

Interview

Ahead of this issue, EMJ spoke to Robert Norman, The University of Adelaide, Australia, an expert in the field of reproductive and women's health. Having contributed significantly to IVF and reproductive endocrinology research, Norman discusses how healthcare systems could improve the early detection and management of reproductive disorders such as endometriosis, PCOS, and ovarian insufficiency.



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“**Women's health is absolutely fundamental to the health of society**”

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Q1 You have contributed significantly to research on polycystic ovary syndrome (PCOS) and are the current Chair of the Australian National PCOS Alliance. How can healthcare systems better manage and support women with PCOS, and where do you think research should be focusing in this field today?

Looking back to the year 2000, we were very divided across the world in understanding PCOS. The Americans had a different definition from the Europeans, and there was little consideration of what the rest of the world thought about PCOS. Within Australia, the results of a survey, which presented identical cases to internal medicine specialists and gynaecologists, showed that they each had completely different views as to what investigations and treatments should be done. We were very divided internationally.

I was lucky enough to be at the Rotterdam consensus in 2003 where we started to see some green shoots across the Atlantic. I think I was the only non-European, non-American at that meeting. When I came back, I met

up with a person called Helena Teede, a physician endocrinologist who just finished her PhD. She was interested in PCOS, but she didn't know anybody outside of Australia; whereas, I knew everybody internationally! Teede has tremendous gifts in diplomacy, organisation, and raising money, and I was lucky enough to be involved with her. I remember her saying to me: “Rob, we've got to do guidelines for PCOS for Australia; we've got all this evidence that patients are unhappy and doctors don't know what's going on.” So, in 2011, we came up with Australian guidelines, which were evidence based, and published them in the *Medical Journal of Australia*. We were then invited by the National Institutes of Health (NIH) to a meeting on PCOS, and afterwards, the organisers took us off into a room on our own and said: “You guys know what you're doing. You're the best in the world and we've got to bring about a change.” So, the NIH came on board with our attitude.

We then did the international guidelines in 2018, this involved people from every continent, and, for the first time, we were getting

unanimity. We've recently updated this and published it last year, and that was with an even wider group of people. So, to come back to your question, how can healthcare systems better manage and support patients with PCOS? I think it's by working together, by basing our decisions on the best evidence available, and getting an international consensus.

Q2 How can healthcare systems improve early detection and management of reproductive disorders such as endometriosis, PCOS, and ovarian insufficiency in women?

Talking mainly about Australia, because that's my experience in this area, I think we are starting to recognise that women's health is absolutely fundamental to the health of society. There's been a tremendous emphasis in Australia on things such as PCOS, endometriosis, pelvic pain, menstrual disorders, and, increasingly, menopause. This all originated because there were a number of support groups that went to prominent politicians and highlighted that there was

a significant lack of funding in these important areas. This was particularly significant for endometriosis, and I think there were about five or six female parliamentarians that raised this, and the government has now put large sums of money into endometriosis research and education. There's also now a recommendation that medical schools must put aside a mandatory amount of time for teaching about endometriosis, menopause, and PCOS, and there's a big demand for GPs to have strong education in areas such as menopause. We also have the trades unions who are pushing for menstrual leave, IVF leave, and there's even talk now about taking time off for menopause.

The other thing that we've highlighted is something we call period poverty, and this is where menstrual products are made available free of charge to young girls and to people who can't afford them. There's been a strong message that if you go to the toilet anywhere publicly, there's toilet paper, so why are there not menstrual products?

Thanks to the work of several groups, value-added tax has been taken off all period products.

We've also developed excellent guidelines for endometriosis. We've just produced a premature ovarian insufficiency guideline together with the European Society of Human Reproduction and Embryology (ESHRE), and we have got both an ESHRE- and an Australian-approved unexplained infertility guideline.

Clinically, there are also many new developments occurring. Endometriosis is usually diagnosed by laparoscopy, which is expensive, and many laparoscopies have to be done to make the diagnosis. However, the government has funded important work investigating non-invasive methods, such as blood tests, to push progress in that area. I think Australia is almost the world leader at the moment in diagnosis using ultrasound methods. This has been coupled with deep learning and AI, so we're hoping that we can move away from laparoscopies completely.



In summary, we've pioneered political advocacy, we've delivered good medical practice, we've had very strong patient support, we've developed new diagnostic protocols, and we're trying to get education to medical schools and to all doctors.

Q3 Obesity is a growing global health issue. How does obesity specifically affect women's reproductive health, and what public health strategies would you recommend to address this issue?

Obesity has been a Western disease for a long time, but we now know that it's an international disease affecting many different countries. Thus, it has become an international problem in terms of general health, and particularly, women's health. We've got good evidence from our research that as the rates of obesity go up, rates of PCOS go up. On the other hand, if you're prone to PCOS and you stay at a low weight, you're less likely to get it.

There's also a lot of evidence that natural fertility is affected by obesity for both males and females, and if you do get pregnant, there are many metabolic issues that can occur, such as gestational diabetes. But there's also hypertension, preterm labour, and overall problems with delivery.

Later in life, diabetes mellitus, endometrial cancer, and cardiovascular disease are more common in women who are overweight. So, obesity clearly affects women's reproductive health throughout life, in addition to all the other problems that can affect your general health.

What are we doing about it? Well, one of our recommendations from our PCOS guidelines was to try

and deal with the weight before it occurs. Specifically, weight gain in the teenage years is the big problem. If you can encourage people not to put on too much weight when they're teenagers, they're less likely to get problems later. It's much easier to stop weight gain than just to lose weight. We've been trying to raise awareness among families and the general public about the benefits of maintaining a healthy weight. But one of the problems that we're facing is this issue of the stigma associated with the name obesity. It's almost not correct to use the words obesity and overweight now. We are therefore working through how we use terminology that's not offensive to people, while making sure we can deliver our message. All our programs for women's health deliver lifestyle information, for example, encouraging people to exercise for at least 150 minutes a week and to eat a relatively low-calorie diet that avoids processed foods. We also have medicines that can help with this, including GLP-1 receptor agonists, such as Ozempic (Novo Nordisk, Bagsværd, Denmark), which are having a huge impact, and people are losing large amounts of weight.

Q4 Given your pioneering work in infertility and reproductive health, how do you see access to assisted reproductive technologies evolving?

I think we have a couple of trends emerging. One is the difference between rich and poor, which affects the access to fertility investigation and treatment. In the UK, you've got postcode access to IVF, meaning it's very patchy across your country, but it's also very patchy across the world and the people who probably need IVF the most are the ones who can

least afford it. I originally came from Africa, and I'm aware that the access to IVF is extremely limited there. In Australia, inexpensive access is quite good because the government will fund up to 70% of the cost for any number of IVF cycles.

On the other hand, we're seeing increased complexity associated with assisted reproductive technology. We're using things such as AI, genetic testing, more advanced equipment, and expensive drugs. We're getting better results that way, but it's just pushing up the price and taking it away from a lot of people. So really, what I'm hoping we achieve is for the vast majority of people to receive simpler fertility treatment, and that includes being able to work out who's going to get pregnant by themselves without any help. We've worked with people in Vietnam who have developed a method that doesn't use any drugs at all and matures the eggs in the laboratory. They call that *in vitro* maturation, and that has a lot of promise.

A problem ahead is that we've got increasing privatisation of fertility, so most countries don't have public services for infertility, and it's a place where you can make a lot of money.

Q5 How do environmental factors like pollution, climate change, and endocrine disruptors impact women's health, and what preventive measures could be implemented?

The vast amount of infertility that we're seeing in society, and the decreasing fertility rate across the whole world, is primarily a socioeconomic problem. It has to do with money, political systems, social attitudes, etc. As we see the total fertility rate dropping across



the world, the primary focus we should have is to work out how we can make it more economic for people to have children earlier in life. To achieve this, we need to focus on political change, such as childcare and leave after giving birth. That's the only thing that's going to change our total fertility rate. It's not going to be more IVF.

However, we then have the problem of pollution, climate change, and endocrine disruptors, which we can show are very significant in animals. We do think that the results from semen analysis are becoming more concerning in some countries. These are probably the main harbingers of something in the environment affecting fertility, but at the moment it's difficult to clearly identify the role of pollution, climate change, and endocrine disruptors. There are other people who feel more strongly about these issues than I do, and I think what they're concerned about is totally valid. But I do believe if we're going to raise our fertility rates as a society, it's more important to look at the socio-economic factors rather than the pollutants that we've got.

Q6 In 2009, you founded the Robinson Research Institute, which now includes 450 researchers focusing on preconception, pregnancy, neonatal care, and paediatrics. What accomplishment related to the institute are you most proud of?

When we founded the Robinson Institute in 2009, we had some very successful groups around The University of Adelaide, Australia, focusing on paediatrics, obstetrics, gynaecology, and epidemiology, but they were all kind of working as if they were private businesses; looking after themselves rather than collaborating. So, the concept of the Robinson Institute was to try and get people to work together, to see outside of their little pool, and to encourage collaboration. Our basic concept was that we wanted to look at what we call parenting before conception. So, before an egg and a sperm get together, how can we optimise the environment biologically, environmentally, socially, and economically. We wanted to maintain this concept from before pregnancy right through to the age of 18 years.

But this was a life course, it was a continuum, it wasn't a bunch of separate groups looking at just one piece of that. We put money into that, and we have had people go on to receive huge grants. For instance, in diabetes, one group is looking at things that predispose us to diabetes at a sperm and egg level, in pregnancy, in early life, and in teenage years.

We also have people who are experts in genetics and molecular biology. We've got others who are really good at doing clinical trials or who are well versed with health systems. We cover the whole spectrum of medicine, from basic laboratory and epidemiology right the way through to health systems and changing the way that society operates.

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I would highlight a couple of successes. We've been very successful at IVF, and at one stage, we would have been in the top three or five units in the world. One of the big prizes in Australia is called the Eureka Prize, and this is for spectacular discoveries. This year, two of our groups won a Eureka Prize, one for AI in endometriosis, and the other one for new ways of treating cystic fibrosis.

The work that struck me most in the area of cerebral palsy was the work of Alastair MacLennan, joint Head of the Australian Collaborative Cerebral Palsy Research Group at the Robinson Research Institute, The University of Adelaide, Australia. MacLennan was an expert on medical-legal issues, and he was constantly in the courts giving information about cerebral palsy when obstetricians were being sued because they had allegedly done the wrong thing during labour. He believed this association wasn't accurate. We've now discovered that at least 25% of all cases of cerebral palsy are genetic in origin, nothing to do with labour, and nothing to do with the doctor. This is changing the whole medical-legal environment in our country.

Q7 Are there any exciting developments on the horizon that will be particularly influential to the future of women's health?

I think that, increasingly, genetics is going to play a role. My main interest has been infertility and PCOS, and if we could screen a person for various genes, we could identify specific subtypes rather than simply diagnosing a generic condition in a patient. We will then be able to tailor treatment much more appropriately to that person. I think the personalisation of medicine is going to become more and more important, and that will come through genetics, but also through big data. Specifically, we need to assemble big cohorts together to provide very large amounts of information, and then analyse that data.

I think we are also going to see big changes in the way that women's health is managed. The next thing I hope that will happen is that society will start to see that having children is important. Obviously, people who absolutely do not want children can decide not to do that, but the evidence

is that most couples want one child more than they've actually got, and we need to look at how society can make that possible without people losing their careers for example. Currently, I think Western societies are not doing that very well. Our emphases have become far too economic, and we are neglecting to look after people who would like to have children but who don't want to be at a disadvantage.

Also, returning to the use of AI in diagnosing endometriosis as I mentioned earlier, one of our groups, headed by Louise Hull, The University of Adelaide, Australia, is recruiting thousands of women who have pelvic pain and other pelvic problems. They have a free MRI and a free vaginal ultrasound. They're then inputting all the data so that they can develop diagnostic models through deep learning and AI. One would then hope that that would be rolled out to every ultrasound and every radiology department in the country to aid in the diagnosis of endometriosis, PCOS, early endometrial cancer, adenomyosis, and even ovarian cancer.

