveness as a site of research and so on—but whichever way you cut it, we have gone down. Probably the most dramatic figure is 50,000 participants in 2017-18 down to 28,000.

It is important to point out that that is ABPI data, not actually government data. One of the things that came through in the review, which surprised me, was that nobody has a comprehensive near-real-time view of which trials are happening where. There are different elements. The Experimental Cancer Medicine Centre network has its own tracker, and of course there is the US ClinicalTrials.gov tracker, but there is no synoptic view. That is one of the first things: you have to know what is going on where, and you have to know which areas are performing and which are not.

The problem seems to be largely in commercial, industry-funded trials, which of course by their nature tend to be later phase. The primary

reason is the speed of setting them up and recruiting the first patient. There are lots of other reasons—as you will have seen in the review, I structured it around problem statements—but if you want to zone in on one big thing that we need to change, it is that.

The consequences of that, which are in the report, are stark. One big global pharma company told us that of 18 sites in Europe that carried out research, the UK was the second slowest to set up. Another told us that the UK only gets about half the allocation of patients compared to peer group countries with similar size populations—France, Italy, and Germany—because we are slow to set up and recruit. That is the real world consequence of it.

You can break that down into several parts, as I have done in the report, but it probably boils down to two big things. One is the approvals process itself, the speed of approvals, particularly by the MHRA, which, despite performing magnificently during the pandemic, has been stripped of some of its skies and its capability. The second is the contracting and costing process. In theory, we have a national contracting process that is meant to cover all bases and all trials. In reality, fewer than half of trials actually use it.

Lord Winston, I realise I am teaching you to suck eggs, but you get lots of secondary approvals processes happening at individual sites, and as a consequence the entire process slows up and we become one of the slowest places to set up a trial. The archetypal story you hear is, "We had 12 trial centres across the world. By the time the UK was ready or able to recruit its first patient, we had recruited our numbers everywhere else", and it is a sort of ghost ship trial site that never actually gets used. That is the real-world issue.

Consequently, the recommendations that I made there are actually delivering world-leading approvals processes; Spain seems to do it best. This 60-day total turnaround time includes amendments and various other revisions. The second recommendation is a comprehensive and mandatory approach to national contracts that actually has enforcement. I talk about carrots and sticks, about how that could be done.

Q2 **Lord Winston**: Can I also ask you about what we call the public sector? Certainly, the trials that I have been involved with have generally been based within an NHS service and usually paid for by the drug company involved. What about the NHS involvement? We have recently had an inquiry into clinical academics, and it has been an issue for them too. Would you like to comment on that before we move on?

***Lord O'Shaughnessy*:** Yes. In your report, you talked about the importance of protecting time for research, and it will not have passed your notice that I do not make a specific recommendation about that. There are two reasons for that. One is that it has been done by others. Another is that, however much one wants it to happen at the moment, unless you deal with the actual causes of the reason why that time is impinged upon, it just will not happen. One person who contributed to

the report talked about stripping out the bureaucratic undergrowth, which makes it a lot easier to do research. That is what quite a lot of this is about, particularly in national contracting costing: just do it once, do it well, apply it to all sites, and then it becomes easier to set up trial sites. That is part of it.

The second part is professional and financial incentives. Most of the incentives in the system point clinicians or clinical academics towards more academic research rather than commercial research, and there are some suggestions in the report about how we can address that. Finally, there is something about having much greater accountability for the activity that happens. Like I said, there is not good data about what trials are happening, where, and how well they are performing. As a consequence of what happened in the review, we found that some of the clinical research networks dramatically outperform others. They do not get rewarded or incentivised to do that, and, equally, those that underperform still get their money and are still allowed to crank the handle. There is general lack of accountability for performance.

As a final point, it is not a priority for the NHS leadership. It is two and a half pages in the long-term plan. There is no R&D target for the NHS, even though it is meant to be one of our key industries for the long-term future of the UK. Sorry, there are a lot of factors.

Lord Winston: Thank you. That is a really helpful answer. It is what I would have asked you anyway.

Q3 **Lord Sharkey:** I would like to briefly go back to the Health and Care Bill 2021. When it came before us, we amended the Bill with the help of government to place a significantly greater emphasis on research in the NHS, but, as Lord Winston has mentioned, it is quite clear that we still have problems with research in the NHS. How can we engage the NHS institutions and the people who work in them to make sure that they do what we ask them to do, which is to prioritise research?

***Lord O'Shaughnessy*:** It was a fantastic amendment and I was pleased to see it, but like all these things it is pregnant with possibility rather than delivered.

We did think about that quite a lot, and it is potentially a powerful lever, because it is through that you can actually make the ICSs behave in certain ways. But, ultimately, it is a top-down system, so it has to come from the top. I know that it is unpopular, and to some extent it is counter to the theme of the Hewitt review, which was about trying to reduce the number of targets on integrated care systems and ICBs and the like. But I happen to think that if you have a top-down system, they tend to respond to incentives and instructions from the top, and the NHS is no different. We might wish it otherwise, but that is the reality of it. Unless you set R&D targets, or start measuring at the very first rate and then set R&D targets, you are not really going to change the culture.

It is a long time ago now—I have not seen the research repeated, and I was not able to do it through my review—but when I was in the department as a Minister I commissioned a piece of work that looked at the proportion of R&D activity in the NHS. At the time, it was 1.7% or 1.8%, which was the UK average across the economy. Now, of course, that has all been revised upwards and all the rest of it. I would not be surprised if it is about the same, but we do not know. We all want it to be higher, but we do not have a view about what it ought to be quantitatively. A big part of it is measuring it and then ultimately setting ambitions and targets around it, and some of the rest will follow.

Lord Sharkey: Does that include incentivising it, because at the moment—I think you mentioned it in your report—it does not seem that there is a sufficient incentive for NHS staff?

***Lord O'Shaughnessy*:** Yes. A professional incentive is important, and we talked about the new academy for clinical research, clinical trials. There is also the financial. Critically, there was perhaps a misunderstanding, when the report was published, that the suggestion was that GPs should be paid directly, which is a very American style.

That is not what is envisaged. The idea, and it is a nice description that somebody suggested, is a kind of PI box. The actual unit that is doing the research gets a minimum proportion of the funding that comes to them to carry all the margin on top of the cost of carrying out the work, and they can use that to invest in more research nurses, better data, creating platforms, outreach to patients, or whatever it is.

Again, it is about transparency. One of the things that surprised me is the lack of transparency for the £350 million that we spend on this through the NIHR. It is very poor. One of my conclusions—again, it is not my headline one—is that we need to look again at the model for how what is currently called the Clinical Research Network but is changing its name to the RDN is structured, precisely because it is a very closed environment that does not seem to have appropriate accountability for the money we are spending. Look what has happened: the performance has got worse.

The Chair: We certainly strongly agreed with your conclusion about research targets in the NHS. We were very keen to see some reporting on what research is being done—

***Lord O'Shaughnessy*:** Yes, it would be a start.

The Chair:—as a way of encouraging senior management to make sure there was time for it.

***Lord O'Shaughnessy*:** There is an easy rejoinder to that, which is that 7.5 million people are on waiting lists, and all the rest of it, and it is not possible. Sure, front-line pressures are very bad, and no one underestimates how hard people are working, but that is also true of most countries post pandemic. Almost every country in the world has tremendous pressure on its healthcare services, and yet others are

managing to leap ahead in this area—Spain, Australia, Poland, we could name others. It clearly is possible, but it is only possible if it matters to somebody who has the power to do something about it. That is the bit where, culturally, we are not there yet.

The Chair: We would argue that quite a lot of the research in the NHS is actually geared to making the NHS more efficient and helping to reduce the pressure, but if you do not make time to do the research, you never actually reduce the pressure. That investment is about making things easier for the future. Absolutely.

Q4 **Lord Rees of Ludlow:** Good morning. I want to ask about lessons from the pandemic where lots of large-scale and high-profile clinical trials did take place in the NHS. We can learn from what happened during that period and how it was so different, I guess because everything was done in a hurry; things happened more quickly and with higher priority. The worry is that the engagement with research that we saw during Covid has not been maintained. Would like to comment on that?

***Lord O'Shaughnessy*:** It is interesting to reflect with researchers in the NHS about their experiences of Covid, because, on the one hand, there is obviously an extraordinary track record of success, in the vaccine trials and the treatment trials. You would have seen in the review that the first case study is the Vaccine Taskforce.

On the other hand, everything else stopped, and we are where we are partly because everything else had to stop. That obviously harmed our capacity. People got out the habit of doing research outside of Covid, and we are still recovering from that. Indeed, what the NHS and research is going through is called a Recovery Support Programme. It is also a bit of a mixed blessing, because it had a scarring effect to a degree. Nevertheless, I do think that it showed us the model of how we can do things safely and ethically, but also at tremendous speed. The RECOVERY, PRINCIPLE and PANORAMIC trials, and the Vaccine Taskforce, were a big inspiration for the recommendations in the report.

Speeding up approvals is an obvious example. We are clearly capable of doing it, and we know how to do it, but we need the capacity to be able to do it. That comes back to the MHRA. It also comes back to the idea of not allowing every site to second-guess decisions made by a lead site—there is no reason for that; we did not put up with it when we were moving in matters of days, not weeks or months or even years—and to being fussy about amendments and all those kinds of things.

It is also a bit of the inspiration for the clinical trial accelerator networks, because when we needed to prioritise something that was the biggest health issue for the country, we were able to put in place a system that delivered probably better than anywhere in the world. Are we short of urgent health needs now? No, of course not; we have them by the bucketload. We have to decide to be strategic about it and put in place platforms that can be used by industry and by academia to expedite approvals in the whole process so that we can get trials through quickly

in areas that are important to us for health reasons, for life science reasons, or ideally for both, so that we have genuine connectivity at the strategic level between where our science focus is all the way through to health outcomes at the other end.

Lord Rees of Ludlow: I do not know what credence it had, but a newspaper reported some spokesman saying that we were now less prepared for a pandemic than we were before Covid-19. What would you say to that?

***Lord O'Shaughnessy*:** Is this not day one of the UK Covid-19 inquiry? It might be related. Of course, under your leadership, Lord Rees, we did the Risk Assessment and Risk Planning Committee together, and you will be better a judge than me of whether that is true or not.

It is so interesting—and this is true not just of this area—how so much of the way we behave as an economy and as a society seems to be about recapturing the status quo ante, before Covid, rather than internalising the things that went well as well as the things that went badly. It was such a traumatic experience, we almost want to forget. More than one person in this review said, "If we could just go back to how it was five years ago". We were doing a lot better five years ago, so you can understand the impulse, but the world has changed. We know how to do radically better. We can do not just as well as we were doing five years ago, but twice as well. You will have seen that I set an ambition for that in relation to these commercial trials.

Being prepared to deal with the trauma of remembering the experience in order to learn the good bits as well as the bad bits is also part of the issue, and we have not quite done that yet.

Q5 **Lord Krebs:** I want to go a bit deeper into regulation, because your problem statement number one was that the clinical trial set-up and approvals processes in the UK is slow and bureaucratic, especially compared to other countries. As a prelude to digging into the regulator, that has obviously changed over time because our participation in clinical trials, as you have already said, has gone down over time. Is it that we have got worse, or have other countries got better?

That is a pre-question. My core question is about the role of the MHRA, which you have referred to on a number of occasions. Can you explain why the MHRA is slow and what it needs to do to speed up clinical trials? Are there risks associated with going faster? As a regulator, the MHRA has to be duly cautious. Will the push to speed up compromise patient safety?

Perhaps as a final point, the Government announced £13 million extra money for the MHRA to build capacity. Is that sufficient for the purpose?

***Lord O'Shaughnessy*:** To answer your first question, it is both: we have got worse and other countries have got better. Spain is a really interesting example, because it has made it a national strategic priority to go after commercial clinical trials activity. I have not had direct

conversations with Spain, but they speak quite aggressively about taking business, as it were, away from the UK.

AstraZeneca is globally headquartered in the UK in Cambridge. I do not know if members of the committee have seen it, but relatively recently it has made a £500 million investment in Catalonia—there is a big cluster around Barcelona—all on delivering clinical trials. You talk to them about it and they say, "They can give us everything we need. They'll turn approvals around quickly. There is amazing access to data, clinical capacity", et cetera. It is sad to reflect on that if you want to think of it in entrepreneurial terms, which I think we should, because you would have thought that we would be in a good place to win that kind of business.

On the MHRA, I do not think it is a problem of the leadership or the nature of the MHRA, which is perfectly capable of doing what we want it to do, but if you look at the hard numbers of people it has lost in retrenchments post pandemic and at the kind of people who have left, there has been an exodus of talent from the regulator. That combination of capacity and quality means that it is just not able to do what it wants to do and what theoretically it is capable of doing in the way we want it to do it.

It is not just the MHRA. Generally speaking, the HRA came out of this process pretty well. People seem to be pretty happy with how it is operating, slimming down ethics approvals and speeding that up. There were other bits and pieces, but the MHRA was the main concern. To your other questions about risks and funding, there is only risk if you ask it to cut corners, and no one is asking it to cut corners. We are just asking it to perform in the way it is capable of doing and fund it accordingly, and the £13 million is extremely welcome. Will it do the job? I hope so.

One of my recommendations is that the MHRA should have a task and finish group, delivering on the 60-day approval turnarounds with the HRA. That can all be done with the funding that has been provided. The decision has been made to accept the decision of stringent regulators—the FDA, the EMA, and others—for medicines and medical devices, so I would hope that it will also reduce demand on the MHRA for its services, which means that more can be oriented towards the clinical trial approval process as well.

Overall, I am pretty optimistic that we will be able to fix that part of the pipe. The feeling from the dozens of people we spoke to is that this is the most significant issue we have to address. We can be reasonably optimistic about that.

Q6 **Baroness Neville-Jones**: In your review, you proposed clinical trial accelerator networks. Could you say a bit more about them—maybe what you see as being their purpose, how they operate, and what effect you expect them to have?

***Lord O'Shaughnessy*:** The vast bulk of the recommendations are about trying to improve the overall environment for doing commercial and non-

commercial clinical trials: almost a rising tide. But I also became convinced of the need for the model by which we support commercial trials to change. At the moment, that funding is largely distributed out through clinical research networks that are regional. We fund infrastructure, the money goes out, it is supposed to be a competitive process. I am not convinced that there is that much competition in it. It is a sort of regional infrastructure that is not terribly accountable for performance, and we do not incentivise excellence or address weakness particularly.

The idea of the clinical trial acceleration networks—we have used examples from the US and the UK—is much more about disease-specific platforms; learning the lesson of Covid, if you like, where we had disease or therapeutic modality platforms. The vaccines are a good example. They are focused on an area where everybody agrees that there is an urgent health need, so you can speed things up and set them up in such a way that there are partnerships between all the critical elements in delivering trials—the public sector, NHS, academia, industry—but also with a degree of independence, so they can follow their entrepreneurial instincts.

The final part is privileged access to the approvals processes and so on, so not a different approvals process but a fast lane. The idea behind these is that, over time, it should become the model for how we fund research. So it is not just Buggins' turn redistributed and everyone gets something, but a much more entrepreneurial environment where people have a particularly successful way of delivering trials, or there is a big disease area that we really care about and we want to make sure that attention is spent there, or there is a big pipeline of industry drugs coming through that we want to be able to mainstream here, or whatever it is. In that sort of entrepreneurial environment we can capture that moment of innovation in a particular disease area or around a modality like mRNA vaccines and make sure that we attract that activity here.

You will have seen this relatively modest start on government funding. The Government have talked about funding two or three of these. I believe the approach they will take is to align them with the Life Sciences Vision so that there is a natural buildout from the basic science, which makes sense. I hope it will mean that you get platforms that are industry-partner agnostic but which anybody who has a drug to treat blood cancers, for example, will want to come here to do it, because it delivers world-leading performance.

Baroness Neville-Jones: What is the network bit in that?

Lord O'Shaughnessy: That is a very good question. It would not just be one site. It would involve potentially dozens but certainly a handful of different sites across the UK, which might be hospitals or, over time, primary care, which is an underexploited resource. It is worth stressing that this is a UK wide sector; we have four NHS areas but single science funding. A bit of knitting needs to go between the two, but that is what we mean by the network: you have coverage across the whole population

that, at 67 million people, is large enough and heterogeneous enough to be able to provide recruitment populations for almost every disease in the world.

Baroness Neville-Jones: Do you think they are really ready to hang out their sign saying, "Here we are. We can do these. Come and do it with us"?

Lord O'Shaughnessy: Yes. I was pleased to uncover a lot of latent entrepreneurialism out there that is just covered in bureaucratic sludge. We have to clear all that away. There are people out there who are capable of designing and delivering these platforms, which will be able to deliver thousands of trial participants, if not tens of thousands in time, but for whom the current structure is inaccessible. It does not really like their way of doing things.

Baroness Neville-Jones: It does not really require any government action, does it?

Lord O'Shaughnessy: Ideally, it would not, but in reality you do need a bit of seed funding.

Baroness Neville-Jones: I mean that it is something that those involved and the profession itself can get on with.

Lord O'Shaughnessy: They can as long as they can access it, because a lot of this is done on publicly funded infrastructure.

Baroness Neville-Jones: That is true.

Lord O'Shaughnessy: We have to have a bit of skin in this game, but it should not be totally funded by government.

Baroness Neville-Jones: Do you think the Government will give it priority?

Lord O'Shaughnessy: It is one of the things that they have put this initial tranche of money towards, so I am hopeful, but you know what it is like with these independent reviews; it is all about execution risk. That is why I am glad you are giving it attention, because the biggest risk is that amongst everything else it is just a second-order priority, which I do not think it should be. But then I would say that, because I have spent the last six months thinking about it.

Baroness Neville-Jones: I will give it a push. Thank you.

The Chair: You mentioned the devolved Administrations, and it would be interesting to hear a bit from you about how the co-ordination with the devolved Administrations has worked, or what needs to be done to ensure that it is integrated across the different areas in the NHS.

Lord O'Shaughnessy: It was commissioned by UK Government Ministers but with their English responsibilities, if I can call them that, and then built out towards the devolved Administrations. Obviously, a lot

of the recommendations are UK-wide, regulation being a good example, national contracting and costing being another, and so on. Members of the DAS, whether the Chief Scientific Officer or other civil servants, were very involved in giving evidence, helping to build the report and so on.

Inevitably, it is quite difficult to write these things, because our health systems are all slightly different in a way that is completely agnostic. There probably is a bit of an English bent to the recommendations, but they can be read across. I am off to Edinburgh in a couple of weeks' time, and Cardiff in a month's time, to meet with Ministers and talk about how to implement the bits that are within their purview. So far, I have not heard anything from them such as "No, we can't do it, we're not interested", or anything like that. I am relatively encouraged by that, albeit that execution clearly is different in each of those countries.

Northern Ireland's health system is the one I know least about, frankly, so I would not want to make claims about that, but Scotland and Wales are more agile than England, partly because of size, partly because of culture, partly for other reasons, so they might be the ones to grasp quite a lot of this and quickly implement the bits that are under their control.

The Chair: Will you expect a formal response from them after this?

Lord O'Shaughnessy: Yes, they will be part of the total government implementation plan that is due to be published in the autumn.

Q7 **Baroness Northover:** You have touched on international competitors to some extent—for example, what we can learn from countries that are starting to overtake us in the delivery of clinical trials, and whether we should adopt particular policies that your review examined.

Could I also take it a little wider and ask you about the impact of Brexit? Here we have a situation where there is a different regulator in the UK than across the EU, and potential barriers to the pharmaceutical industry. Clearly there is huge expertise in clinical trials; there always has been in the NHS. The fact that almost the whole population is in it, the emphasis in secondary and tertiary care is on conducting clinical trials, the support from organisations such as what became Cancer Research UK and so on, all helps to drive clinical trials in Britain; I am thinking of Peto's work, for instance, through clinical trials in China.

Here, however, we have had a massive change in our arrangements with the EU, the loss of researchers, and the loss of involvement in the Horizon programme. Clearly the Covid pandemic is a different situation, with the pressures enabling certain things, plus the potential of producing medicines that can then be used internationally, and so on. We are now facing the situation with Brexit, so as you answer on the international comparisons, could you comment on that as well, please?

Lord O'Shaughnessy: Yes, by all means. We have covered some of the international comparison elements, so I will not repeat that, but obviously the speed of approvals and so on is really important.

One topic we have not touched on yet is health data, and you will have seen that it features quite significantly in the report. One of the things that happened during Covid was the use of COPI—Control of Patient Information—notices in order to make confidential patient information available for the purposes of dealing with the pandemic. I do not think we ought to continue operating under emergency legislation, but neither did I see anybody complaining that their data was being used to give them a better chance of accessing an effective Covid vaccine or therapy. It is really important that we have a very explicit public conversation about the use of data to help to improve outcomes in big disease areas.

Of course there are people who are concerned about privacy, but privacy ultimately is the choice of the citizen, and if we can give them the choice to be part of sharing their data for research, that will improve their clinical care.

Baroness Northover: A lot of it could be anonymised anyway, and the cancer registers and such like are a fantastic resource.

Lord O'Shaughnessy: Indeed, but the trouble is that we have never gone through a process of properly asking people or having a conversation about it. To your point about comparisons with other countries, we talk a great game on access to data in this country, but the industry will say, "You're not really delivering it". We cannot approach patients who have been stratified and identified as having a condition or being suitable for trial unless they have already consented to be contacted. It is a Catch-22 situation. Even when we do, and we have them in a trial and they say, "Yes, I'm happy for my health data to be joined up or taken out of primary care", or whatever it is, that often never happens, and if it does it is very slow. Other countries have leapt ahead on that front.

In theory, we ought to be brilliant at that because of the way the NHS is set up: we capture data about health and health processes and outcomes rather than billing data, and we have extensive genomic data assets and lots of other things, but we are not delivering on it. That is a massive issue. You will have seen it is addressed in the report both in terms of patient recruitment into trials and being able to approach people—they can always say no—but it is actually about joining up data once people are in trials, so that you get really deep phenotyping and, now, genotyping. That is a huge asset. We have an advantage at the moment, but other countries are very quickly catching up, and that is something that we strongly need to address, so I would highlight that topic.

On your point about Brexit, in all honesty it did not come up an awful lot. Clearly, we are at a regulatory juncture at the moment, being the only country that is still operating on the CTD as everyone else is moving to CTR. I know there is legislation in front of the House to have our own version of clinical trials regulation.

The truth is that this is all about international convergence. It is not just about Brexit particularly; it is about making sure that trials that happen

here and in the States, in China, in Australia and everywhere else are adhering to the same standards, using the same kind of platforms and capturing the same data, and that the regulators are giving a consistent message about what data they want to see for regulatory purposes when they are licensing drugs and medical devices and so on. Although, for obvious reasons, we have had a hiatus for the last few years, we are now moving very much in the right direction.

Baroness Northover: What about the other aspects that I mentioned such as the capacity for running trials? Researchers are key for running a lot of those trials. You might have people in charge of a trial, but they have to have people to carry them out.

Lord O'Shaughnessy: It is notable that our activity in phase one and phase two trials has not declined, so that is why I do not think it is an issue.

Baroness Northover: Could it be a pending one, an issue that worries you coming down the track when some of these people are not replaced?

Lord O'Shaughnessy: There may be an impact the longer we are outside schemes like Horizon and so on, but I honestly do not think that is our big problem. The big problem is how difficult it is to do research in the NHS, particularly commercial research. If you unpack all of that, people, the workforce, is one part of it, but having access to an international workforce is a small part of a part. Maybe it is an element, but I would not want to overblow it.

The most important thing is making it easy to set up and run trials, for the incentives that come from that to actually land, for the positive externalities to be internalised by the people running the trial so that it is in their interest to do it—they get recognised, rewarded, and so on, not directly paid but in the way we have described—and for there to be a very clear message, from the top down, that research matters.

The final part is the pull through from patients. There are really interesting opportunities, like the NHS app, which is now on 32 million phones across the country. You can choose to be part of the NIHR cohort—it just takes you to another website; it is not very interactive—but the ability to build functionality into the NHS app so that you can set preferences, such as whether you would like to be contacted for which kind of trials and how you want your data to be used, is huge. Again, most health systems cannot offer that. I have not seen it, but I am told that there is that functionality in the product pipeline for the NHS app.

All these factors are more important than the international workforce aspects. I know you are worried about them, and I understand why, but I do not think they are too much of a worry.

Viscount Stansgate: Good morning, and thank you for coming to talk to us. Can we move on to the government response to your report? There was an interim response the same day. Can you give us your thoughts on

that, and where would you like to see the fastest progress made soonest? I will then ask a question about the money allocated.

Lord O'Shaughnessy: It is two and a half weeks since it was published, and I would say, "So far, so good", but it is early days. There were 27 recommendations, and of course you do not want to have any favourite children, but in the end some things matter more than others. I was asked in advance what things I thought mattered more than others. For a variety of reasons, I chose things that offered the biggest opportunity for change or needed to be done most urgently, or both, and those five areas were the five areas that the Government accepted immediately and put money behind. There was nothing that I asked for in that regard that did not come through.

Obviously, it is never straightforward to get these things over the line. Nevertheless, that commitment was given, and funding was allocated to it, and I am happy with the funding that has been allocated. I also said that there should be an implementation plan by the autumn, and they have accepted all recommendations in principle and promised an implementation plan by autumn. I also know that autumn is a very stretchy season, and the spotlight of attention moves on once something has happened. That is why I said earlier, and I would reiterate in answer to your question, that the biggest risk is implementation risk.

Everyone agrees with it; not necessarily all of it, but they are generally happy. We have a set of recommendations. Of course, things can be done differently or improved upon or whatever, but we have a set. Everyone seems to agree with them more or less, so let us get on and do it. However, it is the getting on and doing it which is where these things usually fall down. Obviously, I am not a member of the Government, and I am not even currently sitting in this place at the moment, so it is not my role to make it happen. I do not have the levers to do it. I can continue to agitate for that, but what I say to everybody I speak to about the report is that if they think of it as broadly pointing in the right direction and that the things recommended ought to happen, we all have a responsibility to try to keep the pressure up, because there is the risk that, with an election imminent and various other things to deal with, it will just drop down the list of priorities. That, frankly, is my biggest worry.

Viscount Stansgate: Can I take a specific example? How satisfied are you with the money allocated for the CTANs, and is it your understanding that this is new money or recycled money?

Lord O'Shaughnessy: Those are two good questions. Would I have liked more CTANs to have been funded in the first instance? Sure, but I also appreciate that if we will do them well they need to be genuinely innovative, so there is a case for the thin end of the wedge approach to policy-making, which is that you try and do a small number really well, to really understand how best the model could work, and then build out from there. I am glad that they accepted that point in principle. Sorry, what was your second question?

Viscount Stansgate: It was about the money. Is it your understanding that it is new money or recycled?

Lord O'Shaughnessy: I do not know. We are within a spending review period, so it cannot be that new, but it is money to do something that is needed and that will, I hope, if it succeeds as a concept, be transformative of the way we fund clinical research overall. That is the most important thing here, because we spend quite a lot of money on this area. The NIHR is quite well funded.

Overall spending allocation for health R&D is pretty good, but how do we spend that money, and are we using it to leverage additional funding that will grow the field? That is one reason why I think commercial clinical trials are such an interesting area: because they are a tiny proportion—2%; it was 5%—of the total clinical trial numbers that we do, but they have this outsized impact because it is net new money. It is not taxpayers' money that is being redistributed through the research councils or the NHS; it is often foreign direct investment coming in from the private sector into the UK, and a lot of it directly into the NHS to pay for treatments that would otherwise have to be funded by the taxpayer, so it has this outsized importance.

That is why it is important to have an entrepreneurial mindset, which sadly is missing to some extent, about how we can use this public spending to leverage as much non-public spending as possible. If we have that, which is what I am trying to use the CTANs to engender more of, the total funding pot of sources considered for clinical research will grow, and that, after all, is what we need to see.

Q8 **Viscount Stansgate:** Thank you. My final question is about what you think we should be doing to monitor the success of your report and its recommendations.

Lord O'Shaughnessy: First, I am delighted and grateful that you have taken the time to do this inquiry. I know that it builds on your own work and report. I would hope that the extraordinary group of people who are in this committee, including those with stellar medical research careers who know a lot more about the subject than me, will help to keep the pressure up by keeping the spotlight on this area with the means you have available—Select Committee inquiries, debates in the House and so on, as well as using legislative opportunities to try to get some of these changes to happen, or at least to raise the profile of the topic.

As I say, it is a multi-partner endeavour, so everybody needs to contribute to that, and it was one reason why I felt that it ought to be up to the Life Sciences Council to provide oversight; it is one of the few bodies that has all the relevant parties represented—the NHS, government, academia, industry, patient groups and medical research charities—which of course have an incredibly important role in all of this. Hopefully that answers your question.

Viscount Stansgate: Thank you.

Q9 **Baroness Neuberger:** I have chaired UCLH, which has a fair research agenda and describes itself as a research-led hospital. You talked, I thought absolutely rightly and almost movingly, about us being a top-down system. I just wonder what you think we could do in the NHS as a bottom-up system, and I want to tie that together with what you have said about Spain, because Spain has been very interesting. It is a mixture of top-down and bottom-up, and I think we get that wrong here.

Lord O'Shaughnessy: I was talking to UCLH partners just the other day about the review, and there is a lot of bottom-up interest from your hospital and its partners in north and east London. So you are right. We also have the Academic Health Science Centres, which drive a huge amount of research. I came this morning from the launch of the Paddington Life Sciences hub. Imperial is obviously central too, and we can look around the country and see that a lot of activity comes through that.

That is where a lot of the national impediments, if removed—and, as I say, removed in a way that is safe and ethical and so on—will unleash a lot of activity. Greater Manchester has the highest ratio per capita of clinical trial recruitment in the country, and it is clearly capable of doing really well. If we make it easier to set up and run trials, they will do even better, so a good degree of this is, as I say, releasing the pressure on that entrepreneurialism. I do think that will grow from the bottom up.

Nevertheless, we need clear signals, incentives and transparency—I really want to stress that point about transparency—so that we know who is doing well and who is underperforming and we can do something about it. Special attention, as your Lordships rightly pointed out during the passage of the Bill, needs to be given to research so that it is a priority at every level, including ICSs. What would be the equivalent of Catalonia? It would be Greater Manchester or the north-east—Northumberland, for example—those kinds of areas. We should try to use the money to create more radical change, which is where the CTANs and that kind of thing come in.

What also probably needs a bit of top-down attention is trying to use our primary care assets—in effect, the GP network—to deliver more research. The big late-stage trials in chronic and infectious diseases want to be recruiting people out of primary care who will be seen in primary care and who may even be able to participate in trials from home. My understanding at least, or the evidence that was given, is that there are huge opportunities there and, indeed, a really exciting pipeline of drugs. There are big trials coming that look a lot like the trials that we were doing during Covid, particularly on the vaccines for example, for which we could recruit.

Honestly, primary care is a bit of an afterthought. There is a primary care research strategy, but it is not very thorough. We do not create incentives for GPs to take part in research, and one recommendation was that we should think about how we use the QOF and things like that to incentivise them.

Baroness Neuberger: Primary care is very difficult, and obviously using the QOF is right, but is there not something about pulling the primary care academics together, giving them something of a kick up the backside—to put it basically—and saying, "There's money in this. There's money for your practices, there's money for the NHS, and you're always complaining about how underresourced you are. You can actually bring it in"? When I talk to the academics at UCLH, they understand that, but when I talk to their primary care colleagues, much less so. I am just wondering whether a pep talk is needed, a mixture of incentives and a bit of stick as well.

Lord O'Shaughnessy: Yes, quite possibly. In my experience, GPs are exquisitely sensitive to financial incentives.

Baroness Neuberger: Yes, because of the way it works.

Lord O'Shaughnessy: I think that could get you an awful long way. Again, there are lots of examples not of single surgeries but of clusters of surgeries or even quite big networks that are doing fantastic work all over the country, and often in the most remote places, which is also a factor, because we do not want this to just be about cities; this has to be people all across the country, rural as well as urban. The diversity of our country and the heterogeneity of our population is a huge strength if you are trying to recruit for trials that will sell drugs in China, India, South America, the Middle East, Africa and so on. It needs a bit of central attention to create those networks locally and, with a bit of attention, a l bit of carrot and maybe a bit of stick as well, we could deliver some really good infrastructure and numbers.

Baroness Neuberger: I agree. Thank you very much.

Q10 **Baroness Neville-Jones:** Do you think that the public health system in this country, which used to be really rather important, was revealed under Covid as having fallen down? Do you think it has any role and any future, and can be used and exploited in the area of clinical trials?

Lord O'Shaughnessy: That is a very good question. The fact is that we managed to recruit half a million people to the vaccine cohort. Vaccines and other things like smoking cessations and changes to pollution are probably the most successful public health interventions in the world. They demonstrate what is possible, but it is notable that they were done, in effect, outside the NHS. That is what I am trying to get to with the clinical trial accelerator networks. A lot of really interesting and entrepreneurial activity seems to happen in spite of the structures in the NHS and NIHR rather than because of them. They have to operate outside them. My hope—and it is a hope at this stage, because we cannot confidently expect it to happen—is that by understanding the right model for creating cohorts and platforms, and trying to do that through the NHS and using NIHR money, we will internalise that activity, which in itself will have a positive effect on the way we do research.

The risk, of course, is that we end up just putting everything through the NHS, and as you quite rightly point out it is only one part, albeit the biggest part, of our public health system. There is the credible argument that we should be doing it via other means, whether through the UK Health Security Agency or whatever. That is a perfectly reasonable criticism. This is probably quite an NHS and NIHR-focused report, and you could certainly envisage building these cohorts, as we have with things like Our Future Health and UK Biobank, which sit outside the NHS. The trouble is that they then have to interact with the NHS, and if the NHS does not feel a sense of ownership or co-production with these bodies, it does not always play that nicely, so we need to find a way of overcoming that problem. I do not know if I have cracked it.

Baroness Neville-Jones: It is worth looking at, is it not?

Lord O'Shaughnessy: Yes, 100%.

Q11 **Viscount Hanworth:** It seems to me that there is a conundrum that needs to be deconstructed. On the one hand, you have talked about removing bureaucratic sludge, which I think we all understand, but on the other hand there is the fact, which is recognised in your report, that some of the bureaucratic agencies lack sufficient manpower. Can we honestly expect politicians to be able to cope with this conundrum and to deconstruct it in a sensible way, or will they simply try to remove bureaucracy willy-nilly?

Lord O'Shaughnessy: That is a very fair point. Once you break it down into the component parts, the seeming paradox evaporates because, on the one hand, it is quite simply just getting approvals done quickly, which is a matter to some degree of slimming down the process or running elements of it in parallel rather than sequentially. You can make some reforms to it; it is not really so much a deregulatory approach as it is a smarter regulatory approach. However, it is about capacity. If you want to do more, unless you can find a way to dramatically improve your productivity you need more capacity, and the benefits, the return on investment for doing that, are pretty high. There is something to be said for having more capacity and more expertise back in our regulators in order to be able to do that, because our performance has worsened. It is a very tangible thing.

The second issue is what it actually feels like on the ground. If you are in the NHS or a teaching hospital, a university hospital, and you want to set up a trial, it is a nightmare. To bring it home, I get sent things on various channels including Twitter. A doctor tweeted about a patient who would, in theory, be eligible for a trial that this doctor was trying to set up, but the MHRA had been sitting on an amendment to the trial protocol for months. As a consequence, that patient has now passed the point at which they would be eligible for a trial because their prognosis is so poor. That is the reality of it; partly it is just about speed and being able to move quickly.

Another issue is the whole bureaucracy of doing trials. A lot of it is not that the bureaucracy does not need to be done but that it does not need to be done 17 times. It needs to be done once, and it needs to cover as many aspects of the trial as humanly possible, everything from costing for imaging through to exclusion and inclusion criteria. It is information governance, and you need to have a common approach to doing it—for one site to do it and for every other site to be made to accept the decision of that NHS trust.

Viscount Hanworth: Does that mean exalting the MHRA and making it a leaner and possibly more numerous organisation?

Lord O'Shaughnessy: It needs more people, and it needs more expertise back. It has lost a lot of people, good people, so it is about size, but it is also about quality. It is also about not having trial sites continually second-guessing decisions that have been made by other trial sites, which, let us face it, are their colleagues, their peer groups. They would accept their decisions in many other clinical situations, so why are they having to do their own due diligence on a trial that has already been approved by one site? That should not happen. It is completely unnecessary.

There is a certain degree of precaution around the very small tail-end risk of something going wrong, and foundation trust directors want to fulfil their duties and their obligations, which is why I suggested that the current indemnity schemes need to be expanded—so that you can obviate the need for boards to do their own due diligence because they are indemnified for that.

Viscount Hanworth: A universal indemnity?

Lord O'Shaughnessy: That tail-end risk is minuscule but it is there, and of course anybody would be thinking that they have to cover themselves by going through their own process. If you can indemnify that risk, you remove one credible reason for sites doing their own due diligence. I would hope that that would lift an awful lot of the burden of setting up trials.

Q12 **Lord Winston:** Can I ask you something slightly different that is quite an important issue? As someone who has done a number of clinical trials, I never got that interested in the actual trials as a process-driven process, but as a researcher I have always been excited about asking a basic question and trying to answer it. I wonder whether you feel that one of the problems is that clinical trials are not really as attractive to a lot of researchers as something for which you might get rather more brownie points and certainly tend to get a paper in a higher impact journal. Of course, there are exceptions, but I wonder if that is a problem in the way we are regarding them within the NHS and in academia.

***Lord O'Shaughnessy*:** I absolutely bow to your expertise on this, Lord Winston, but I think you are absolutely right. We hear that the high-credibility, high-esteem activity is to do earlier-phase, more academic

trials that are linked in some way to basic science happening in a university setting, and that commercial trials are not seen as important. As you rightly point out, given that those trials are usually working out effect sizes of medicines that we already know are effective to some as yet unsubstantiated degree, there is potentially a lack of novelty or excitement in doing large-scale trials. That is why we have tried to think about what the incentives would be for individuals, the credibility that would flow from it and the idea of having an academy or similar professional body specifically for clinical research, but also for repatriating some of the money that comes from trials into hospitals.

One thing we heard was, "I do a trial, but I don't get any benefit. My patients might get benefit, but my team, my unit, as a PI in my team, does not particularly get any benefit. We don't see any of the financial upside from it. If we want to do more of them and we want to appoint another clinical research nurse, I have to ask the board for it, and they'll say, 'You've not done the trials yet, so we're not going to fund it'".

You are laughing because this obviously resonates, but it is a typical story, which is completely nuts because that is money coming in but disappearing into a black hole at trust level. A lot of this is just about transparency and saying, "If there's this amount of money coming in, some of it is paying for costs. There's some margin on the top. Some of that gets distributed to the unit, to the R&D department, to the trust. Everyone benefits". I did a third-third-third rule of thumb, but at the very least every trust should have an approach to doing it that is explicit and that reports transparently. Hopefully, at the very least, that means that those PIs and their teams get some financial income coming to them and they can expand their activities. That in itself will be an exciting, dynamic experience rather than, as you say, perhaps a slightly painful one with an opportunity cost that involves doing less clinical work or doing less research that their peers would value, it being rather a status-driven institution, as you know.

The Chair: Thank you very much for giving evidence to us today. It has been a really interesting session. As you see, the committee has been very engaged with this. A transcript has been taken and it will be sent to you within the next few days for any minor corrections you want to make. If there is anything you would like to flag up to us as a committee that you think would be of interest to us or that we might want to look at, we would be very pleased to hear from you. Thank you.