HOUSE OF LORDS

Preterm Birth Committee

Corrected oral evidence: Preterm birth

Monday 19 February 2024

3.15 pm

Watch the meeting

Members present: Lord Patel (The Chair); Viscount Colville of Culross; Baroness Cumberlege; Lord Hampton; Baroness Hughes of Stretford; Baroness Owen of Alderley Edge; Baroness Seccombe; Baroness Thornhill; Lord Winston; Baroness Wyld.

Evidence Session No. 3 Heard in Public Questions 30 - 49

Witnesses

I: Dr Catherine Aiken, Associate Professor and Honorary Consultant in Fetal and Maternal Medicine, Cambridge University Hospitals; Professor Asma Khalil, Professor of Obstetrics and Maternal Fetal Medicine, St George's Hospital, University of London.

Examination of witnesses

Dr Catherine Aiken and Professor Asma Khalil.

Q30 **The Chair:** Thank you, both of you, for taking time out of your busy schedules to help us with our inquiry. We are now broadcasting on the parliamentary channel and the whole session will be on the record, so it would be helpful if you could introduce yourselves and give your designation.

Dr Catherine Aiken: I am an associate professor and honorary consultant in maternal and fetal medicine at the University of Cambridge.

Professor Asma Khalil: I am a professor of obstetrics and maternal fetal medicine. I work at St George's Hospital in London and at Liverpool Women's Hospital, and I have different hats. I am a vice-president of the Royal College of Obstetricians and Gynaecologists.

Q31 **The Chair:** Thank you. You are both softly spoken. Unfortunately, quite a few of us, including me, have ossified ears, so please shout as loudly as you can into the loudspeaker—we will not mind—so that we can all hear you and, most importantly, get you on record.

Let me start with the first question, which is quite clinical. How does one

identify women at risk of preterm labour and, therefore, preterm birth? What are the criteria? That is not about primary prevention, but about secondary prevention. What treatments are available? How evidence-based are those treatments and where is there a lack of evidence? Is that evidence used in national guidelines, and is it followed? That is a long question, but break it down into bits.

Dr Catherine Aiken: The first thing you touched on was how secondary screening for preterm birth is currently conducted in the NHS. It is done by universal risk factor-based screening, which every woman gets when she books a pregnancy. That is undertaken by a community midwife. There is a long list of preterm birth-related risk factors that every woman should go through. Any woman who screens as being at intermediate or high risk from those lists of questions should be referred to a specialist preterm birth clinic.

Among the 110 maternity units that deliver more than one preterm birth a month in the UK, there are probably 80 to 85 preterm birth specialist clinics, which has been a rapid and welcome increase over the last few years. Those preterm birth clinics have the remit to take that risk factor-based screening and to perform specialist screenings—cervical length scanning and sometimes other tests such as quantitative fetal fibronectin—to sub-stratify those women further with regard to their risk, to treat modifiable risk factors, and to apply treatments for preterm birth where applicable.

Q32 **The Chair:** The identification of women at risk is quite important. I presume that is done through proper history taking. History taking is done by a variety of people of different grades and professions. Are the guidelines related to history taking well applied across the country?

Dr Catherine Aiken: The essential first step, which is the risk factor-based screening, needs to be taken at grassroots level for every woman who comes for pregnancy booking. It is done, essentially, by the community midwife. A long list of risk factors are asked about in a national standardised screening tool. The detailed history taking should be done within the remit of a specialist preterm birth clinic, which is when you really get into the weeds of exactly what has happened to that woman in previous pregnancies and exactly what the cervix looks like. Teasing out the history and figuring out the appropriate treatment on that second round of screening is a very specialist skill indeed.

Professor Asma Khalil: The challenge with this approach is the fact that the majority of women who have preterm births do not necessarily have these risk factors. Having what is almost a checklist approach is not sophisticated enough to provide an individualised risk assessment. If a woman had a previous preterm birth, for example, that is one of the strongest risk factors. If you have had one previous preterm birth, your chance of having another is 15% to 30%. If you have had two previous preterm births, your chance of having another is up to 60%. If you have had one previous term pregnancy, your risk is less.

So if I am the midwife, I just have a checklist, and I am taking the history from the patient, I might say, "She's had one previous preterm birth, so she's high risk", but I would not be taking into account the fact that she has had four previous term deliveries. What would be ideal is a prediction model that takes into account the presence as well as the absence of the risk factors. These risk factors do not all have the same strength of association with the outcome of a preterm birth. Some may be stronger than others. Despite the fact that that is the current practice and is easy to implement, it is not the best approach to identifying women who have a high chance of preterm birth.

Q33 **The Chair:** What is the treatment for those who are identified as possibly at risk?

Professor Asma Khalil: A number of interventions have been studied. Some studies have shown that they are effective. Other studies have shown that they are not. The NICE guideline on preterm births that was published in 2015 and updated in 2022 made some recommendations regarding some of these interventions. If, for example, a woman has had a previous preterm birth and has a short cervix, measured between 16 and 24 weeks and with a cut-off at 25 millimetres, they recommended offering vaginal progesterone as a pessary or a cerclage, which involves putting a stitch around the cervix. If a woman has a short cervix, we know that that is a strong risk factor for preterm birth and we can offer vaginal progesterone. If the woman has a short cervix and a history of trauma to the cervix—for example, a cone biopsy or surgery on the cervix—we can offer cervical cerclage.

So there are a number of interventions, and studies have looked at those. Those supported by evidence have been reviewed as part of the NICE guidelines, and recommendations have been made.

The Chair: How effective are these treatments? Can you give numbers?

Professor Asma Khalil: A number of randomised controlled trials and meta-analyses or systematic reviews have shown that vaginal progesterone could reduce by up to 40% preterm births that occur prior to 34 weeks in women with a short cervix

Dr Catherine Aiken: The key difficulty here is that we have a range of interventions, all of which have some evidence that they are at least partially effective in the right group of women. The difficulty is disentangling the evidence to figure out exactly which woman should get which intervention. This is really nicely summarised in the NHS England's *Saving Babies' Lives* document, which says: "The evidence base cannot determine precisely in which women, and in what circumstances, each intervention will be most effective". That is NHS England's stance on it.

When you get through the weeds of the evidence, that is probably where we are in this field. We have some evidence that the things we offer are at least partially effective and will be effective for some women, but we

do not have really good, systematic evidence to say, "If I give this woman here in front of me this treatment, she will do well".

Q34 **The Chair:** Moving now to the identification of women at risk and what could be done, if mothers come in in preterm labour, what evidence-based treatments are there to stop the preterm labour or prolong the pregnancy?

Dr Catherine Aiken: If someone is in preterm labour, we focus mainly on optimisation to mitigate the risk of preterm birth. Critical things include preparing the baby for a preterm delivery. That will involve giving steroid injections to the mother which mature the baby's lungs and help to prevent gut complications for the baby. We also give the mother an infusion of magnesium, which is very important to protect the baby's brain from the consequences of the preterm birth. There are other important things such as giving antibiotic therapy promptly, because infection is a major source of morbidity for tiny preterm babies who are born.

Making sure that the woman is in the right place for birth is an absolutely critical intervention. We know that, for babies who are born before 27 weeks, their survival is reduced by at least 25% if they are born outside of a suitable level 3 tertiary neonatal unit, for example.

If the woman is in active preterm labour, all of those things need to be considered, as well as whether it is safe to transfer and whether we can prolong the pregnancy. Sometimes drugs to prevent uterine contractions are also used. Nifedipine is a key example of that. Those are, again, partially effective, but they may buy crucial time for the interventions that will improve the baby's outcome to be applied.

Q35 **The Chair:** What treatments are available during the obstetric period that would improve the outcome for the baby?

Dr Catherine Aiken: The primary thing that improves the outcome for the baby is usually prolonging gestation, particularly at the very early stages.

The Chair: How successful are we at doing that?

Dr Catherine Aiken: We are moderately successful. One intervention that Professor Khalil mentioned is giving progesterone, which is the key hormone that is very high in women in late pregnancy. There is evidence that giving more of that vaginally prolongs pregnancies by a matter of weeks. The median duration in various trials—exactly how effective it is—differs depending on when it is first applied.

The mechanism of action of the stitch that is put around the cervix—the cerclage—is, honestly, not quite known, but it is generally considered to be a mechanically strengthening factor for the cervix, which has a tendency to open.

There is also pessary treatment, which is offered in many preterm birth clinics and, again, attempts to support the neck of the womb and protect against preterm birth that way.

Q36 **The Chair:** Are the guidelines that you mentioned up to date and followed universally, or do they lead to variation in care?

Professor Asma Khalil: The problem with the guidelines is that they often lag behind the evidence, such as from a randomised controlled trial. Guidelines that are published are due to be updated, let us say, every three to five years. Therefore, if the guideline is published this year and a randomised controlled trial or study is published next year, the guideline will not be updated until it is due to be.

There may occasionally be a case for updating a particular question or area in the guideline—for example, if evidence becomes available that we should update the recommendation—but the truth is that guidelines tend to lag behind the evidence. Therefore, we might look at whether to increase the frequency of reviewing guidelines that need to be updated, or whether there is a mechanism by which a body is responsible for saying, "There's emerging evidence that addresses some of the research questions in these guidelines or could impact or change some of the recommendations in them", which should trigger a review of the guidelines.

The NICE guideline on twin and multiple pregnancy, for example, was updated and published in September 2019. I was a reviewer of this guideline, and we looked at the screening and prevention of preterm births in twin and multiple pregnancy. At that time, we did not make a recommendation about screening or prevention. However, because some evidence has recently been published looking at this particular area, there is a draft consultation on the NICE guideline that is particularly pertinent to the screening and prevention of preterm births in twin and multiple pregnancy. In fact, there are significant changes in the recommendation. This update to the NICE guideline recommends screening cervical length assessment in twin and multiple pregnancy and, if the cervical length is short, offering vaginal progesterone.

The Chair: Guidelines are falling behind advances, for whatever reason, and you are saying that that results in variation in care. Dr Aiken, do you have anything to add?

Dr Catherine Aiken: It is entirely reasonable to say that the guidelines need to be updated more frequently. Certainly, the guideline in this particular area is NICE guideline 25, which was last updated in June 2022. There is also NHS England's *Saving Babies' Lives* guidance, which was last updated in July 2023. The Royal College of Obstetricians and Gynaecologists also has a specific guideline regarding exactly how you do cervical cerclage. The British Association of Perinatal Medicine guidelines also have a toolkit on the questions that you are asking about optimisation of the preterm birth.

Between those overlapping sets of guidelines, there is broad concordance on what should be done. There are also areas of difference. They have all been updated at different times, which possibly accounts for some of that difference.

The Chair: Would it be better if we had one guideline that is followed rather than multiple ones?

Dr Catherine Aiken: That would be a step towards reducing variation.

Q37 **Viscount Colville of Culross:** I want to pick up on what you said, Professor Khalil, about us needing to look at the absence of risk as well. Does that mean that we should be looking at a population-wide screening for things such as length of cervix or fibronectin? The screening reviews have said not to do it population-wide, but if the absence of risk is so important, does that not lean towards doing population-wide screening?

Professor Asma Khalil: In the UK, we have a national screening committee that looks at whether—

The Chair: We are talking now about primary prevention, not secondary prevention.

Professor Asma Khalil: Was your question about primary or secondary? If you are doing it routinely in the population, that is primary.

The Chair: The question is about screening.

Professor Asma Khalil: If what you envisage is that we should screen all pregnant women for preterm birth and offer those identified as high risk an intervention, that would usually be the remit of the National Screening Committee. The National Screening Committee looked at whether we should routinely screen for preterm birth—for example, using cervical length—and its conclusion was that it is not recommended.

When it looks at the evidence, it does not look at just whether this marker or this parameter is a good screening test. It looks also at whether you have an intervention, how effective it is, and the health economics, for example. There are various aspects that it would consider before recommending offering population screening. At the moment, it is not recommended.

Q38 **Baroness Hughes of Stretford:** I would like you to clarify something you said at the outset, Dr Aiken. I am interested in the point you made about risk factor-based screening, which, for the most part, is the first opportunity a community midwife will have to try to identify women and babies who may be at risk.

How confident are you that in all parts of the country that particular process is done so that women at risk will almost certainly be identified? You said that they would go into a higher-level and more sensitive screening process. Are you confident that all the people who should go on into some more sensitive screening process get into it? It is important that the first gate a woman gets to is working equally effectively in all

parts of the country. Do you have a view on whether that is the case?

Dr Catherine Aiken: It is almost certainly not done equally in all parts of the country, and it cannot be reasonable to assume that it would be, because it is done by an enormous range of people. Community midwives are hard-pressed and hard-pushed; they have enormous remits in their roles. It cannot be that every community midwife is applying this tool equally to the same standard and is hearing the risk factors in the same way. Even the same person applying the same tool cannot always come up with the same result.

That is why the tool has to be as simple and as broad brush as possible. As Professor Khalil says, it is a blunt instrument. It aims to cast the net as widely as possible. It is channelling women in for the consideration of high-level care. Certainly not all women who get referred to specialist preterm birth clinics carry on down a specialist preterm birth pathway.

Q39 **Baroness Thornhill:** Thanks to your persistent questioning, Chair, we have segued very nicely into my question. I wanted to ask, quite neutrally, whether the witnesses think there is inconsistency in practice, but you have been very clear that there absolutely is. Put very simply, what are the main barriers to gaining that consistency? How do we achieve it?

Dr Catherine Aiken: We certainly need better evidence on what the best thing to do is. If we take the example of preterm birth clinics offering a first-line therapy for women with short cervical length, at the moment 20% are offering progesterone as the first line, 60% cerclage, and 20% combined therapy. That exemplifies the variation in practice across the country.

There are opportunities to reduce variation through a more networked approach. The neonatal teams are way ahead of us in those terms. They have been maturing neonatal network practice across the country for over 20 years. There are now 17 maternal medicine networks to cover all areas of the UK, but they have been in place for only the last few years. They need more investment and more funding, and they need strengthening in order to make sure that women are diverted to the right services more consistently and with less variation regionally in the UK.

Q40 **The Chair:** You did not mention treatment using antenatal steroids. Is there variation in giving those?

Dr Catherine Aiken: The best data that we have on that suggests that over 90% of women in whom antenatal steroids were indicated received them. That data is from 2022. What is difficult about that is that there is a narrow window of optimal time to give antenatal steroids, which is between two and seven days prior to the preterm birth occurring. We know that antenatal steroids are not a benign intervention, and that their overuse puts children who do not deliver preterm at a slightly increased risk of neurodevelopmental difficulties.

We know that there are a large number of people who got antenatal steroids when they probably did not need them or got them outside the optimal two to seven-day window prior to preterm birth. The overall statistic that over 90% of women who should have got them did get them hides a lot of variation in practice, where the steroid use was not optimal or was unnecessary in a large group of other women.

Professor Asma Khalil: Of course we should ensure that there is training, that protocols are consistent and that guidelines are followed, but it is a bit more complex than that. The incidence of preterm births varies across the country, for example, for a number of reasons. Is it because we may not be applying screening and prevention, or is it also because of the population and its demographics? In the north of England, where the population is more socioeconomically deprived compared to the south—we know that socioeconomic deprivation is a risk factor for preterm births—there is a higher incidence of preterm births.

Also, across hospitals or maternity units in the country, there is variation in the incidence of preterm births, which could be partially explained by the nature of the services that each maternity unit provides. If I work in a tertiary-level hospital where we have tertiary-level neonatal facilities, I will by definition have a higher incidence of preterm births compared to smaller hospitals, because women who go on to have spontaneous preterm births will be transferred and deliver in this hospital, as well as those who need an iatrogenic or medically indicated preterm birth. Someone with pre-eclampsia or fetal growth restriction will be transferred to deliver in this unit. That partially contributes to the variation in the incidence of preterm births.

Probably the best figures that you get on the outcomes of these premature babies are from the National Neonatal Audit Programme. The latest data is from 2022. It looked at various outcomes, including the mortality rate. The mortality rate of babies born very prematurely—before 28 weeks—was about 6%, but there is variation across the country; it is between as low as 4% and as high as 8%. That is where we need to focus. It is not easy to change your demographics. We cannot change the nature of the services as maternity units. This is how the system is structured. We really should aspire to the outcomes for these babies being the same wherever the women give birth.

Baroness Thornhill: Thinking about it as a process, it is interesting that you said that the guidelines lag behind the evidence. The following of the guidelines and them being translated into practice provides these massive variations. What is the real barrier? Who is really holding the ring for all this? You have mentioned a lot of names and acronyms for different things, but who is top trumps? How do we get that level of consistency?

Professor Asma Khalil: If I were brave enough, I would say that the Government have a duty to deliver consistent care and consistent outcomes across the country. If that means that we need to invest resources in ensuring the implementation of these guidelines, with

enough resources and training for all healthcare professionals, and a sufficient workforce, that is what we should do.

Dr Catherine Aiken: One of the problems we have is that there are so many pressures on maternity services from different sides, and maternity services are under a great deal of pressure already at baseline. The number of agencies with different mandates and approaches to the same problem is generating part of the problem.

Q41 **Baroness Cumberlege:** When we were doing the national maternity review, which was called *Better Births*, we included the vision to implement a continuity of care model. For the committee, it is the same person, usually the midwife, who will be with the mother through the pregnancy, through the birth, and postnatally. What really convinced us was that, when we looked at the research, it demonstrated that women who received midwife-led continuity of care were 24% less likely to experience preterm birth. We felt that that was a goal that was worth working towards. Do you agree that it is, or is this so difficult that we should not even pursue it?

Professor Asma Khalil: I would support it, and I am aware of this evidence. I am aware also of the recommendation on continuity of care in the *Better Births* document, which you led on. The challenge is how to deliver continuity of care safely when we have a shortage of staff and midwives able to provide safe care to our pregnant women even without continuity of care. You need more midwives to be able to provide continuity of care. It is better for the patient, and the evidence supports continuity of care. The challenge is how to deliver it when you do not have a sufficient workforce to do so.

The Chair: Is there any evidence that continuity of care delivered by a midwife—of course, the point you make about a shortage of staff is very important—will deliver a reduction in preterm births? You either have the evidence or you do not.

Professor Asma Khalil: There is observational evidence associated with a reduction in preterm births. When NICE reviews the evidence, it requires higher-quality, level 1 evidence from a randomised controlled trial to make a recommendation. As I mentioned, when NICE looks at the evidence, it is not just about the evidence to support the intervention, but about other aspects of the implementation such as its cost effectiveness. There are other aspects before you make a recommendation for intervention.

Dr Catherine Aiken: I agree with Professor Khalil's stance on this. Continuity of care is a wonderful aspirational model. The practicalities of it in current maternity services are an entirely different matter.

Q42 **Viscount Colville of Culross:** How effective are we at identifying women at risk of giving birth preterm? We have already talked about screening and the problems with secondary and primary screening in trying to identify this. However, we have also been told to look at health

records, which are not sufficiently co-ordinated or whose impact midwives are not trained enough to be able to understand. The example we have been given is that, for instance, if a woman had previously had surgery on her cervix, the midwife might not have knowledge of that impact. Is that a concern for you?

Dr Catherine Aiken: It comes back to the screening tool being only as good as the person who is implementing it and the information that they have available to them. It is crucial that everyone who screens is trained to the standard that the screening tool requires. Where health records really come into this is the availability of health records nationally. The fact that preterm birth may have happened in a different hospital and the precise details of what happened during that time might be crucial. Cervical surgery may have been carried out somewhere else, and a preterm birth specialist really needs to know what length of cervix was removed and the exact procedure done. We do not have a co-ordinated enough system for those records always to be available at the right time, and in a sometimes very short timescale, for that information to be used in the treatment of the person in front of you at that time.

Professor Asma Khalil: Ideally, you want almost a two-step screening. The pregnant woman will meet the midwife at the booking visit, they will have almost a standard questionnaire or checklist, which is nowadays often done electronically, and one of the questions might be, "Have you had surgery on the cervix, or the neck of the womb?" If you tick the "yes" box, that should automatically trigger a referral to a preterm birth clinic, where this patient would see a specialist who had a detailed discussion about the type of the surgery and, if it involved removing part of the neck of the womb, or the cervix, how much. If it was done in a different hospital, they would contact the other hospital and get the records.

You want to ascertain whether this woman is at a particularly high risk of preterm birth and whether that level of risk might require intervention. The NICE guideline recommends, for example, that if a woman has had a previous cervical trauma, such as excision of part of the cervix, cone biopsy or LLETZ, and has a short cervix, she should be offered a cervical cerclage or stitch. That level of detailed management is difficult to expect a midwife to do. They may not have the relevant experience or knowledge, or the time, to do that. That is when it would be extremely beneficial for the preterm birth clinics to go through that level of detail, make a management plan and follow up on these women.

Viscount Colville of Culross: Dr Aiken, you talked about the lack of co-ordination sometimes between different hospitals and throughout the health service when it came to health records. Why is that? I thought that the health service had one of the greatest databases in the country.

Dr Catherine Aiken: The health service has an awful lot of health records and so on, but as an individual clinician requesting information from another service, that is done piecemeal. That is a request where there are not necessarily established pathways. I may email Professor Khalil and get an email back tomorrow with the relevant information.

Equally, in other cases I will ask for information and not get it. It is not a consistent system, and there are not ways of data sharing as easily and simply as there should be for maximally effective care.

Q43 **Viscount Colville of Culross:** That is very important. We have also heard about the Tommy's digital tool, QUiPP, and how supportive it is for reducing still and preterm births. However, there has been a study that shows that 90% of women receive appropriate treatment, whether they use this tool or not. How useful is the QUiPP app and should it be rolled out nationwide?

Dr Catherine Aiken: There is evidence from the studies they have done that it is an effective tool that can support preterm birth decision-making.

Viscount Colville of Culross: Does that mean that it should be rolled out nationwide?

Dr Catherine Aiken: That is a step further, and it requires health economic analysis and things that I do not have to hand. I know only of the evidence they have produced on the efficacy of their tool.

The Chair: On the basis of evidence-based guidance, has it been tested properly to recommend that it should be adopted nationally?

Dr Catherine Aiken: I do not know of an economic analysis that would support that. Perhaps Professor Khalil does.

Professor Asma Khalil: The value of the QUiPP app is mainly in women who are presenting with threatened preterm births—for example, coming with abdominal pain or some tightening. The truth is that the majority of these women do not go on to preterm birth. Therefore, the value is probably in triaging these women—"Which of them will actually go on to preterm birth?"—and then considering all the aspects or components of how to optimise the care of these premature babies. That may involve transferring the woman to a hospital with neonatal units with adequate facilities, or giving antenatal steroids, magnesium sulphate or antibiotics. For the majority who will not, you do not need all these interventions, some of which could be harmful.

Fibronectin, which is a component of the app, is a good negative test. If there is a negative, it means that it is unlikely that this woman will go on to preterm birth, but it is not necessarily a very good positive test, because the majority of women who have a positive fibronectin do not go on to preterm birth.

To your question, whether we have enough evidence to recommend its routine implementation depends on how beneficial you find it in your clinical pathway or your management algorithm. It may be beneficial if I work in a small DGH where I think a woman might be at risk of preterm labour and I have to transfer her because I do not have the facilities. If I work in a hospital with a tertiary-level neonatal unit, I do not necessarily have the benefit of having to transfer this patient, because I am the unit that she will be transferred to.

Another aspect is how much clinicians trust the result. In women presenting with threatened preterm birth and whose pregnancy is less than 30 weeks, for example, the NICE guideline is to admit and to do this optimisation because of the early gestation and the implications for a baby born at this premature or preterm gestation. Saying yes or no is a very simple answer. It is a bit more complicated than that.

Viscount Colville of Culross: Professor Khalil, you are a very experienced professional. Do you use the QUiPP app?

Professor Asma Khalil: I do not use it in my hospital.

Viscount Colville of Culross: Why not?

Professor Asma Khalil: It is more that we did not feel there was a need, or maybe because of resources. At St George's Hospital, we do not use it at the moment.

Q44 **Baroness Owen of Alderley Edge:** You spoke earlier about the need for predictive modelling. I was going to touch on the need for the QUiPP app as well. If the QUiPP app is not appropriate, is it that a data model has not yet been created that is picking this up? What kind of predictive model do you envisage being needed?

Professor Asma Khalil: There have been studies that attempted to combine various risk factors. They use statistical modelling, called multivariate logistic regression, where they combine the presence as well as the absence of some of those risk factors and develop an individualised risk for each woman. Some of them combine the cervical length assessment, as well as maybe biochemical markers, to try to improve the predictive accuracy. These prediction models are not perfect—they do not give you 95% accuracy, for example—but they are better than what we are currently offering, which is just a checklist approach.

The other question for the national screening committee is whether there is an effective intervention for women who are identified as high risk. That is often a struggle when it comes to looking at any screening marker.

Baroness Owen of Alderley Edge: We spoke about the scenario in which Dr Aiken would write to Professor Khalil. Why is it not all attached to your NHS number? I carry an NHS app around with me and I have my NHS number. Why is everything that I have ever been treated with not all on that list so that I can show it to my doctor, who can then scan a QR code and it would be on their computer?

Dr Catherine Aiken: That would be great.

Professor Asma Khalil: It is something that you could recommend or encourage the system to implement. We did it in Covid. It is really challenging to share digital records. The Government aspire to having an app or a QR code, so that if a patient has booked in Cambridge but

happens to be in London and comes to my hospital, I will be able to have access to all their records. Unfortunately, that is not happening at the moment. We would like to achieve that. It seems to be challenging, so far.

The Chair: Dr Aiken, you nodded. Are you in agreement?

Dr Catherine Aiken: Yes. Our hospitals use all types of systems. Sometimes they have different systems for their maternity records and for their regular records, and sometimes those do not even speak to each other. Their primary care records will be somewhere else entirely, the data controller for which is the general practitioner. That needs to be addressed at national level.

Q45 **The Chair:** I agree. It has come up before in other inquiries that England needs to establish a national number like Scotland, which has its CHI number.

In your answers to Viscount Colville and Baroness Hughes about different people seeing women at risk or women who are going to have babies, you said that there is a lack of co-ordination. Should the networks that exist not be made responsible for making sure that all the professionals who engage with women at risk of preterm labour work in a co-ordinated way, including history taking?

Dr Catherine Aiken: Yes, absolutely. There is always a role for the networks in education. The new maternal medicine networks that have been set up are very active in running educational components of what they do. Ultimately, some issues need a very experienced specialist to work through the history and to appreciate the detailed differences between one woman's experience and another's. We need as much training as possible on risk factor-based screening.

The Chair: Is there a way of making sure that all the networks work in a co-ordinated way and do not each have a different way of working?

Dr Catherine Aiken: There is a national specification for networks and a broad set of criteria that they need to meet. There is a dichotomy between nationally standardising everything and making it work in local pathways as they are. There are some extremely good local implementation toolkits. The PERIPrem toolkit in the south-west and the west, for example, is a good bridge between what exists nationally as top-level guidance and implementation of services into what is present in a local network. There is a gap between the national ambition and the care that can be delivered on the ground in different places, depending on how things intersect with existing services.

Q46 **Lord Winston:** You mentioned national ambition. Just 30 years ago plus a month, Peter Radetsky from California or Texas—I forget which—published an article in *Science*, the world's leading scientific journal, on preterm birth and its mechanisms. He looked at fibronectin, gap junctions in the muscle, and a whole range of other mechanisms that are still puzzling us. He said in that article that preterm birth was a national

disgrace at the time and that things needed to improve. How far have we improved in understanding preterm birth?

Dr Catherine Aiken: The elephant in the room here is that we know very little about the mechanisms even of normal birth that occurs at the appropriate gestation, at term. The science lags far behind where it sits in many other fields. The fact that we do not know in detail the molecular pathway that leads to the onset of normal labour and delivery is way below the standard that you would expect in most fields of medicine.

The real problem when we play around the edges of fibronectin levels and so on is that we do not know the basic molecular pathways, which gives us very few targets to intervene on. You can identify the key targets where you will be most effective only if you know what is going on in the system as a whole. That is one of the key things here. It is exemplified by the fact that only two new drugs have been approved globally and licensed anywhere for pregnancy-specific conditions in the last 30 years since the article in *Science* that you refer to was written.

Lord Winston: One is Makena, which has just been removed.

Dr Catherine Aiken: Makena has been removed from the market, so we are left with atosiban, which does not work.

Lord Winston: Is it not axiomatic in medical research that you do not give a treatment before you have made a diagnosis? That is essentially the problem. We are dealing with a mechanism that we do not understand. Would you agree with that?

Dr Catherine Aiken: That is a fundamental part of what is going on here. We have some things that we know are partially effective. We do not know exactly how they work. A cerclage works, we believe, by somehow strengthening the neck of the womb. We apply those treatments because there is some evidence of efficacy, but you are right that, without laying the pathway bare and understanding what is going on, it is very hard to know where best to intervene or where we go from here.

Q47 **Lord Winston:** I would be very grateful, then, if both of you could explain to the committee generally why we still regard the randomised controlled trial, preferably blinded, as the gold standard for clinical research. What is the difficulty of doing it in this situation with preterm birth? It is not an aggressive question.

The Chair: Feel free to give your own view.

Dr Catherine Aiken: It is a very good question.

Lord Winston: It is an important philosophical point.

Professor Asma Khalil: I agree with you that we still do not fully understand all the mechanisms of preterm birth, but I am a bit more positive. We have made some progress over the last 30 years.

Lord Winston: You have published lots of cohort studies, which are very useful. I have looked at them and am grateful for them, but it does not get down to mechanisms.

Professor Asma Khalil: You are absolutely right, but, back to your supplementary question on whether we need level 1 double-blinded randomised controlled trials for everything, I do not think so. I do not think that is necessary. That can sometimes hinder our progress in managing some diseases. There are many conditions where designing high-quality double-blinded randomised controlled trials is extremely difficult, if not impossible.

Particularly in my field, which is fetal medicine, randomising women for placebo or no intervention is not acceptable for patients. Therefore, for conditions where it is difficult or maybe not feasible to do randomised controlled trials, the NIHR asks for feasibility studies first. It asks researchers to do some of the work, including qualitative work, with the patients and the clinicians: is it feasible or acceptable for the patient to be randomised?

One arm is no intervention. If I was a patient with an increased chance of preterm birth and you tried to tell me, "You might be randomised for no intervention", when the other arm is a cerclage, for which there is at least some evidence, even if not high-quality, in support, I might not accept the risk of being randomised to nothing. I would want the intervention, even if it is not supported by level 1 evidence. That makes doing randomised controlled trials in this area very challenging.

Lord Winston: Is that not why clinical trials of a sophisticated type are needed? Women who are in premature labour with a baby are desperate, frightened and anxious. We know that there are claims that the ring pessary around the cervix improves things, but they are unsubstantiated. Of course, the psychological effect of knowing that they have had this treatment may be quite relevant, but when you look at more controlled trials, it does not show any advantage at all.

Professor Asma Khalil: You are absolutely right. Particularly for the pessary, the evidence is very controversial, including from randomised controlled trials. There are some that showed that it is beneficial, and others, including those that are conducted in the UK, that showed no effect. Therefore, most of the guidelines that looked at the evidence did not recommend the routine implementation of a pessary in women with increased risk of preterm birth. We still need to aspire to and demand having the level 1 evidence to back up our recommendations, but that can be difficult and challenging.

Q48 **Lord Winston:** What would you recommend this committee to do about claims for research? What should we be advising Government with regard to trying to improve academic activity in this area?

Dr Catherine Aiken: I would be looking at funding more basic science research in this area and asking, "What are the pathways?" Preterm birth

is undoubtedly the final common pathway of a number of pathologies. We know that there is a strong component of placental dysfunction that feeds into preterm birth, for example. Those are targetable areas that we can look at, but the idea of starting at the bottom of the pathway, when the preterm birth is imminent or occurring, is very challenging. It is a tiny portion of the entire paradigm of preterm birth, which begins pre-conception and ends with the long-term health of the child. We should not focus all the intervention in that small gap. There should be a mandate from this committee to fund preterm birth research that is much more wide-ranging and longitudinal in its scope.

Professor Asma Khalil: I would take this opportunity to highlight a group I am particularly interested in, which is twin and multiple pregnancy. This group is particularly at an increased risk of preterm birth. Some 20% of babies born premature come from twin or multiple pregnancy. The chance of cerebral palsy is about six to seven times higher in twins compared to singletons. The problem is that, if you look at the randomised control trials that focused on preterm birth, a fraction of them focus on twin and multiple pregnancy.

What is not unique to preterm birth but applies to all conditions is that most trials exclude twin and multiple pregnancies up front. Where they include them, the numbers are so small that it is difficult to extrapolate the evidence in this particularly high-risk group. I would use this opportunity to say that this is a high-risk group, particularly for preterm birth, and that we need better quality evidence of interventions in twin and multiple pregnancies to reduce the risk of preterm birth.

Q49 **The Chair:** You mentioned twins. Professor Khalil, you have a special interest in them. You just mentioned the figures that multiple pregnancies are higher risk for preterm labour. Is it the same for monozygotic as dizygotic? I know the difficulty of identifying antenatally whether they are dizygotic or monozygotic, but does IVF contribute to this, and by how much?

Professor Asma Khalil: IVF does contribute to the increase in number of twin and multiple pregnancies. There is a difference in the risk or the chance of preterm birth. During the pregnancy, we do not always know whether they are monozygotic or dizygotic. We manage them based on ultrasound scans, which tell us whether they are monochorionic or dichorionic, so whether they share one placenta or have two separate placentas. That is how we manage them. We do not even routinely test them at birth to see whether they are identical.

We know that preterm birth is twice as high in monochorionic compared to dichorionic twins. There are a number of reasons why. To some extent at least, we know some of the mechanisms for why there is an increased risk of preterm birth in monochorionic compared to dichorionic twins. They tend to have similar risk factors, such as smoking, socioeconomic deprivation and short cervix, to preterm birth. It is just the fact that, over the years, people have tended to extrapolate the evidence from singletons to twins, which has proven to be wrong on several occasions.

Interventions that work in singletons do not necessarily work in twins. Therefore, I would use this opportunity to call for twin-specific evidence for any intervention.

The Chair: Thank you very much. I know that we have not exhausted questioning you and learning about this, but I am afraid that the time is up. Thank you for coming today. We appreciate it very much. Thank you for all your help today in answering the questions. Of course, you can stay for the next session, if you wish, but you might have better things to do in life than listen to us. Thank you.