Interviews

Maggie Shepherd discusses her research in the pertinent field of monogenic diabetes, and its common misdiagnosis. Pia Leete sits down to highlight the importance of pancreatic immunopathology in diabetes research, and the work being done to improve global equity.

Maggie Shepherd

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Q1 What inspired you to pursue a career in nursing, and to start research?

I was about 14 or 15 when I first decided that I wanted to be a nurse. I started volunteering at my local hospital, and also volunteered at the Red Cross. Both of these experiences convinced me that yes, this was the role for me. So, I started nursing at 18 at King's College Hospital in London, UK, and have been nursing in the National Health Service (NHS) ever since.

In terms of starting research, that was a bit more of a chance encounter, really. I had been working as a diabetes specialist nurse in London for 8 years, and then was planning a move down to Devon, UK. So, I sent my curriculum vitae round to the diabetes teams around Exeter. It just happened that Professor Andrew Hattersley, who leads the team in monogenic diabetes, and who had started 6 months prior, was looking for a diabetes research nurse, initially collecting samples from individuals with an autosomal dominant family history of diabetes; so, that is how my research career first started. I subsequently went on to do a PhD to gain an understanding of patients' and professionals' attitudes to genetic testing in diabetes; and postdoctoral awards investigating the impact of a genetic diagnosis and treatment change from insulin to tablets, and also the impact of a diagnosis of neonatal diabetes. My later work has focused on correct identification of monogenic diabetes, and translating these research findings into clinical care.

Q2 You lead the National Genetic Diabetes Nurse Project. How does this project help raise awareness on monogenic diabetes, and support patients and their families?

I started the National Genetic Diabetes Nurse Project in 2002, because I was very aware that we had been finding genes that caused monogenic diabetes, which is diabetes caused by change in a single gene. We were providing this information to clinicians and families, but at that point in time, there was very little understanding of monogenic diabetes, although we were publishing papers and presenting at conferences. As I had a background as a

diabetes specialist nurse, I thought that there could be a better way of effectively translating these research findings into clinical care. So, I approached the Department of Health to try and gain funding to train diabetes specialist nurses across the UK in genetic forms of diabetes. That was a model that we carried on until 2021, with regional genetic diabetes nurses, who worked half a day per week on monogenic diabetes, and continued to work as a diabetes specialist nurse for the rest of their time. We used a model of training the trainers: the genetic diabetes nurses attended training three times a year in monogenic diabetes. Then we would provide PowerPoint presentations for them to give talks to other healthcare professionals about monogenic diabetes across their regions to raise awareness, with the idea of trying to identify more, and to make sure patients meeting the criteria had genetic testing. For those with a positive result, they were then changed to the optimal treatment, and we made sure that their family members had appropriate follow-up. However, there were still areas of the UK without a genetic diabetes nurse.

In 2021, I contacted the NHS England diabetes programme, and aimed to work with them to increase awareness of monogenic diabetes even more. They were able to provide us with some financial support, so we were able to change our 2-day course in monogenic diabetes into a virtual format, and offer this to healthcare professionals in England at no charge for the past 4 years. These have been attended by clinicians and nurses, nationally and internationally. We recorded the talks in advance, and developed the programme so that people could listen to the talks, and then we have a live question and answer session. Over the past 2 years, we have run that course four times, and have had over 1,000 delegates attend. As part of that, we aimed to identify a named consultant and diabetes specialist nurse in every Trust with a diabetes service in England. In 2 years, we now have 95% of Trusts with an identified monogenic diabetes lead. The vast majority of those have both a diabetes consultant and a diabetes specialist nurse as named leads. We only have 5% of Trusts in England with a service who do not currently have a named monogenic diabetes lead. The idea behind it is that it does not matter where you live, wherever you are, with diabetes; there will be somebody in the local diabetes service with training in monogenic diabetes. In fact, around 80–86% of teams now have additional staff, as well as the named leads who have attended the training as well. We run some virtual masterclasses that staff can attend to increase their skills, and all of our training videos are available on www.diabetesgenes.org for healthcare professionals to access in their own time for free, if they cannot spend 2 days attending the 2-day course, or would like to revisit the content.

Q3 Your current research involves identifying patients with monogenic diabetes who have been misdiagnosed as having Type 1 or Type 2 diabetes, and co-ordinating the transfer of these patients to the most appropriate treatment. How common is misdiagnosis, and how can this be improved?

One of our colleagues, Lewis Pang, identified the prevalence of monogenic diabetes as being 248 per 1 million of the population, with an anticipated 12,000 (77%) cases in the UK that still have not received a confirmed diagnosis.[1] Historically, the time between the initial diabetes diagnosis and getting the correct genetic diagnosis was around 10–12 years. That is clearly something we want to improve, to make sure that people get the right diagnosis as soon as they possibly can.

It really is about raising awareness, raising recognition. Another colleague, Bev Shields, developed a maturity onset diabetes of the young (MODY) calculator, or a diabetes application,[2] where clinicians can enter eight different clinical characteristics very easily, with a patient sitting in front of them in clinic, which can help to identify how likely it is that the patient has monogenic diabetes. There are lots of different aids to differential diagnosis. Of course, we try to publicise and raise awareness of this through conference presentations, publications, podcasts, etc. Obviously, patients can access all the information on our website, and can put their details into the calculator as well.

Q4 What does the current diagnostic/treatment landscape for monogenic diabetes look like, and what are the unmet needs in this area?

I think the key thing is that anybody who meets criteria for genetic testing should be accessing that genetic testing, under the NHS. As testing is now centrally-funded, costs should not be a barrier for anyone in the UK when accessing genetic testing, which is the only way we can confirm monogenic diabetes. More than 30 different genes have been identified as causing different types of monogenic diabetes. Each have different clinical characteristics and different treatments. By performing genetic testing, and finding the specific gene that is affected in that case, we can then advise the best treatment for that patient. For example, those who have glucokinase MODY do not need any treatment or any follow-up, so they can be discharged from diabetes screening. For patients who have *HNF1A* or *HNF4A* MODY, they are best treated with a low dose of a sulfonylurea. Many, but not all, of these patients can be taken off insulin, and get better glycaemic control on a low dose of sulfonylurea. However, about 50% of the cases of neonatal diabetes are caused by changes in the potassium channel, and these patients are best treated with a high dose of sulfonylurea. So, the key thing, really, is that the optimal treatment depends on the gene that is affected. By doing genetic testing, we can identify which gene is affected, and then we can offer the optimal treatment for that patient, as well as the best advice and management for their care going forward.

Q5 What is the role of genetic testing in diabetes, and what is its impact?

Doing a genetic test is the only way to get a correct diagnosis. Typically, a sample is tested for all known genes that cause monogenic diabetes in one go. So, in a number of cases we will be able to confirm that the patient has monogenic diabetes. However, in some of the cases, we get a negative result, which means that those patients do not have a change in a gene that we know causes monogenic diabetes, so they still may have an atypical Type 1 or Type 2 diabetes.

> **"Identifying the correct genetic diagnosis can have an impact on treatment."**

Identifying the correct genetic diagnosis can have an impact on treatment. However, there are some types of monogenic diabetes that have a wider impact. For example, in *HNF1B* MODY, many of these patients will have a renal developmental abnormality, such as renal cysts, or a single or horseshoe kidney that may impact on their kidney function or uterine abnormalities; for example, a bicornate uterus or uterus didelphys. Patients with *HNF1B* typically have a very small pancreas, so the exocrine pancreatic

function can also be affected, and these patients may need treatment with Creon. So, the impact can be wider than just diabetes.

Another example is mitochondrial inherited diabetes and deafness (MIDD). Typically, patients with MIDD will have a bilateral sensorineural deafness, and early-onset diabetes, and they can have other features as well. These patients tend to need insulin within a couple of years. So, the impact of a genetic diagnosis can include getting an answer for patients for what has caused their diabetes, but may also indicate what has caused some other symptoms that they may have. Sometimes, even though some of those may not seem that positive, it can be helpful to get an explanation of what Is causing these other features in patients, and perhaps in other family members.

Q6 One of your research interests involves bridging the gap between research and clinical care. What steps are needed to overcome this gap?

I was appointed as one of the National Institute of Health and Care Research (NIHR) 70@70 senior nurse research leaders a few years ago. That was a 3-year part time appointment, and it focused on developing opportunities for nurses and midwives to undertake clinical and research careers, and support progression to a clinical academic career. Historically, there have not been clearly defined pathways for nurses, midwives, or other allied healthcare professionals to undertake a career that combines both clinical work and research at a senior level. However, Ruth May, who is the Chief Nursing Officer for England, recently launched a research strategy, which highlights the importance of nurses at all levels becoming involved and engaged in research. A similar initiative was launched by the Chief Midwifery Officer, and also the lead for allied healthcare professionals.

Within our own organisation, we have developed a nurse, midwife, allied healthcare professional, and healthcare scientist research strategy, which is focused on engaging clinical staff at all levels in research. This could be individuals just being aware of what research is going on in the organisation, which they can signpost patients to, or it may be an awareness of research roles within the organisation, or undertaking their own research.

We have also set up a scheme that we have been running for about 4 years now: the Chief Nurse Research Fellow programme, where individuals who might not have been exposed to research before have 1 day out of clinical practice fortnightly for 1 year to learn more about research, and consider potential opportunities to engage more in research in the future. The Chief Nurse Research Fellows also undertake a project based on a clinical problem in their area, to get them interested in the early stages of what research within their role and their organisation could look like. We have also set up a clinical academic network of individuals within the organisation, who are doing research at different levels; some are pre-PhD, some are post-PhD, but the idea is to provide a supportive, collaborative network, with possibilities for mentorship, and practice interviews for those who are applying for research funding. We all talk about evidence-based care, and that evidence has come from research, so I think it is vital to see research as a crucial component of clinical care, and show nurses, midwives, and allied healthcare professionals how they can turn clinical questions into potential research. Different professions will see things from a different perspective, so we can all have a role to play in research.

Q7 You were awarded the Aster Guardians Global Nursing Award 2023. Can you tell us more about what led to you receiving this award?

Aster Guardians Global Nursing Award is an initiative that has been developed by Aster DM Healthcare to recognise the great work that nurses are doing across the world, and to inspire others to join the profession. The first award was in 2022, and it was won by an amazing Kenyan nurse, Anna Qabale Duba, who had been doing some fantastic work with women and girls in terms of healthcare and education, and improvements within her own village in Kenya.

I saw the details of the award, and thought it would be a great opportunity to highlight some of the work that we do in Exeter, because we offer genetic testing for neonatal diabetes for anybody

diagnosed with diabetes under 6 months of age, anywhere in the world. For those countries that cannot afford it, we are able to offer that testing for free. I thought that it would be fantastic to draw attention to the work that we are doing, and to raise awareness of this service, because if countries across the world know that if they have a baby below 6 months of age who is ill, and if they test the glucose and it is raised, they can refer to us for genetic testing, at no cost to them if they cannot afford it.

So, I put in an application. There were five different categories, and I provided evidence for my work in the following categories: leadership, research, clinical care, and education. My application involved a description of the work that I did in each of those four areas, and then the application was verified by the external auditors Ernst & Young (EY; London, UK).

This year, over 52,000 registrations were received from nurses from 202 different countries, who were then were shortlisted to 10 finalists. We had an interview with the Grand Jury, which included senior individuals from the World Health Organization (WHO), United Nations (UN), International Council of Nurses (ICN), and other groups. We had a virtual interview with the Grand Jury, and that was an opportunity to talk about the different work that I had been doing, including monogenic diabetes, my own research, the clinical care that I am involved with, the educational initiatives that I have developed, and the leadership that I have been involved with, including the Florence Nightingale Foundation Leadership Scholarship.

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For the next year, this is leading to more opportunities to talk to different forums and countries about monogenic diabetes and the work that we do, as well as championing the cause of nursing, and promoting the profession. So, this was a fantastic opportunity for me. Meeting the other nine finalists was hugely inspiring: to talk to them, and listen to the work

that they have been doing. We have been in touch regularly since, so it is a very supportive group as well.

The Aster Guardians Global Nursing award is about to open for nominations for next year, so I am trying to encourage lots of nurses from the UK to apply. It is a great opportunity to raise the profile of nurses, and to encourage a new generation of nurses to come through the system. I think it shows the variety of work that nurses can do in all sorts of different areas.

Q8 Over the years that you have been practicing as a nurse, how have you seen the field change in terms of advancements to the technology used?

There have been absolutely huge advances, specifically in diabetes. I remember the first ward that I worked on when I qualified in 1984 was in King's College Hospital, and the equipment we had then was so different; for example, the blood glucose monitors were very large, and took 2 minutes to give you a reading. We were putting drops of urine in a test tube to see how much glucose was in the urine. Move forward 40 years or so, and we now have patients who are able to monitor their blood glucose through sensors, with an immediate blood glucose result. Not only do we have insulin pens, but we also have insulin pumps and closed loop systems. So, I think that the advances in the technology have just been phenomenal. Managing diabetes is still really difficult, I would not underestimate that at all, but I think that technology has made things so much easier. When we are in the clinic, we can download a patient's blood glucose results onto our computer from the system they are using, which makes things much simpler to assess. I am sure that there will be lots more advances in the future, as well.

There has been a huge increase in the different types of medications that can be used for diabetes, some with some hugely beneficial results. And, of course, genetic testing. Obviously, genetic testing has been around for a long time, but we used to test for a single gene at a time. So, we would look at a patient's clinical characteristics and think: "that looks like *HNF1A* MODY," or "That sounds like glucokinase MODY, maybe we will just test for that genetic change." Now, however, with the systems that we use, we can test for all known genes in a single test.

Q9 As an educator, where can we expect to see your focus lie in the coming years?

One focus for me is looking at the next generation of nurses coming through. I want to focus on how we can inspire people to join the NHS and other healthcare systems, and to take on a career in nursing, for example. However, it is also about the people who are already in nursing or healthcare, and how we can inspire them to undertake roles that are perhaps a little bit outside the box, or incorporating research or genetics, for example, into their role. There is a move to bring genetics into mainstream care, and that is something that I have been involved with, with our work in monogenic diabetes, by training diabetes healthcare professionals in genetics. Obviously, COVID-19 prompted us to use virtual platforms more than we ever did before, which has given lots more people the chance to access training that may have been inaccessible before; they can just log in from their own home online. That kind of virtual technology is really helpful as well.

One thing that I have been involved with more recently is podcasts, which are a really good way of getting information across. In fact, within our team, we have been talking about developing podcasts on monogenic diabetes because it makes the information so much more accessible. There are lots of different initiatives, and I am sure that there will be more ideas that can come through in the future. For me, it is about keeping your mind open to different ways of communicating information, to make it effective for people.

References

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