O&G MAGAZINE

CANCER

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Editorial Communications
O&G Magazine Advisory Group
RANZCOG
Djeembana | 1 Bowen Crescent
Naarm (Melbourne), VIC 3004 Australia
(t) +61 3 9417 1699
(e) OGmag@ranzcog.edu.au

Advertising Sales
Minnis Journals
(t) +61 3 9836 2808
(e) minnis@minnisjournals.com.au

Printer
SouthernImpact
(t) +61 3 8796 7000

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The College

Cancer

RANZCOG acknowledges and pays respect to the Traditional Custodians of the lands, waters and communities across Australia, on which our members live and work, and to their Elders, past, present and future.

Women's health

The College

RANZCOG recognises the special status of Māori as tangata whenua in Aotearoa New Zealand and is committed to meeting its obligations as Te Tiriti o Waitangi partners.

RANZCOG New Zealand Committee
Te Kāhui Oranga ō Nuku
Dr Susan Fleming **Chair**

Aotearoa New Zealand National Office
Catherine Cooper **Head**
Level 6, Featherston Tower,
23 Waring Taylor Street,
Te Whanganui-a-Tara (Wellington) 6011
PO Box 10611,
Te Whanganui-a-Tara (Wellington) 6140
(t) +64 4 472 4608
(e) ranzcog@ranzcog.org.nz

RANZCOG State and Territory Committees
Engagement and Rural Health
Mel Pietsch **Head**
Suite 13, 18 National Cct
Barton, Ngambi (Canberra), ACT 2600
(t) +61 2 6100 1160
(e) mpietsch@ranzcog.edu.au

Australian Capital Territory
Dr Sim Hom Tam **Chair**
Robyn Walton **Member Engagement Lead**
Suite 13, 18 National Cct
Barton, Ngambi (Canberra), ACT 2600
(t) +61 2 6169 3993
(e) act@ranzcog.edu.au

New South Wales
Dr Mark Ruff **Chair**
Robyn Walton **Member Engagement Lead**
Suite 2, Ground Floor, 69 Christie Street
St Leonards, Warrang (Sydney), NSW 2065
(t) +61 2 9436 1688
(e) nsw@ranzcog.edu.au

Queensland
Dr Senaka Abeysundera **Chair**
Sylvia Williamson **Member Engagement Lead**
Suite 2, Level 2, 56 Little Edward Street,
Spring Hill, Meanjin (Brisbane), Qld 4000
(t) +61 7 3252 3073
(e) qld@ranzcog.edu.au

South Australia/Northern Territory
Dr Kate Walsh **Chair**
Terri Herrero **Member Engagement Coordinator**
First floor, 213 Greenhill Road
Eastwood, Tarndanya (Adelaide), SA 5063
(t) +61 8 7200 3437
(e) sa-nt@ranzcog.edu.au

Tasmania
Dr Frank Clark **Chair**
Michelle Turner **Member Engagement Lead**
Djeembana, 1 Bowen Crescent,
Naarm (Melbourne), Vic 3004
(t) +61 3 9114 3925
(e) vic-tas@ranzcog.edu.au

Victoria
Dr Samuel Newbury **Chair**
Michelle Turner **Member Engagement Lead**
Djeembana, 1 Bowen Crescent,
Naarm (Melbourne), Vic 3004
(t) +61 3 9114 3925
(e) vic-tas@ranzcog.edu.au

Western Australia
Dr Fiona Langdon **Chair**
Claire Siddle **Member Engagement Lead**
34 Harrogate Street,
West Leederville, Boorloo (Perth), WA 6007
(t) +61 8 9381 4491
(e) wa@ranzcog.edu.au

From the President

Dr Benjamin Bopp
President

Like the zodiac, the medical term 'cancer' references the Latin for crab because many cancers, when spreading, extend into surrounding tissues like the legs of a crab.

It's an unfortunately negative association for a fine (and flavoursome) creature and those born under that star sign.

Whether a person is medical or not, little in life is as confronting as seeing a person die, particularly slowly from the effects of cancer. As a junior medical student, I witnessed a loved one with a chronic leukaemia lose his seven-year cancer battle.

It was 1985 and Dad was 53.

Following heart disease, dementia and stroke, cancer is a leading cause of death in Australia. Unfortunately, cancer touches all our lives at one time or another.

But just as technology has moved on, so has medicine. That fatal condition in 1985 is now eminently survivable. With advances in many sciences, DNA technologies, targeted pharmaceuticals and other treatments, the potential for individuals to live well beyond many more types of cancer is here.

This issue of *O&G Magazine* addresses numerous topics ranging from primary cancer prevention to cancer epidemiology to ovarian cancer screening and management through to palliative care and pain management.

As our world slowly renormalises post covid, it has been a pleasure to attend numerous hospital site visits in person and liaise with colleagues and trainees across Australia and New Zealand. The recent, face-to-face RANZCOG presentation events in Brisbane and Wellington have allowed us to finally celebrate the elevation of some of our new Fellows and Subspecialists.

There will be further events this year (in Christchurch to coincide with the New Zealand ASM in September and on the Gold Coast in October to align with the RANZCOG ASM). These events also provide opportunity for the College to acknowledge scientific leaders in Women's Health whose primary and translational research drives so many clinical advances.

A memory shared by my cohorts from Queensland University in the 1980s is of a thorough and no-nonsense immunology tutor who, like most in his position, was starting his academic career and having to deal with a rabble of obnoxious medical students. His name was Ian Frazer and he went on to be the co-inventor of the HPV vaccine. His work means that, for the first time, we may be on the threshold of completely eradicating a type of cancer!

Not all cancers are the same, many have very uncertain aetiologies and to defeat them all will take a lot of time and money and, most importantly, dedicated investigators.

Another sign of progress was, several years ago whilst in private practise caring for someone in pregnancy, we diagnosed cancer of the cervix at 17 weeks. In medical school days the treatment for this devastating situation was an immediate radical hysterectomy with obviously loss of the pregnancy and future fertility.

The local gynaecology oncologist performed the appropriate staging procedures including laparoscopic lymphadenectomy mid-trimester, chemotherapy was given, and baby then delivered by caesarean section at 34 weeks before further chemotherapy. Within two years there was another pregnancy and another baby. Complete hysterectomy had been successfully delayed until family completion.

So, reflecting on the changes in diagnosing, treating and preventing cancer that have been witnessed in the last 35 years gives us all hope for the future.

Please enjoy this Spring issue of *O&G Magazine* and we hope you'll join us on the Gold Coast for our Annual Scientific Meeting in October.

From the CEO

Vase Jovanoska
Chief Executive Officer

At the time of writing this, **July Council Week** is nearly upon us and we look forward to welcoming our College Board and Council to Council Week at Djeembana, College Place in Naarm. Council Week July 2022 will mark the first time in three years that the RANZCOG Council has been able to meet for the annual Council Dinner in Melbourne, so it is a significant occasion, a long time in the making.

I would like to take this opportunity to thank our membership for participating in RANZCOG's Discrimination, Bullying and Harassment survey which, after some months, has culminated in the learnings and outcomes being consolidated into the **Fostering Respect Action Plan**. The Plan which is currently being reviewed and considered by the College Board and Council will provide a tangible set of actions by which we will work and strive to create a culture within our workplace and the O&G speciality across Australia and New Zealand that is free from, and does not tolerate, bullying, discrimination, and harassment.

RANZCOG acknowledges the Bunurong people, the traditional custodians of the lands on which Djeembana, College Place is located. RANZCOG took part in **National Reconciliation Week** in June and hosted a special event lead by Natarsha Bamblett, member of the First Peoples' Assembly of Victoria, Indigenous leader, facilitator and storyteller at Djeembana, to have open and vulnerable conversations about the inequities of Indigenous Australians within the wider community.

NAIDOC Week celebrations are also held across Australia in July each year and is an opportunity for all Australians to learn about First Nations cultures and histories and participate in celebrations of the oldest, continuous living cultures on earth. This year's theme was *Get Up! Show up! Stand up!* This year, RANZCOG hosted an Indigenous birthing, pregnancy, and healthcare panel discussion with some incredible Indigenous women who spoke of their experiences as mothers and advocates of woman's health, giving us rich insight into the Indigenous women's experiences in healthcare. The College continues to work on our Reconciliation Action Plan to bridge the gap through meaningful engagement with Aboriginal and Torres Strait Islander people.

The College recently held two **Fellowship Awards Ceremonies**; the Queensland ceremony was held at the Brisbane City Hall on Sunday 22 May with 170 guests in attendance, 30 Fellows and 3 Subspecialists were elevated. A very special ceremony was held in Aotearoa New Zealand in June with 21 Fellowship and 4 Subspecialist elevations at an event which combined Māori tikanga (custom) and RANZCOG protocols. A special feature of the evening was Kaumatua Luke Crawford introducing a mauri stone (sacred stone) – a piece of Ngai Tahu pounamu (greenstone) gifted to He Hono Wāhine and RANZCOG by Kaumatua Wendy Dallas-Katoa. Elevating Fellows and awardees were invited to add their energy or essence to the stone by touching it as they went onto the stage.

At the time of writing this article, we are very much looking forward to three major events on the RANZCOG calendar being the **New Zealand Annual Scientific Meeting**, 22–23 August in Ōtautahi Chirstchurch themed Doing things differently; Tu ora mai , live in health; the **New Zealand Flourish Women Health Summit**, an interactive event bringing together a wide range of people and organisations interested in women and health for a series of facilitated conversations, and the **RANZCOG Annual Scientific Meeting** at the Gold Coast Convention Centre between 7–12 October, which will be the first time in three years that we have the opportunity for a face-to-face ASM.

The RANZCOG webinar series has continued over the past few months with the **Vaginal Birth after Caesarean (VBAC) webinar** which took place on Tuesday 14 June and was attended by over 300 people, both RANZCOG members and consumers. Hosted by RANZCOG President, Dr Benjamin Bopp, the multidisciplinary panel of experts discussed mode of birth for subsequent pregnancies after a

caesarean section and each option – whether a labour with a view to safe vaginal birth or planned caesarean section – has both potential risks and benefits. The recording is available on the RANZCOG Vimeo channel if you would like to view the session. At the time of writing, we are also about to host a **Contraception, sexual health, and fertility webinar** in mid-July as well as a webinar on **Perimenopause** in September. Stay tuned on the College's media channels for further information about our webinars.

I am happy to confirm that RANZCOG's bid to host the **2026 AOFOG World Congress in Sydney** was successful. President Dr Ben Bopp presented the College's bid at the AOFOG Council meeting in May which also showcased a unique video that was created for the bid. The video also features immediate past-President Dr Vijay Roach and Chair of the RANZCOG Sexual and Reproductive Health Special Interest Group, Prof Kirsten Black and can be viewed here: https://vimeo.com/713593231.

I am pleased to report that the College received a response to our **Australian Medical Council (AMC) 2022 Monitoring Submission** with no outstanding conditions. The AMC commended the College on our initiatives to encourage Indigenous students in Australia to enter the FRANZCOG program, and advocacy and support programs in Aotearoa New Zealand; several pilots including online communication skills courses to support trainees in effective communications with colleagues, patients and their families and two emotional intelligence and sustained wellbeing courses; improved levels of trainee satisfaction pertaining to the quality of exams; comprehensive and appropriate processes for addressing bullying, harassment and discrimination issues. The full report can be accessed on our website.

The **AMC 2023 Full Accreditation Report** will be submitted in May 2023. The process is extensive, consultative, and marked by milestones over the coming months, including formal hospital site visits, a visit to College Place, exam observation and a final written submission to the AMC.

I am pleased to announce that RANZCOG's **new website** also launched in June. The new website is a fresh, clean and functional interface and I thank all those involved in the development of the project. As always, we continue to improve our platforms and services, so we encourage you let us know if you have any feedback regarding the website.

Have you read about changes to CPD?

Continuing Professional Development (CPD) is an essential part of maintaining your RANZCOG Fellowship, and we are committed to making it as straightforward as possible to meet your CPD requirements.

Recently, changes have been made to the way RANZCOG delivers CPD, to simplify the process and ensure that all of our Fellows are supported in gaining hours.

Read about the changes on the RANZCOG website:

ranzcog.edu.au/cpd

Changes comes into effect from 1 July 2022.

More information:
E cpd@ranzcog.edu.au

LEADERS IN FOCUS

Dr Nisha Khot
MBBS, MD, FRCOG, AFRACMA, FRANZCOG

This feature sees Dr Nisha Khot in conversation with women's health leaders in a broad range of leadership positions. We hope you find this an interesting and inspiring read.

Join the conversation on Twitter
#CelebratingLeadership @RANZCOG @Nishaobgyn

Dr Michael Carrette FRANZCOG (ret)

This issue of *O&G Magazine* comes to you at a time when we are witnessing an unprecedented (how we have come to hate this word!) invasion of government into the personal lives and healthcare choices of Americans. In Australia, we have watched with horror as events unfold in USA. The 'justification' provided by those who made the decision to overturn Roe vs Wade was that abortion is a dangerous procedure and people seeking abortion needed to be 'protected'. Experience around the world has unequivocally demonstrated that restricting access to abortion only reduces the number of safe (ie. not dangerous) abortions. We are already hearing evidence of the dangerous situation many women now find themselves in directly because of restricted access to abortion.

Closer to home, new laws to decriminalise abortion in South Australia have only just come into effect in July 2022. In WA, abortion is still regulated by the Criminal Code. While abortion is available in all states and territories, we cannot deny the existence of a postcode lottery for abortion rights and access.

It seemed entirely appropriate to feature Dr Michael Carrette in this *Leaders in Focus*. Dr Carrette was the first doctor to use mifepristone for abortion in Australia. For 18 years, he was one of very few doctors providing surgical abortions in Cairns. When he retired in 2016, women from Far North Queensland (FNQ) had to travel thousands of kilometres to access surgical abortions. I am grateful to Prof Caroline de Costa for introducing me to Dr Carrette. I hope readers will be as fascinated as I was by Dr Carrette's life as a musician and singer before he came to medicine and specifically, O&G. Although Mike has retired, he continues to explore his various passions including building his own harpsichords and flying his ultralight aircrafts.

Could you please tell me about your early years? Who were your early influences?

I was brought up in England by my mother whose Irish husband had disappeared shortly after I was born. She was 40 years old and was caring for me and her elderly parents. She worked as a teacher to make ends meet. My mother, two grandparents and I lived in a very modest house and clearly expectations were on me from an early age to improve the social and financial situation.

My mother made me learn to play the piano. So far so conventional, but it was the one thing that set me on my life and my career. By the age of 8, I was fairly musical and had an attractive treble voice. My mother got me an interview at the choir school of Canterbury Cathedral and I was accepted. What followed was far and away the happiest time of my life. For five years we choirboys lived in the cathedral precincts and lived and breathed history and music. I sang on television, on stage and in operas.

At the age of 13 it was time to go to 'high school'. My family's middle-class background required that

I go to a 'good' school. There was no money for such a thing, but the school we fancied had a few scholarships ready to be awarded for various things. With my musical background the deal was I would have reduced school fees if I played the organ in chapel, sang in the choir, played in the orchestra and in the cadet force band. I really did not enjoy my high school years.

At 18, I faced the next problem. I had enough 'A-levels' to go to university, but no hope of a good medical school and no money to pay for it. It turned out I had a godfather who had been a celebrated surgeon at Barts in his day. I think there might have been a person on an interview committee who was of a musical bent. It also turned out that the local government authority where we lived had a scheme to give financial support to those seeking higher education but were of limited means. So pulling various strings, and involving much luck, I enrolled at Charing Cross Hospital in 1962.

At this point I feel compelled to mention Doris. My mother had a good friend at teachers training college called Doris. Doris had a partner called May. Doris told my mother that since she was destined never to have children, the next best thing was to help someone else's child through life. My journey through schools and university was largely thanks to Doris. When my mother told me about this, (me being young, innocent and living in an unenlightened age) I always assumed that Doris has some terrible disease that prevented her having children. The truth occurred to me much later and when it did, it was a revelation.

The next episode was nearly the end of everything. After the first two years at Charing Cross, we had a pre-clinical exam. I failed, mostly because I had discovered rugby football, beer and nurses. My grants were cut off. Fortunately, I was allowed to retake the exams after six months, but I had to work all day on the books and all evening as a bartender. But I made it the second time. Never have I been so mugged by reality and come so close to failing. I still dream about it and awake stressed.

What prompted you to choose a career in O&G?

I chose O&G largely because to the young Dr Carrette, it was such a mystery. It also seemed that there could be no finer life for a man than sustaining women through that most important expression of being a human being. It is the only specialty that combines medicine, surgery and psychology. Childbirth is so exhilarating and rewarding. I have had a very full career that has brought me much joy.

What advice do you have for junior doctors aspiring to a career in O&G?

The life of an O&G specialist will allow you to participate in the joys of your patients while earning their lasting affection and gratitude.

I still experience this in my retirement; my former patients recognise me, while my children and grandchildren report being told 'your dad delivered me' on regular occasions.

Dr Michael Carrette

How did you come to be involved in reproductive healthcare and abortion care?

When I first arrived in Cairns I became involved with Cairns Family Planning, before it was incorporated into Brisbane. This was a time when many chemists refused to stock the OCP and when a woman could not have a 'tubal ligation' without her husband's consent being witnessed by the hospital superintendent. We did a lot of 'extended sterilisations' at the Catholic hospital. It was called a hysterectomy. Being a lifetime atheist, I always considered religion an enemy and treated it as such.

I started to perform surgical abortions in Cairns in 1998, which was as soon as there existed a local facility which allowed this. At times I scarcely had time for much else. A short time ago I analysed my patients' data and it turns out I have performed over 9,000 such procedures!

What were the defining moments of your career?

My career highlight was being the first to use mifepristone in Australia. My involvement with Queensland abortion law reform is another defining moment in my career. For both of these my thanks are largely due to Prof Caroline de Costa. Caroline had an ambition to be the first to introduce medical abortion into Australia. She had the academic know-how, the drive, the contacts, the plans. What she lacked were the patients, since hers was an academic post. I had a busy abortion practice ,the only one in North Queensland, and thus what started as a partnership of necessity became a team and a lasting friendship.

What is your reaction to the news from USA with regards to Roe vs Wade? Should we in Australia be concerned?

Roe vs Wade is too terrible to think about. It will be a long learning exercise for the people of USA where I can see disaster as the SCOTUS lurches right while the people steadily march left.

We here will, I hope, never have a similar problem. We do not have a 'cult' mixing radical religion, anti-gay rights, anti-abortion and guns. However, this should not mean that we let our guard down. Abortion rights in Australia were hard won after many years of steady campaigning. There is much that we have not achieved as yet in ensuring equitable access to abortion across regional, rural and remote Australia.

Over the course of your working life, what are some of the big changes you have noticed in O&G?

The most obvious change is the gender balance. I worked with Doctors Bob, Patrick, another Bob, Tom, Roger, Paul, Desmond, and Michael. Only later did Dr Liz McKenna arrive followed by a host of other female O&Gs. To be frank, this change is a mixed blessing. There is a perception that the ladies are the more gentle and caring. I can't comment on loving and caring, but have observed many registrars (and colleagues) operating and can tell you men are mostly careful, meticulous, efficient surgeons and this, to me, shows that they care about their patients.

The other problem is obvious and inescapable. It is not hard for me to observe that the most loved and trusted obstetricians are those who have devoted their life to obstetrics, who have been on call 24/7 for year after year in the same practice with very little leave. This is not a gender-based criticism but rather a reflection of the 24/7 nature of obstetrics.

What role did RANZCOG play in your life? What has been your involvement with College activities?

I did some work for the College creating learning resources for trainees on the subject of abortion. The reach of the college is tenuous in FNQ, but when the hospital lawyers were threatening, the law ambiguous and medical indemnity providers being no help at all, the College was unequivocally on our side and very reassuring it was too. I do think the College could be more involved with women's rights on a broader front by advocating for a federal approach to abortion rights and action on domestic violence.

If you had the ability to, what would you change?

Looking back, I would not change anything. I have been terribly lucky in my association with wonderful colleagues. Music (Mozart and Bach amongst others) has been ever-present. I have had the opportunity to make a difference in many ways. The boy with very few prospects who grew up in England has come a long way thanks to the generosity of the likes of Doris who faced discrimination and marginalisation in their lives.

What has kept you busy post-retirement?

I am enjoying living close to my family, making trips to the cottage in Tasmania and listening to a lot of music. I am determined to create a herb garden outside the back and this has kept me happily occupied in retirement.

I hope you have enjoyed reading this interview with Dr Michael Carrette. My aim with this column is to feature women's healthcare professionals who can inspire readers, especially the next generation of O&Gs. Your feedback and suggestions are very welcome. If you have any recommendations for colleagues or mentors you would like to see featured, please get in touch. I look forward to hearing your thoughts on the current format of this feature and any ideas for improvement.

He Hono Wāhine

Smear Your Mea

Dr Leigh Duncan (Ngā Mahanga, Taranaki Tūturu)
MBChB (Otago), Dip. Obs (Auckland),
MRCOG, FRANZCOG
Chair of He Hono Wāhine

Bailey Parata (Ngāi Tahu, Te Atiawa)
Kaitohutohu Hauora Wāhine Māori
Māori Women's Health Advisor

In June, RANZCOG Aotearoa held their Fellowship Elevation and Award Ceremony. The night was filled with amazing achievements of our new Fellows, as well as our award winners. One award presented was RANZCOG's Māori Women's Health Award, which is awarded to individuals, or a group, that has made a significant contribution to Māori women's health outcomes. Due to COVID, there was a backlog in awards to be presented. Our 2020 Award winners, Smear your Mea, were presented their award for their incredible work. Talei Morrison was diagnosed with advanced cervical cancer aged 41. She found a lack of resources that resonated with her as a wahine Māori. Because of this, she launched an extremely successful health campaign to encourage wāhine Māori to get their cervical smear test.

The aim of the Smear Your Mea campaign is to protect the health and whakapapa or genealogy of wāhine Māori, to safeguard the health of future generations. Their mission is to raise awareness and promote advocacy and support through the detection, treatment and prevention of cervical cancer for wāhine Māori. The Smear Your Mea campaign continues to bring cervical screening to the people at many communities and kaupapa Māori events – public holiday events, marae days, community health days, Kapa haka, Waka Ama sporting fixtures.

Prof Sandra Morrison accepting the award on behalf of Smear Your Mea

(Left to right): Dr Kasey Tawhara, Te Ururoa Flavell, Nadine Riwai, Prof Sandra Morrison, Elaine Kameta, Tiria Waitai, Eruera Keepa.

In 2019, Talei's brother Eruera, Chair of the Smear Your Mea Trust, presented to the Māori Affairs Select Committee's Inquiry into health inequities for Māori. They reported that Talei was failed by the current health system framework and advocated for policy change. The Committee's final report referenced Talei's journey, recommended changes to the national screening program, and also recommended practitioners undergo cultural safety training for their professional development.

The Smear Your Mea campaign was nominated for the RANZCOG Māori Women's Health award to acknowledge this inspirational mana wahine, who even through her terminal illness was determined to advocate for wāhine Māori. We also acknowledge her whānau who continue to drive this community-funded campaign in her memory.

The Smear Your Mea campaign is an exemplar of how we can provide culturally safe education, advocacy, and treatment to our Māori whānau, creating positive health experiences and improving health inequities. There will be several changes when the new primary screening test is introduced. Self-testing will be an option. A vaginal swab can be taken privately at a health clinic, or it can be taken by a clinician if preferred. The health care provider can also arrange for the tests to be done out of clinic, for example, at home, or in a non-clinical setting in the community. A speculum exam is not needed for the new test. However, if the test shows HPV is present a follow-up test will be needed.

The Ministry of Health will be looking at ways to make screening even more accessible in the future, which may include a future approach of a national mail-out of self-testing kits, if they are found to work safely and well for participants.

Smear your Mea were our 2020 Māori Women's Health Award winners alongside Prof Bev Lawton (Ngāti Porou). Prof Bev Lawton was nominated for her mahi as the principal investigator of a community-based Kaupapa Māori research project called He Tapu Te Whare Tangata, designed to improve access to and uptake of cervical cancer screening in a way more suited to Māori needs. This research was also integral in getting self-testing for HPV recognised and agreed to for wāhine.

Get to know College staff: various LIDT members

With so many people working behind the scenes with a shared passion for excellence and equity in women's health, here's a chance to get to know College staff and the diversity of skills and experience they bring to our vision and mission.

This issue, we focus on the Leadership, Innovation and Development Team (LIDT), which comprises the senior leadership of RANZCOG. Featured here is a quarter of the LIDT membership.

The LIDT share information about each business area with other leaders, including new projects and/or initiatives that may impact other units, discuss current and future operational challenges and communicate shared information in a consistent manner with their teams and direct reports.

Andre Khoury

Head of Communications and Public Affairs

Working closely with the President and Chief Executive, Andre is responsible for the oversight and coordination of all communications and public affairs of the College, including providing strategic advice and managing external media relationships and day-to-day media issues.

An expert media, strategic, and communications professional with more than 10 years' experience, Andre's skill is in managing issues and providing high-level advice to senior executives, having an authoritative knowledge of health, general, financial and business media, as well as an understanding of not-for-profit, government and public company communications. In addition, his networks extend throughout the national media, health and business sectors, and regulators and authorities.

Andre's career encompasses experience with Australia's integrated corporate, markets, financial services and consumer credit regulator; one of the four largest financial institutions in Australia; the medical regulator in Australia; and specialist medical colleges.

Andre holds a Bachelor of Communication (Journalism).

Iffath Afroze

Head of Governance

Iffath leads the Governance and legal team. During her three years at RANZCOG, she worked on the College's governance, contract management, compliance with Regulations, Legislation, oversight of legal matters, appeals and independent external consultations. Iffath's team manages RANZCOG elections, Constitution, Regulations and Policies and organisation-wide committee's terms of reference.

Iffath has more than 10 years of corporate governance experience and has worked in not-for-profit organisations for the past five years. Her career encompasses managing compliances with Regulatory bodies, Legislation and ensuring that the Board processes run efficiently and effectively.

In her most recent role, Iffath managed a successful application to register a higher education provider with Tertiary Education Quality and Standards Agency (TEQSA). Iffath holds a Degree in Law and Commerce. Iffath is a member of the Governance Institute of Australia. In addition to being a registered Lawyer in India, she is working on her registration as a Lawyer in Victoria with the Victorian Legal Admissions Board (VLAB).

Andrea Hayman

Head of Training Programs

Andrea has stepped into the world of speciality medical colleges after vast experience in the Vocational Education and Training Sector. Andrea has dealt with the dynamic VET environment, she supported and implemented requirements of VET Quality Management System, incorporating Australian Skills Quality Authority (ASQA) requirements. These included compliance, instructional design, preparation, maintenance, coordinating and evaluating teaching and learning resources across a range of qualifications and various units of competency. Andrea ensured that all requirements for qualifications were covered, and the licensing requirements of courses were maintained. She provided support in developing appropriate skills and knowledge to fulfill strategic and operational objectives. Working with third-party organisations in expanding opportunities, Andrea's quality assurance and compliance management fostered relationships that were beneficial to all stakeholders.

Andrea believes in lifelong learning and holds a Bachelor of Business specialising in Accounting and Finance, a Graduate Diploma of Education, Graduate Certificate in Education and Training for Sustainability, and six Diplomas covering sustainability, adult education, human resources, leadership and management and business.

Stephen White

Deputy Director of Education

Stephen heads up the Curriculum, Evaluation and Accreditation unit within the Education Directorate, providing leadership in the areas of curriculum and training program development, evaluation of training and trainee experiences, and accreditation of training sites. He also plays a leading role in activities regarding the College's own accreditation by the Australian Medical Council and Medical Council of New Zealand.

With an Honours degree in English Studies, Stephen worked in academic publishing for eight years in the UK before moving to Australia. He then spent 11 years in a senior management role in curriculum and learning resource development in the vocational education and training sector, before shifting into the specialist medical college world. Stephen worked on strategic education projects – including curriculum development – for the College of Anaesthetists, before joining RANZCOG in early 2020.

Matthew Stewart

Head of Examinations

Matthew is responsible for leading the examinations team, overseeing the development and delivery of the College's written and oral exams. The examination team currently help develop and deliver exams for the FRANZCOG, DRANZCOG, CWH and Subspeciality programs.

Matthew joined RANZCOG in 2022 after a 17-year career as a healthcare professional and educator, having worked in a range of metropolitan, rural and remote settings as an Emergency Department Registered Nurse and Registered Paramedic. For the last seven years, he has been heavily involved in the education and assessment of undergraduate and registered healthcare professionals. In addition to his duties at RANZCOG, he still actively teaches and course directs a range of programs such as the Advanced Life Support level 2 and Pre-hospital Trauma Life Support Courses.

Matthew currently holds registration as a Registered Nurse and Paramedic. He has a Bachelor of Nursing, Graduate Diploma of Paramedicine and Master of Emergency Health. He has delivered one baby so far in his career.

Guest Editorial

A/Prof Orla M McNally
FRANZCOG, CGO

Dr Deborah Neesham
FRANZCOG, CGO

Gynaecological cancers represent a large burden of disease for women and their carers in Australia and New Zealand. In 2017, with 5,823 new cases, they accounted for 9.3% of cancers diagnosed in women, with uterine cancers being the most common. By 2021 it was estimated that the risk of having a gynaecological cancer was 1 in 23 (4.4%) by the time a woman reaches 85 years of age. Globally a cancer diagnosis will also be made in 1 in 2000 pregnancies with the majority of these being breast cancers and accordingly the need for consensus guidelines for pregnant women with cancer is increasingly recognised.

Tracking a parallel course with the obesity epidemic in the western world, the number of women receiving care for uterine cancer continues to rise. While the majority have early disease and will likely be cured with surgery, the survival rates for advanced disease are dismal so the recognition of molecularly distinct endometrial tumours that may benefit from target-based therapies going forward is showing exciting promise and indeed, at the same time, may save many others the toxicity associated with traditional adjuvant therapies such as radiotherapy and chemotherapy.

In contrast to the tsunami of uterine cancers, the number of cases of ovarian cancer (now recognised as including ovarian, fallopian tube and primary peritoneal cancers, OFP) appears to be falling and published mortality rates in Australia are showing a downward trend.[2] The falling incidence has been linked to oral contraception usage over time which reduces ovarian cancer risk with increasing length of use up to ten years, as well as the recognition of at-risk women with genetic mutations with the opportunity to intervene at the appropriate time with risk reduction strategies such as bilateral salpingo-oophorectomy, acknowledging that there is no current recommendation for population screening or screening of any high-risk women. Whether salpingectomy alone proves to be a significant strategy to reduce risk remains to be seen and is being explored in a number of ongoing international studies. The advent and effectiveness of poly ADP-ribose polymerase inhibitors (PARPi) in women with OFP cancers with a BRCA mutation (somatic/germline) means that for the first time ever gynaecological oncology specialists are beginning to talk about 'cure' even in women with advanced disease at diagnosis.

While each gynaecological cancer may be considered as a unique disease and indeed by definition rare, as a group, gynaecological cancers represent the fourth most common cancer diagnosis in women and are most appropriately managed by the same multidisciplinary group of medical practitioners. This is particularly important with the implication of strategies set to eliminate cancers such as cervical cancer. Australia and New Zealand are considered world leaders in this regard with the success of the national HPV vaccination programs for primary prevention and robust screening programs for secondary prevention. Ongoing efforts will still be required in at-risk groups, Māori and Indigenous Australian women, for whom screening rates remain low. The latter is more reflective of the global burden of gynaecological cancer with cervical cancer being the most commonly diagnosed cancer and continuing to increase in incidence and be responsible worldwide for most gynaecological cancer deaths with the highest burden of disease in regions with a low sociodemographic index (SDI).[3]

Gynaecological cancer care is well established in Australia and New Zealand, and it is great that this issue is dedicated to cancer. It is by no means exhaustive in covering all aspects of cancer care but it provides many important updates as well as inspiring contributions from a consumer, a general practitioner involved in end-of-life care and a community project team providing local support in close collaboration with medical practitioners.

With ongoing advocacy and dedicated research, we as a medical profession can continue to strive to provide holistic care for women at risk of, and diagnosed with, gynaecological cancers and cancers in pregnancy.

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The epidemiology of gynaecological cancers

Clin. Associate Professor Emma Allanson
MBBS(Hon), MPHTM, FRANZCOG, PhD, CGO
Consultant Gynaecologic Oncologist,
King Edward Memorial Hospital for Women
Western Australian Gynaecologic Cancer Service

Dr Chloe Ayres
MBBS, FRANZCOG, CGO
Consultant Gynaecologic Oncologist,
King Edward Memorial Hospital for Women
Western Australian Gynaecologic Cancer Service

In 2021, there were 6,576 new cases of gynaecological cancer diagnosed in Australia, and in 2019 there were 1322 new cases of gynaecological cancer diagnosed in New Zealand.

As a group, this represents 9.3% of cancers diagnosed in women, with endometrial cancer being the most commonly diagnosed gynaecological cancer in both countries, coinciding with the worldwide obesity epidemic. It is estimated that an Australian female has a 1 in 23 (or 4.4%) risk of being diagnosed with a gynaecological cancer by age 85. Gynaecological cancer as a group represents 10% of cancer-related deaths in women, with ovarian cancer being the most common cause of gynaecological cancer-related death. With over 21,000 women in Australia living with a gynaecological cancer at the end of 2016 (diagnosed in the preceding five years), there are important survivorship issues to be considered.[1,2] (Table 1)

Endometrial cancer

Endometrial cancer is the commonest of both the gynaecological cancers and the uterine malignancies, accounting for more than 90% of the latter. Both the incidence and mortality associated with endometrial cancer are increasing in Australia and New Zealand. Obesity, nulliparity and diabetes are all increasing in incidence and are all independently associated with the risk of developing endometrial cancer. Obesity accounts for up to half of all endometrial cancers in high-income countries, and we are no exception. Sixty percent of Australian women are overweight or obese and more than 10% of Australian women have a BMI of 35 or more.[3] Furthermore, the fertility rate has fallen in the last decade from 1.9 births per woman to 1.5 and the incidence of diabetes has increased since 2001 to 1 in 5 Australian women.[4]

The biggest change we are seeing in endometrial cancers is in its classification. We are increasingly moving away from classifying endometrial cancer as type 1 and type 2, as described by Bokhman in 1983, whereby type 1 cancers associated with obesity and metabolic syndromes were considered to have a more favourable prognosis, and those with type 2 cancers, occurring independent of these risk factors, behaved more poorly. The Cancer Genome Atlas (TCGA) published a comprehensive genomic analysis of endometrioid and serous endometrial carcinomas in 2013, and we now understand these endometrial cancers to be classified as being a part of four distinct molecular subgroups; POLE ultramutated, microsatellite instability hypermutated, copy-number low, and copy-number high. This molecular classification is increasingly guiding prognostication and the use of adjuvant therapy.[5]

Ovarian cancer

Ovarian cancer encompasses the epithelial, germ cell and sex cord stromal histologies, with epithelial cancers being the most common and the most lethal. Ovarian cancer is the ninth most common cancer diagnosed in New Zealand women, and three Australian women die every day from ovarian cancer.[1,2] One of the significant risk factors for the development of epithelial ovarian cancer is having a familial cancer syndrome such as a BRCA mutation or Lynch syndrome. While the incidence of ovarian cancer has remained largely unchanged in the last three decades, the age standardised mortality rate in Australia has decreased from 8.8 deaths per 100,000 females in 1982 to 6.5 deaths per 100,000 in 2019.[1] Radical surgical management, advances in chemotherapy including the use of intraperitoneal chemotherapy (which may or may not be heated), and molecular targeting agents such as poly adenosine diphosphate–ribose polymerase inhibitors (especially for patients with BRCA mutations) and vascular endothelial growth factor (VEGF) receptor inhibitors have likely all contributed to this reduction in mortality.

Cervical cancer

Cervical cancer is the 11th and 12th most commonly diagnosed cancer in women in Australia and New Zealand respectively, and in both nations represents just over 1% of all gynaecological cancers diagnosed and of cancer deaths in women.[1,2] Risk factors for the development of cervical cancer include human papilloma virus (HPV) infection, smoking, number of sexual partners, concurrent immunosuppression including with the Human Immunodeficiency Virus (HIV), and prolonged use of the combined oral contraceptive pill. Persistent infection with high risk types of HPV remains the greatest risk factor for the development of cervical cancer. Both Australia and New Zealand have national immunisation and screening programs to prevent cervical cancer and have seen significant decreases in incidence and death from disease in the last 30 years. The use of population-based HPV vaccination programs is demonstrated to result in reductions in both HPV infections and in the detection of high-grade cytological cervical abnormalities,[6] which results in the corresponding reduction in cancer diagnoses and the clear pathway we are on to the elimination of cervical cancer in our nations. If the combined approach of HPV vaccination and co-test screening coverage is maintained at the current rates, cervical cancer is likely to be eliminated as a public health issue in Australia by 2035. Cervical cancer rates will fall below 4 in 100,000 and the associated mortality will fall below 1 per 100,000 women. Despite this there remains challenges, with Māori women and Indigenous Australian women continuing to have a high incidence of, and mortality from, the disease.[7]

Vulvar cancer

Vulvar cancer is rare and represents about 5% of malignancies of the female genital tract. It includes cancers of the mons pubis, labia majora and minora, clitoris and Bartholin's gland. Squamous cell carcinomas account for 85–90% of cases, whereas basal cell carcinomas, melanomas, invasive Paget's disease, Bartholin's gland carcinomas (where a variety of histologic types may occur), and sarcomas are much less common. Vulvar cancer is typically diagnosed in women over the age of 60 with the highest proportion of cases among women over 80.

The age standardised incidence of vulvar squamous cell carcinomas (SCC) has not changed significantly. However, over the past 30 years, HPV-dependent vulva cancer rates have increased by 84% in women under the age of 60. These findings are consistent with an increase in the proportion of HPV-attributable cases of vulvar cancers as a result of changing sexual behaviour in women born from the 1950s onwards, and increased exposure to HPV in this group.[8] We are also now seeing that differentiated VIN (dVIN) (HPV-independent and frequently lichen sclerosus associated) has a greater risk of, and more rapid transit to, vulvar squamous cell carcinoma. Furthermore, dVIN-associated vulvar cancers have an increased risk of recurrence and higher mortality (93% vs 68% five-year survival)[9] than those arising from HSIL, which has changed the way we manage these patients.[10]

Vaginal cancer

Vaginal cancer is one of the rarest gynaecological cancers and represents 1–2% of malignant neoplasms of the female genital tract. Squamous cell histology accounts for the majority of cases and risk factors include HPV exposure, genital tract dysplasia, cervix cancer and smoking. It is more common in women over the age of 60, however, vaginal adenocarcinomas in particular can occur in younger women, including with in utero DES exposure, which we see infrequently

		Uterine	Ovarian	Cervix	Vulva	Vaginal
Estimated number of new cases diagnosed	Australia (2021)	3267	1720	913	433	116
	New Zealand (2019)	686	260	187	64	17
Estimated rate of all new female cancer cases diagnosed	Australia (%)	4%	2.4%	1.3%	0.6%	0.2%
	New Zealand (per 100,000)	18.4	7.1	6.7	1.4	0.4
Estimated number of deaths	Australia	349	1042	237	107	30
	New Zealand (per 100,000)	113	208	50	14	
Estimated contribution to all female deaths	Australia (%)	1.7%	4.8%	1.1%	0.5%	0.1%
	New Zealand (per 100,000)	3.2	5.6	1.7	0.3	
Chance of surviving 5 years (all stages)		85%	48%	74%	73%	52%

Table 1. Australian Institute of Health and Welfare (AIHW)[1] data on gynaecological malignancies and New Zealand Ministry of Health.[12,13]

now. Secondary vaginal cancer that arises from metastases elsewhere [cervix (30% cases), endometrium (20%), colon/rectum (10%), ovary (5%) or vulva (5%)] is in fact more common than primary vaginal cancer.

Gestational trophoblastic neoplasia

The malignant spectrum of gestational trophoblastic disease (GTD), collectively called gestational trophoblastic neoplasia (GTN), can arise from any type of viable or non-viable pregnancy and includes invasive mole, choriocarcinoma (CC) and the even rarer placental-site trophoblastic tumour (PSTT) and epithelioid trophoblastic tumour (ETT). GTN occurs in 15–20% of patients diagnosed with GTD and is fortunately highly sensitive to chemotherapy.

Women from Asia and women at the extremes of reproductive age have the highest incidence. In Australia, there is no nationally coordinated program for the registration or management of GTD which makes assessing incidence and trends difficult. There are State-based registries in Victoria, Queensland, South Australia and New Zealand. WA is close to establishment. The Queensland Trophoblastic Centre (QTC) published their experience over a three-year period from 2012–2015. 407 patients were diagnosed with GTD, of which two had PSTT (0.49%), one CC (0.25%), one ETT (0.25%). 41 were diagnosed with persistent disease (GTN) following a molar pregnancy. All women were cured of their disease, however, one woman with underlying anxiety died by suicide at the end of her treatment, giving an overall survival rate of 97.4%.[11]

Gynaecological malignancies comprise nearly one in ten cancers in Australian and New Zealand women. These women require multidisciplinary care from diagnosis, through treatment, and surveillance. Gynaecological oncologists are available to provide care in all Australian states and territories and across New Zealand.

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Molecular profiling in endometrial cancer

Dr Melissa McGauran
Fellow Gynae Onc RWH

Dr Niveditha Rajadevan
Gynae Oncologist RWH

Uterine cancer is the fifth most common cancer in Australian women and the most common gynaecological malignancy, with women having a 1 in 44 (2.3%) risk of uterine cancer by age 85.[1] Coinciding with rising obesity rates, the incidence of endometrial cancer continues to increase. The majority of women are diagnosed with early-stage disease and surgically managed, with an excellent overall five-year survival rate of 85%.[1] The outcome for women with advanced-stage or recurrent disease, however, is poor with only a 17% five-year overall survival if distant disease is present.[2]

When women are diagnosed with endometrial cancer, risk stratification for recurrent disease currently relies on an assessment of stage, grade and histopathological subtype. Higher stage, higher grade and histopathological subtypes of serous and clear cell carcinomas are associated with poorer prognosis. It is known that the majority (~80%) of women with early-stage endometrial cancer have a good prognosis (95% five-year overall survival), whereas the remaining 20% have at least one risk factor (high-risk histological subtype, higher grade, deep myometrial invasion, lymphovascular space invasion) which is associated with worse prognosis.[2] The challenge for clinicians is determining which patients with early-stage endometrial cancer truly have low-risk disease, and subsequently a low risk of recurrence, versus high-risk disease. Low-risk disease can generally be managed with surgery alone whereas it is recommended that high-risk disease is managed with surgery followed by adjuvant therapy (radiotherapy and/or chemotherapy).[2]

In 2013, The Cancer Genome Atlas (TCGA) published a comprehensive genomic and proteomic analysis of the different endometrial cancer histopathological subtypes. This led to the identification of four distinct molecular subgroups of endometrial cancer with distinct prognostic outcomes.[3] The identification of these molecular subgroups, enabled an objective and reproducible classification system, not relying purely on histological subtype, stage and grade and thus eliminating the issue of reproducibility/inter-observer variation between pathologists. However, due to cost and time constraints, the TCGA classification was not suitable for routine clinical use and so different molecular classification tools using surrogate markers with prognostic signatures consistent with the TCGA subgroups have been explored and validated.

In 2017, the ProMisE classification (Proactive Molecular Risk Classifier for Endometrial Cancer) was introduced.

The ProMisE classification identifies four prognostic molecular subgroups: dMMR (mismatch repair deficient), POLE mutation (DNA polymerase epsilon), p53 abnormal (p53abn) and p53 wild-type/no specific molecular profile (p53wt/NSMP). Molecular testing can be performed on endometrial curettage samples, prior to definitive surgery and potentially guide management, including the timing and extent of surgery. Furthermore, testing can be performed on formalin-fixed specimens, rather than relying on fresh tissue which is more costly and not as widely available.[4]

Tumours with a POLE mutation have the most favourable prognosis whilst the p53abn subgroup is associated with the worst prognosis.[5] A recent study from the Netherlands and Denmark has shown five-year recurrence rates of surgically staged patients to be 36.7% (p53 abn), 13.4% (dMMR), 42.9% (NSMP/p53 WT) and 0% (POLE mut).[6] Irrespective of stage and lymph node status, patients with p53 abn tumours have poor clinical outcomes.[6] Kommoss et al[4] described patients with a p53abn tumour to generally be older, with a lower BMI, mostly serous histopathology and diagnosed at both a higher stage and grade. Conversely, p53wt/NSMP tumours were generally low-grade, low stage and endometrioid histopathology.[4]

Given the distinct prognostic outcomes associated with each of the four molecular subgroups numerous studies are underway to assess how this knowledge can be used to guide both surgical as well as adjuvant treatment decisions. For example, given the favourable prognosis for women with

Molecular Subtype	% of endometrial cancers	Prognosis
POLEmut	~10%	Favourable
NSMP	~50%	Intermediate
dMMR	25–30%	Intermediate
p53 abn	15%	Poor

POLEmut tumours, studies are attempting to determine whether adjuvant therapy can be reduced or avoided altogether in this patient cohort. In contrast, because women with p53abn endometrial cancers are known to have a poorer prognosis, improved outcomes with combination chemotherapy and pelvic radiation versus pelvic radiation alone have been assessed.[2] dMMR endometrial cancers appear to be more susceptible to radiation therapy and appear to have little benefit from chemotherapy.[2] Furthermore, molecular profiling in endometrial cancer can identify those who are more likely to respond to immunotherapy (dMMR) and ongoing research is investigating those more likely to respond to progestogens (NSMP).[2] dMMR is found in 25–30% of all endometrial cancers and in most cases is due to tumour methylation; however, 10% of dMMR endometrial cancers are associated with Lynch syndrome and if methylation is absent referral for genetic counselling is recommended for formal testing.

The role of lymph node assessment in endometrial cancer (either sentinel lymph node or lymphadenectomy) continues to be debated, with a wide range of practices throughout the world. Each molecular subtype has an associated risk of lymph node metastases: 44.8% of p53 abn, 14.2% POLEmut, 14.9% dMMR and 10.8% p53wt. Knowledge regarding molecular subgroups in endometrial cancer can help guide lymph node assessment for women, particularly those with p53abn tumours.[7] There is also scope for molecular profiling in endometrial cancer in assisting decision making regarding fertility-sparing management and what constitutes optimal surveillance following treatment.[4]

In the era of personalised cancer medicine, molecular classification should be considered for all endometrial cancers and performed routinely in all high-grade tumours particularly when the result will impact treatment decisions.[2] For accurate molecular classification, all four of the molecular subtypes must be tested (rather than a single test in isolation), as up to 5% of carcinomas have more than one subtype.[8] However, whilst molecular classification does increase the cost associated with pathological testing, and not all countries worldwide will have sufficient resources to perform testing, it has the ability to guide management and improve outcomes for women, and may actually reduce overall healthcare costs by avoiding unnecessary adjuvant treatment.

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Cancer in pregnancy

Clin. A/Prof Emma Allanson
MBBS, MPHTM, FRANZCOG, PHD, CGO
Consultant Gynaecologic Oncologist
King Edward Memorial Hospital for Women
Western Australian Gynaecologic Cancer Service

Dr Michael Burling
BHB MBChB PGDipOMG FRANZCOG CGO
Staff Specialist in Gynaecological Oncology
Westmead, Liverpool and Westmead Private hospitals

Dr Shih-Ern Yao (he/him)
MBBS (Hons), FRANZCOG, GradCertPallCare, CGO
Consultant – Gynaecological Oncology
Adjunct Senior Lecturer – Obstetrics &
Gynaecology, Monash University

Dr. Kristen Moloney
MBBS FRANZCOG CGO
Royal Brisbane and Women's Hospital

Dr Niveditha Rajadevan
Gynae Oncologist RWH

General principles

Cancer in pregnancy is extremely rare, affecting approximately 1 in 2000 pregnancies. A rise in incidence is expected and is becoming evident in population-based studies. Delayed child-bearing and non-invasive prenatal testing (which may detect asymptomatic cancer) are the most likely contributory factors.[1]

Involvement of a multidisciplinary team is crucial to the sound and evidence-based management of any malignancy, and this is particularly applicable to cancers in pregnancy which remain uncommon. Given dilute experience in gestational cancer management amongst both treating specialists and centers, collaboration is key and should involve discussion between senior oncologists, maternal-fetal medicine specialists and perinatologists. Key resources are available through the International Network on Cancer, Infertility and Pregnancy[2] including a 2019 publication which provides international consensus-based guidelines.[3]

In an effort to address the paucity of Australian data on cancer in pregnancy, the Cancer Council of New South Wales are co-ordinating a state-wide investigation into gestational cancers.[4] The results of this project will inform the creation of evidence-based and patient-centred resources, leading to improved quality of care and better support for women with cancer in pregnancy in Australia.

The overarching principle of gestational cancer management is to manage the malignancy on its merits, and then determine what allowances can be made for the pregnancy and the fetus. When making decisions about investigation and management, the aims are:

1. To account for both maternal and fetal concerns
2. To facilitate standard maternal treatment if possible
3. To prevent iatrogenic prematurity

Cervical cancer in pregnancy

Approximately 5% of pregnant women will have abnormal cervical cytology and routine antenatal care should include a cervical screening test if due. Colposcopic examination of the pregnant cervix should be undertaken by an experienced colposcopist. Indications for urgent referral to a gynaecologic oncologist include LBC prediction of invasive disease, colposcopic impression of invasive carcinoma, and histologically confirmed invasive carcinoma. The National Cervical Screening Guidelines are a great resource, providing a clear and succinct strategy for the management of HSIL on cytology in pregnancy.[5]

Colposcopy in pregnancy is undertaken with a view to excluding invasive disease. High-grade lesions diagnosed during pregnancy can be safely deferred for treatment until after delivery because progression

to invasive disease during the pregnancy is rare. Of those cases that do progress, most are microinvasive and amenable to curative treatment. Biopsy is safe during pregnancy but is not usually necessary unless invasive disease is suspected.

Once a tissue diagnosis of invasive cervical cancer in pregnancy has been made, the next step is to determine disease extent. Radiologic staging investigations in the non-pregnant patient include MRI pelvis and FDG–PET.[6] In the pregnant woman, most clinicians would make allowances for the fetus by instead using CXR with abdominal shielding and MRI. As in the non-pregnant patient, a variety of treatment options are available but are dependent on stage of disease and maternal desire to continue the pregnancy. When considering these options, it is useful to first consider standard management, then consider how such management might be adjusted to account for the pregnancy. Table 1 provides a guide for comparing standard management versus pregnancy-adjusted options for early-stage disease.

Ovarian cancer in pregnancy

As in the non-pregnant state, most ovarian malignancies are diagnosed after surgical excision with majority presenting as asymptomatic adnexal masses, commonly detected on ultrasound examination. Approximately 2.4% of pregnancies are complicated by an adnexal mass, and 1-6% of these masses are malignant.[7-10] Ovarian cancer ranks behind breast, haematologic, thyroid and gastrointestinal tract[11] as the most common primary sites for cancers diagnosed during pregnancy but remains the second most common gynaecological malignancy after cervical cancer. Epithelial subtypes make up approximately 50% of cases, (half of which are borderline tumours), germ cell tumour representing another third and rarer tumour types and metastases making up the rest of presentations.

When symptomatic, complaints are similar to those regularly reported during pregnancy (eg. abdominal swelling/discomfort, back/pelvic pain, constipation and urinary frequency), making diagnosis even more challenging. Other times when an adnexal mass has been diagnosed in pregnancy have been after adnexal torsion or incidentally at caesarean delivery.

Ovarian tumour markers (eg. AFP, CA125, hCG, LDH, inhibin) are not as useful in pregnancy as levels may be influenced by gestational age, fetal abnormalities and maternal comorbidities. Consequently, the use of ultrasound and MRI to characterise adnexal masses are more heavily relied upon when suspicions for ovarian cancer are raised. Features such as solid components, papillary projections, septations and vascular elements or evidence of loco-regional disease should prompt referral for gynae oncology opinion and management. CT should be avoided as exposure has been linked with miscarriage, congenital abnormalities, IUGR, neurological effects[12-16] and childhood cancer and leukaemia.[17-18]

Surgical intervention is generally indicated where suspicion for malignancy is significant or when lesion size may confer an increased risk for rupture, torsion or labour obstruction. Surgery is preferably performed in early second trimester by a multidisciplinary team (gynae oncologist, high risk obstetrician, neonatology, anaesthetics, midwifery and allied health) with cases diagnosed later often able to be managed expectantly. A unilateral salpingo-oophorectomy +/- staging should be performed through an incision which will maximise exposure, avoid tumour disruption and minimise manipulation of the pregnant uterus. Peritoneal washings and thorough inspection of the abdominopelvic cavity should be performed and biopsies from suspicious areas taken for pathological assessment. Frozen section may be utilised if this would change the patient's wishes for intra-operative management. The role of primary cytoreduction in the setting of advanced stage disease would not generally be considered if other treatment options (eg. neoadjuvant chemotherapy) are available.

Ultimately, pathological confirmation is key to guiding the ongoing management of both patient and pregnancy and should be discussed at a

Table 1. Standard management for cervical cancer versus pregnancy-adjusted options for early-stage disease.

FIGO stage	Standard management	Pregnancy-adjusted management	
IA1 (+/- LVSI)	Cone biopsy +/- pelvic lymphadenectomy	Cone biopsy +/- pelvic lymph node assessment. Vaginal delivery can proceed provided cone margins are negative.	
IA2-IB2 <22 weeks	Radical hysterectomy + pelvic lymphadenectomy or primary concurrent chemoradiation	Pelvic lymphadenectomy with further action dependent on nodal status	
		Node positive Termination* and primary chemoradiation	Node negative Watchful waiting until fetal maturation followed by caesarean- or postpartum radical hysterectomy.
IA2-IB2 >22 weeks		Neoadjuvant chemotherapy or delay treatment until after delivery	
**If termination is declined, careful counselling regarding poor prognosis is required (nodal positivity confers FIGO Stage III disease)*			

multidisciplinary level with recommendations for treatment highly dependent on gestational age, extent of disease and patient wishes. Further surgery is generally reserved until after delivery and systemic chemotherapy can and has been used safely during pregnancy, but needs to be balanced against chemotherapeutic side effects and possible risks (eg. congenital malformation, premature labour, IUGR, neonatal marrow suppression).

Non-gynaecologic malignancies in pregnancy

Breast is the most common cancer in pregnancy with an incidence of 2.3 to 40 cases per 100,000 women.[19] Over 90% of patients will present with a palpable mass.[20] The histology of tumours appears to age-matched women who are not pregnant but the stage of disease at diagnosis is more advanced which incurs a worse prognosis. This is likely due to a delay in diagnosis.[21] Diagnosis is made on USS and core biopsy. Surgery and chemotherapy are the main treatment of choice. Radiotherapy, endocrine therapy and target therapy are generally contraindicated.

Colorectal cancer is the seventh most common type of cancer diagnosed in pregnancy, with an estimated incidence of 7–8 per 100,000 pregnancies.[22] Diagnosis can be challenging as the signs and symptoms are masked by pregnancy. Approximately 60% present at an advanced stage (at least stage III) and 86% are generally in the lower rectum.[24] Diagnostic investigations like endoscopies can be difficult but may be necessary depending on the clinical suspicion. Management principles are the same as other cancers in pregnancy.

Lymphomas, most commonly Hodgkins lymphoma, are the fourth most common malignancy in pregnancy occurring in approximately 1 in 6000 pregnancies.[25,26] Diagnosis is often delayed due to an overlap of features characterising both the malignancy and pregnancy (weakness, sweating, shortness of breath, pain).[5]

Treatment options are generally dependent upon histological diagnosis, stage at presentation, gestation, and maternal wishes regarding the pregnancy. Given the rarity of haematological malignancies in pregnancy, multidisciplinary involvement is important. Given the increased risks of chemotherapy to the developing fetus in the first trimester, if possible, chemotherapy should be delayed until the second trimester unless this compromises maternal outcome.[25] If treatment cannot be delayed beyond the first trimester, then pregnancy termination may be required. Broadly, acute leukemias should be managed without delay as any delay may seriously affect maternal prognosis. Conversely, lymphoma treatment may be delayed without maternal risk.

Rare cancers in pregnancy

In Australia, despite lung cancer being the fourth commonest cancer diagnosed in women and the leading cause of cancer related mortality,[28] its incidence in pregnancy is rare. Adenocarcinomas are the most common histology, accounting for approximately 80% of cases.[29] >97% of women are diagnosed with locally advanced or metastatic disease; possibly due to symptoms being attributed to other causes or a reluctance to investigate in pregnancy.[29]

Treatment options are largely drawn from expert consensus opinion, case reports and standard treatment options in non-pregnant women. Given this, and that maternal outcome in lung cancer is generally very poor with many women succumbing to their disease within the first year after delivery,[29] multidisciplinary discussion is vital. Obstetricians and neonatologists should be involved in the decision-making process.

The management of rare gynaecological tumours in pregnancy including endometrial, vulval and vaginal cancer is derived largely from case reports, expert opinion, and extrapolation from management outside of pregnancy.

Endometrial cancer diagnosed shortly after pregnancy (whether first trimester loss or term pregnancy[30]) is generally associated with a favourable prognosis. Most are reported to be low grade and can be managed as standard. Uncommonly, endometrial cancer may be diagnosed on uterine sampling on a woman who is subsequently found to be pregnant. In these cases, standard of care does not allow for continuation of the pregnancy.[31]

There is an increasing incidence of vulval cancer in young women, which may result in diagnoses during pregnancy.[32] Early vulval cancer can be managed similarly to outside of pregnancy, including radical wide local excision and sentinel node biopsy, although the management needs to be tailored to the pathological features of the malignancy and the gestation of pregnancy.[33] The sentinel node biopsy can be performed with technetium-99 and a gamma detection probe with omission of lymphoscintigraphy.[31] Caesarean delivery is advised. In the very rare occurrence of an advanced vulval cancer, care should be tailored to the gestation at diagnosis, and may include the use of neoadjuvant chemotherapy in pregnancy prior to delivery and definitive management.

Vaginal cancer is exceedingly rare in pregnancy with limited case reports.[31] The approach to management is multidisciplinary team consensus based, and depends on stage, with extrapolation on treatment options from the more commonly seen cervical cancer in pregnancy.

Complete hydatidiform molar pregnancy with co-existing fetus is uncommon and reported to occur between 1 in 10,000 and 1 in 100,000 pregnancies. Management should be tailored to take into account the features of the live fetus (karyotype and anatomy) as well as the potential for pregnancy complications in the woman, including pre-eclampsia.[31]

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Ovarian cancer screening

Dr Lachlan Baxter
BSc, MBBS (Hon)
4th year RANZCOG ITP registrar
King Edward Memorial Hospital, Perth

Prof Paul A. Cohen
FRANZCOG MD
Western Australia Gynaecological Cancer Service
Clinical Professor, UWA
Director of Gynaecological Cancer Research
St John of God Subiaco Hospital, Perth

Ovarian cancer is the seventh most common cancer among women globally, with 46% survival five years after diagnosis.[1] In 2020 there were more than 313,000 new ovarian cancer diagnoses worldwide and more than 207,000 deaths due to the disease.[2] Ovarian cancer has a poor prognosis because it presents with non-specific symptoms (Table 1) and is diagnosed at an advanced stage in more than two-thirds of patients. Late-stage presentation has a five-year relative survival rate of 30%, compared to 93% for early-stage disease.[3] Consequently, there is a pressing need for an effective screening test that would allow earlier detection of ovarian cancer in asymptomatic women with the goal of reducing the number of deaths due to the disease. The cancer antigen-125 (CA125) blood test and transvaginal ultrasound scan (TVS) have been the most extensively studied screening tools to date but have not reduced ovarian cancer mortality in randomised controlled trials.

Ovarian cancer screening in the general population

The low prevalence of ovarian cancer, and relatively poor specificity and positive predictive value of CA125 and TVS used alone on a single occasion can result in false positive screening results that lead to unnecessary surgical interventions. In 2018 the US Preventive Services Task Force issued a recommendation against population-based screening for ovarian cancer, based on a review of four randomised screening trials.[5] The two largest studies were the Prostate, Lung, Colorectal and Ovarian screening trial (PLCO) and the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS).[6,7] The PLCO trial included 68,557 women undergoing yearly CA-125 and TVS compared to no screening in a US population. No reduction in ovarian cancer mortality was observed (RR 1.18 95% CI 0·82–1·71) and 3285 women experienced a false positive result with 1080 of those undergoing surgery. Improved sensitivity, specificity and positive predictive value has been achieved with two stage screening strategies where an increase in serial

Patient reported symptomatology	Incidence in women subsequently diagnosed with ovarian cancer
Abdominal pain/ discomfort	62%
Abdominal swelling/ bloating	57%
Fatigue	47%
Urinary tract symptoms -urgency/frequency	27%
Early satiety	16%
Decreased appetite	20%
Back pain	48%
Constipation	21%
Weight change	11%
Vaginal bleeding	13%

From Goff B. Symptoms associated with ovarian cancer.[4]

Table 1. Symptoms associated with ovarian cancer.

serum CA125 triggers a TVS.[8] The UKCTOCS was a randomised control trial of 202,638 women receiving either no screening, TVS, or multimodal screening (MMS) comprising a proprietary algorithm – the Risk of Ovarian Cancer Algorithm (ROCA), which incorporates historical CA-125 levels and current CA-125 levels to triage women to additional investigation with TVS. UKCTOCS is the largest randomised trial of ovarian cancer screening and one of the largest randomised trials ever conducted. At a median follow up of 16.3 years (IQR 15.1 – 17.3) there was no reduction in ovarian cancer deaths in either the MMS or TVS group, with hazard ratios of 0·96 [95% CI 0·83–1·10] for MMS vs no screening and 0·94 [0·82–1·08] for TVS vs no screening. There was a 'stage shift' observed at diagnosis, with a 24.5% lower incidence of stage IV disease and a 47.2% higher incidence of stage I/II in the MMS arm, but although some cancers were detected earlier this did not translate to a decrease in disease-specific mortality. UKCTOCS did not include analyses by ovarian cancer histotype, which is a limitation of the study. Such analyses would likely not have been feasible for the rarer histotypes but would have been possible for high-grade serous ovarian cancer which is the most common subtype.[3]

Ovarian cancer screening in high-risk populations

Approximately 10% of patients with an epithelial ovarian malignancy, and 17% of those with high-grade serous carcinomas, will have a genetic predisposition (Table 2).[9] Women with pathogenic germline variants in BRCA1/2 have a risk of developing an ovarian malignancy of 17–44%, compared to the general Australian population risk of 0.9% by age 80.[10,11] The definitive, and currently only, evidence-based strategy for individuals at high risk of ovarian cancer due to pathogenic germline variants is a risk reducing bilateral salpingo-oophorectomy.[12] Whilst this is highly effective in reducing ovarian cancer incidence and mortality, it carries with it the implications of surgical menopause and loss of fertility in reproductive age group women.

The Cancer Genetics Network and Gynecologic Oncology Group assessed 3818 women at elevated risk of ovarian cancer every three months with CA-125, yearly TVS, and a reflex TVS in event of rising CA-125.[13] Whilst nine ovarian cancers were identified, there were 20.7 false positives for every case of cancer detected. The United Kingdom Familial Ovarian Cancer Screening Study enrolled 4531 women at high risk using a similar screening strategy.[13] Whilst this study showed a shift towards a lower stage at diagnosis in screened women most of these women were diagnosed at the time of a risk reduction surgery, not as part of the screening protocol. Australian guidelines currently recommend against screening in asymptomatic high-risk individuals.[12]

What is happening in current practice?

Despite evidence that screening for ovarian cancer does not reduce mortality, screening occurs frequently. A recent survey study of 1264 high-risk women enrolled in an Australian breast cancer cohort with more than 832 respondents (response rate 65.8%), and 531 clinicians (GPs and gynaecologists), with 252 respondents (response rate 47.4%), found that 15% of women had been screened for ovarian cancer in the preceding two years despite national guidelines that recommend against it.[14] Although most clinicians agreed there was no reliable way to detect ovarian cancer at an early stage, and that screening can lead to unnecessary investigations and surgery, about half agreed that they would usually order a CA125 and TVS upon patient request. Inappropriate screening is performed for a variety of reasons including patient expectations, medicolegal concerns, and a belief that screening reduces mortality. Many patients believed that screening would improve survival and overestimated their personal risk of ovarian cancer. Previous studies have found that up to 50% of clinicians in the US request ovarian cancer screening for average risk women.[15,16] Interventions to reduce inappropriate screening are likely to require complex individual and system-based approaches that incorporate patient and clinician education, behavioural change strategies, decision support tools and regulatory processes.

Future prospects

In recent years there has been a paradigm shift in our understanding of the aetiology of high-grade

Pathogenic gene variant	Lifetime risk of epithelial ovarian/fallopian tube/ primary peritoneal cancer risk
BRCA1	44% to age 80 years
BRCA2	17% to age 80 years
RAD51C	11% to age 80 years
RAD51D	13% to age 80 years
BRIP1	6% to age 80 years
PALB2	5% to age 80 years
MLH1, MSH2, MSH6, PMS2 (Mismatch repair genes/Lynch Syndrome)	MLH1 – 11% to age 70 years MSH2 – 17% to age 70 years MSH6 – 11% to age 70 years PMS2 – 3% to age 70 years

From eviq.org.au.[12]

Table 2. Lifetime risks of epithelial ovarian/fallopian tube/primary peritoneal cancer for specific pathogenic germline gene variants.

serous carcinoma, the most common and lethal 'ovarian cancer' histotype. The advent of next generation sequencing technology enabled genomic analyses of omental metastases and fallopian tubes in patients with advanced disease and showed that in situ lesions in the tubal epithelium – serous tubal in situ carcinomas (STICs) – are the precursors to high-grade serous carcinoma.[17] It is now accepted that most high-grade serous 'ovarian' cancers originate in the distal fallopian tube.[18] Thus, in high-grade serous cancer, malignant cells on the ovarian surface are in fact metastatic deposits of fallopian tube origin, which challenges the concept of stage I 'ovarian cancer'. Given the tubal origin of high-grade serous carcinoma, efforts have been focussed on early identification of small fallopian tube cancers such as cytologic sampling of the fallopian tubes using hysteroscopic brush cytology.[19] Further, opportunistic salpingectomy, which is the removal of fallopian tubes during hysterectomy or instead of tubal ligation without removal of ovaries, reduced ovarian cancer risk in a population-based cohort study in British Columbia.[20]

RANZCOG now recommends consideration be given to opportunistic bilateral salpingectomy at the time of hysterectomy for benign gynaecological disease and that the risks and benefits be discussed with the patient on a case-by-case basis and that consideration should be given to bilateral salpingectomy instead of tubal occlusive procedures for female sterilisation.[21] In high-risk individuals, such as carriers of pathogenic germline variants in BRCA1/2, current Australian guidelines do not recommend bilateral salpingectomy as a risk reducing strategy due to lack of evidence of safety.[11] Clinical trials of risk reducing bilateral salpingectomy and delayed bilateral oophorectomy performed closer to the age of natural menopause in high-risk individuals have recently opened to recruitment in Europe and the US.[22]

There is potential for additional protein biomarkers as screening tools to be used in combination with CA125 such as human epididymis protein-4 (HE4) as well as biomarkers such as TP53 autoantibodies, circulating tumour DNA, microRNAs, and DNA methylation, but these require further development, validation, and testing in randomised controlled trials.[3,23] Novel imaging technology such as radiomics and radiogenomics may improve detection and form part of a multimodal screening approach.[24] Resources from the UKCTOCS trial will likely play a key role in future biomarker research and validation as many longitudinal serum samples were obtained during the trial with linked clinical data.

Conclusion

Currently evidence does not support ovarian cancer screening in healthy asymptomatic women regardless of their level of risk. Novel technologies offer considerable promise, and ongoing research for a cost-effective screening test that reduces ovarian cancer mortality is an imperative. In the meantime, strategies such as opportunistic salpingectomy in low-risk populations, and identification of genetic risk with counselling and appropriately timed risk-reducing salpingo-oophorectomy, are integral public health measures to reduce ovarian cancer incidence and mortality.

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Advances in treatment of ovarian cancer

Dr Kasia Michalak
MBBS (Hons), BMedSc
Senior O&G Registrar
Royal Women's Hospital

Dr Monique Topp
Medical Oncology Fellow
Peter MacCallum Cancer Centre

Ovarian cancer is a devastating diagnosis affecting 1 in 87 Australian women in their lifetime.[1] Patients are often diagnosed at an advanced stage portending a poor prognosis. The five-year survival rate is 48%.[1] Ovarian cancer is a heterogenous disease, comprised of different histological subtypes with distinct aetiologies and molecular profiles that can potentially be exploited by targeted treatment approaches. Recently, new advances in molecular sequencing have enabled more rapid and cost-effective profiling. This has come alongside the advent of PARP inhibitors which have revolutionised the treatment of ovarian cancer, improving progression-free survival (PFS) and potentially curing some women. This review will focus primarily on the implications of molecular profiling for the treatment of epithelial ovarian cancer.

Aetiology of ovarian cancer

Tumourigenesis may be caused by a wide range of genomic mutations, in combination with various non-genetic risk factors. The most common genetic causes of ovarian cancer are homologous recombination deficiency and mismatch repair.[2]

Homologous recombination deficiency (HRD)

Homologous recombination (HR) is the high-fidelity method employed by cells to repair double-stranded DNA breaks. In HRD, breaks are repaired using alternative error-prone techniques that lead to aberrant DNA, predisposing the tissue to tumour development.

The best-known ovarian cancer susceptibility genes, BRCA1 and BRCA2, code for proteins involved in homologous recombination DNA repair. Mutations in HR genes may be germline, inherited in an autosomal dominant fashion, or somatic, present only in the neoplastic tissue. BRCA mutations can be found in any histologic subtype of ovarian cancer but are most frequently found in high-grade serous ovarian carcinomas (HGSOC). Germline BRCA1 and BRCA2 mutations confer a lifetime risk of ovarian cancer of up to 49% and 21% respectively,[3] hence the recommendation for risk-reducing bilateral salpingo-oophorectomy between the ages of 35–40 in BRCA1 mutation carriers and 40–45 in BRCA2.[4,5]

In Australia, germline BRCA mutations are found in 14.1% of ovarian cancer patients (17.1% in those with HGSOC), 44% of which have no reported family history of breast or ovarian cancer.[6] A further 6–7% have a somatic mutation in BRCA1 or BRCA2.[2,7] Additionally, HR pathway alterations have been documented in a further 25% of HGSOC,[7] including HR pathway genes such as RAD51C, RAD51D and PALB2 (6–10%) and by epigenetic silencing of HR genes, such as methylation of BRCA1 (7–17%) or RAD51C promoters (1.5–3%).[8,9]

Mismatch repair deficiency

The second most common cause of epithelial ovarian cancer is due to mutations in the DNA mismatch repair (MMR) pathway, which account for another 10–15% of ovarian cancers.[2] MMR is a method for recognising and removing mismatched base pairs during DNA replication in otherwise complementary paired DNA strands. Lynch syndrome (also known as hereditary non-polyposis colorectal cancer or HNPCC) is an example of an ovarian cancer susceptibility syndrome in which mismatch repair deficiency is the culprit. The four genes linked to Lynch syndrome, MLH1, MSH2, MSH6 and PMS2, produce DNA mismatch repair proteins. Mutations in these genes confer a lifetime risk of ovarian cancer of up to 17%.[10]

Molecular profiling in epithelial ovarian cancer

For women diagnosed with ovarian cancer, identification of specific genetic mutations has implications for treatment. Cancer Australia recommends that women newly diagnosed with invasive epithelial ovarian, fallopian tube or primary peritoneal cancer, regardless of their age or family history, should be offered assessment of their genetic risk.[11] While mainstream genetic testing for BRCA1 and BRCA2 germline mutations has been integrated into routine cancer care for many women, integration with familial cancer clinics is necessary for all women with a positive result to discuss personal cancer risk and arrange cascade testing for relatives. Given the treatment implications, namely access to PARP inhibitors, somatic mutational testing is now also standard of care. Furthermore, although not standard in Australia, a range of assays referred to as 'HRD tests' have been developed to identify HRD cancers beyond those with BRCA mutations that may also be sensitive to PARP inhibitors.[12]

Next generation sequencing is a term for DNA sequencing technology introduced in the mid-2000s which allows for massively parallel DNA sequencing and hence rapid and economical tumour

genomic profiling for individual patients. This has shifted the focus of genomic profiling from that of mainly risk assessment, to that of therapeutic planning. Alongside improvements in diagnostic tests have come multiple potential targeted therapies for ovarian cancer, including biomarker-driven treatments undertaken in the setting of a clinical trial.

Treatment for ovarian cancer

The cornerstone of treatment for ovarian cancer remains maximal cytoreductive surgery followed by chemotherapy. More recently, the importance of frontline maintenance therapy has been realised, with expanding indications for PARP inhibitor therapy, establishing a new standard of care for HRD ovarian cancers.

Since the 1990s, carboplatin-paclitaxel chemotherapy has remained the standard systemic treatment for ovarian cancer and is successful in shrinking tumour burden in 70–80% of patients. Unfortunately, up to 85% of patients with advanced ovarian cancer have a recurrence after completing chemotherapy.[13] Ovarian cancers with BRCA gene mutations or other HRD have an increased platinum sensitivity and improved prognosis.[14] They also show a superior response to PARP inhibitor therapy and maintenance PARP inhibitor use following platinum response has been shown to extend PFS.

Poly ADP-ribose polymerases (PARPs) are proteins that are key regulators of DNA damage repair processes. PARP inhibitors are a class of drugs that

Table 1. Indication and access of PARP inhibitors

PARP inhibitor	Indication and access		
Olaparib	PBS listed: Maintenance monotherapy in 1st line or following recurrence in platinum sensitive ovarian cancer with BRCA1 or BRCA2 mutations (germline or somatic[1])		
	Efficacy		
	SOLO1	Olaparib 300mg BD vs placebo Population: gBRCAm with PR/CR after chemotherapy	
		Analysis subgroup: ITT gBRCAm	PFS in months: NR vs 13.8 (P < 0.001), HR 0.3 (0.23-0.41)
	PAOLA1	Olaparib 300mg BD plus bevacizumab vs placebo plus bevacizumab Population: PR/CR chemotherapy	
		Analysis subgroups: ITT (all patients) • HRD[2] (BRCAm) • HRD[2] (excl. BRCAm) • HRP	PFS in months: 22.1 vs 16.6 (P < 0.001), HR 0.59 (0.49-0.72) 37.2 vs 21.7, HR 0.31 (0.2-0.47) 28.1 vs 16.6, HR 0.43 (0.28-0.66) 16.9 vs 16, HR 0.92 (0.72-1.17)
Niraparib	PBS listed: Maintenance monotherapy in 1st line advanced platinum sensitive ovarian cancer with BRCA1 or BRCA2 gene mutation (germline or somatic) PBAC April 2022: recommended for the treatment of women with advanced HG ovarian cancer following completion of 1st line platinum-based chemotherapy, *only if they have a BRCA mutation*.		
	Efficacy		
	PRIMA	Niraparib 300mg vs placebo Population: CR/PR after chemotherapy, stage III patients must have residual disease after surgery	
		Analysis subgroup: ITT (all patients) • HRD[2] (BRCAm) • HRD[2] (exl BRCAm) • HRP	PFS in months: 13.8 vs 19.2 (P < 0.001) HR 0.62 (0.5-0.76) 22.1 vs 10.9 HR 0.4 (0.27-0.62) 19.6 vs 8.2 HR 0.5 (0.31-0.83) 8.1 vs 5.4 HR 0.68 (0.49-0.94)

[1] Tumour testing of somatic BRCA status for access to Olaparib, Medicare item no. 73301
[2] Myriad MyChoice HRD Plus assay, HRD GIS-score ≥ 42 (genomic scar)
PBS: Pharmaceutical Benefit Scheme
gBRCAm: germline BRCA mutation
NR: not reached
CR/PR: complete response/partial response
ITT: intention to treat
BRCAm: BRCA mutation
HRP: homologous recombination proficient

block the action of these proteins. When given to women with BRCA-mutated tumours, the resultant excessive accumulation of unrepaired DNA strand breaks leads to cancer cell death, a phenomenon called 'synthetic lethality'. In 2019, three promising phase III studies of PARP inhibitors for upfront maintenance therapy in ovarian cancer – PRIMA,[13] VELIA[15] and PAOLA-1[16] – were simultaneously published and altered the management of ovarian cancer. Four randomised double-blinded studies incorporating PARP inhibitors into frontline maintenance therapy have shown positive results, even suggesting cure,[17] leading to FDA approval. SOLO-1[17] showed that patients with a BRCA mutation who received a PARP inhibitor following platinum response had an additional median 3.5 years free of disease progression and at five years 48% of patients were progression free compared to 21% with placebo. PRIMA[13] found that among patients with newly diagnosed advanced ovarian cancer who responded to platinum-based chemotherapy, those who received the PARP inhibitor niraparib had significantly longer PFS than those who received placebo. This was true regardless of whether the patients had tumours with HRD or not, though the PFS was longer if they had HRD. PAOLA-1[16] found that in patients with advanced ovarian cancer receiving first-line standard therapy including bevacizumab, the addition of maintenance olaparib provided a significant PFS benefit, which was substantial in patients with HRD-positive tumours, including those without a BRCA mutation.

These studies have altered the way that maintenance therapy for ovarian cancer is prescribed and are improving the prognosis for women with ovarian cancer.

PARP inhibitors have improved the PFS in platinum sensitive tumours; however, 10–15% of tumours are platinum resistant at baseline and in those that recur following initial platinum response, resistance to platinum-based chemotherapy eventually arises. Attention is now being turned to targeting molecular changes unique to platinum resistant ovarian cancer.

Summary

Recent improvements in multipanel genetic testing, alongside targeted therapies exploiting tumour biomarkers, are being integrated into treatment guidelines for ovarian cancer. Every patient with ovarian cancer should be referred for genetic counselling and offered germline testing for BRCA mutations. Those without a germline genetic mutation should be offered somatic testing. Deleterious BRCA mutations and homologous recombination deficiency are now recognised as predictive biomarkers for the use of PARP inhibitors in women with ovarian cancer. Maintenance therapy with a PARP inhibitor is strongly recommended in women with these mutations.

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Cytoreductive surgery for ovarian cancer

Dr Lachlan Baxter
BSc, MBBS (Hon)
4th year RANZCOG ITP registrar
King Edward Memorial Hospital, Perth

Dr Lucy Holden
BSc, MD
1st year RANZCOG ITP registrar
King Edward Memorial Hospital, Perth

Dr Nooraishah Yasin
MBBS, FRANZCOG
3rd Year CGO Fellow
King Edward Memorial Hospital, Perth

The mainstay of treatment for advanced epithelial ovarian cancer (EOC) remains a combination of surgical debulking and systemic therapy. There have been considerable treatment advances in both the primary and recurrent setting over the past several years. New assessment tools to identify patients most suitable for primary upfront surgery, the rise of neoadjuvant chemotherapy (NACT) as well as the development of treatments based upon patient and tumor genetics have shown promise in improving disease-free survival and overall survival. The expanding role of Poly ADP-Ribose polymerase (PARP) inhibitors offers a further armament in the treatment of ovarian cancer in both the primary and recurrent setting. Whilst ovarian cancer remains the most lethal of all gynaecological malignancies (with over 1000 deaths in 2019), there is considerable promise on the horizon.[1]

Primary management of advanced ovarian cancer

Whilst the standard of care for advanced EOC remains the application of maximal surgical effort in a primary debulking surgery (PDS) to resect all visible disease followed by adjuvant platinum and taxane-based chemotherapy, the role and timing of surgery has been refined on the basis of recent studies. The application of maximal surgical effort in order to obtain the least residual disease possible remains the largest prognostic factor in determining progression-free and overall survival.[2-4] But this surgical effort often carries with it perioperative morbidity and mortality due to the extent of surgical resection and frailty in this patient cohort.[5] There exists no consensus on which patients will benefit most from PDS, although various scoring systems to determine surgical resectability and suitability for surgery exist.[6,7] There has been an increasing trend to utilise NACT here and internationally especially for stage 4 EOC where resectability is less assured or not possible due to frailty.[8,9]

The publication of EORTC 55971 and the CHORUS trials both demonstrated non-inferiority of NACT to PDS in advanced ovarian cancer with similar progression-free survival and overall survival.[10,11] Both studies also demonstrated lower perioperative morbidity.[10,11] This is not without controversy with two subsequent studies (the JCOG0602 and SCORPION trial) not showing non-inferiority of NACT and superiority of NACT respectively.[12,13] However large population based retrospective studies have shown that PDS is associated with better outcomes.[14,15] Despite this controversy Farrell et al conducted a survey of Australian gynaecological oncologists in 2018 showing a significant increase in the use of neo-adjuvant chemotherapy in 2017 vs 2007 (43% vs 16%).[16] The outcome of the currently underway TRUST trial, a randomised multicentre trial seeking to determine optimal surgical timing in

advanced ovarian cancer, should be reported in 2024 and will likely further define which patients benefit greatest from PDS.[17]

Laparoscopic debulking in ovarian cancer

Given the improved perioperative outcomes inherent in minimally invasive surgery there has been hope that its safety and equivalence in ovarian cancer may be demonstrated. Most information regarding its safety has been in early-stage disease patients and post NACT settings where emerging data suggests it may be safe and feasible with equivalent oncological outcomes.[18,19] The role of laparoscopic primary debulking surgery is less clear. Whilst retrospective feasibility studies exist and it may be suitable in select patients, the tumour distribution, limitations of laparoscopic vision and surgical necessity are yet to be addressed by randomised trials compared with open surgery.

Surgery for recurrent disease

Secondary surgery (SCS) was historically considered appropriate in patients who had a long disease-free interval following primary surgery and chemotherapy with oligomestastatic or very small volume disease. There are multiple predictive models that have been developed to identify the patient that would most likely benefit from SCS. This includes the DESKTOP AGO Criteria, Memorial Sloan Kettering (MSK) Criteria and the Tian/iModel Score.[20-22]

The selective use of surgery in recurrence has been supported by two randomised controlled trials DESKTOP III which showed an improvement in progression-free survival (14.0 months to 19.6 months) and SOC 1 which showed an improvement in PFS of 5.5 months in the surgery group GOG 213 showed that the hazard ratio for death (surgery vs no surgery) was 1.29 (95% confidence interval [CI], 0.97 to 1.72; P=0.08), which corresponded to a median overall survival of 50.6 months compared to 64.7 months.[23-25] The key to SCS requires a tailored application to patients that will benefit the most with a good functional status, low volume disease and a high likelihood of complete resection.

Anti-angiogenic treatment

The use of antiangiogenic therapy in advanced ovarian cancer has been refined following increasing evidence supporting its usage in high-risk patients with advanced disease. Recent subgroup analysis of GOG 218 and the British ICON7 trial showed patients with newly diagnosed stage IV EOC disease with residual or unresectable disease experienced an overall survival benefit (in the subgroup analysis of GOG 218 this was a difference of 10 months vs placebo).[26,27]

Other indications for the use of antiangiogenic therapy includes recurrent disease and platinum resistant EOC with an improvement in PFS.[28,29]

PARP inhibitors

PARP inhibitors (PARPis) prevent the repair of single stranded DNA breaks and are thus particularly effective against tumours with existing DNA repair mutations. Because of this PARPis were initially employed in the setting of BRCA mutated disease (either germline or somatic) in the recurrent setting.

The publication of the SOLO1 study in 2018 assessed the use of a PARPis (olaparib) in the upfront setting as maintenance therapy following standard surgery and chemotherapy in a patient with either a germline or somatic BRCA mutation.[30] 391 patients were included in the study with 60% of the olaparib patients remaining disease free at three years vs 27% in the placebo arm.[30] Further trials assessing PARPis in the upfront setting have continued to demonstrate a progression-free survival increasing with their upfront usage.

Genetic testing for ovarian cancer

Guidelines recommend that all women diagnosed with epithelial ovarian cancer undergo germline genetic testing, particularly for BRCA1/2 mutations.[31] This testing helps determine risk for the patient and their family, as well as guiding further treatment. To improve uptake of this service, some units have implemented 'mainstreaming,' whereby systematic genetic testing is implemented via oncology clinics.[32] Positive genetic testing for a BRCA1/2 mutation has significant implications on patient's families. Relatives who then go on to be diagnosed with the mutation themselves are advised to undergo specialist input regarding their breast and ovarian cancer risk, with risk reduction surgery recommended. Surveillance CA 125 blood test and pelvic ultrasound are not recommended in those known to have BRCA1/2 mutation.

Heated intraperitoneal chemotherapy

Heated intraperitoneal chemotherapy (HIPEC) has existed since the 1980s and its role in treatment of epithelial ovarian cancer has varied during that time. It broadly encompasses the perfusion of heated chemotherapy (primarily cisplatin in most studies) intraoperatively immediately following cytoreductive surgery. This confers a higher concentration localised to the peritoneal cavity, the chief site of tumour recurrence, and provides the synergist effect of hyperthermia. OVHIPEC 1 was a multicentre trial whereby 245 patients with newly diagnosed stage III epithelial ovarian, fallopian tube, or peritoneal cancer were randomised to interval cytoreductive surgery with or without the addition of HIPEC following administration of neoadjuvant chemotherapy.[33] These patients had been referred for neoadjuvant chemotherapy as their disease was too advanced for primary cytoreductive surgery or initial surgery was suboptimal. Results from this study showed longer disease-free recurrence and survival time in those who received HIPEC. Rates of adverse events were similar in both groups and there was no negative impact on health-related quality of life.[34] PRODIGE-7, another multicentre trial, randomised 265 patients with colorectal peritoneal metastases to HIPEC plus cytoreductive surgery or cytoreductive surgery alone.[35] This study, however, found an absence of overall survival benefit with the addition of HIPEC and higher rates of late postoperative complications. The conclusions from this paper have drawn much criticism and it has been suggested that it should not be used to discredit other studies.[36] Further studies into HIPEC such as HYNOVA, an ongoing Australian study, as well as the eventual outcomes from OVHIPEC-2 will likely go some way to determining the role of HIPEC in advanced ovarian cancer treatment into the future.[37,38]

Conclusion

Whilst the essential tenants of ovarian cancer treatment remain cytoreductive surgery either before or after platinum and taxane-based chemotherapy, there is ongoing refinement in its implementation and the augmentation of new systemic therapies. Ovarian cancer treatment must be individualised to the patient's clinical status, institutional strengths and availabilities and tumour biology. As the outcomes from more quality multicentred randomised trials in the field are reported, it is likely there will be further refinements in care provision to improve outcome for ovarian cancer sufferers.

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Cervical dysplasia in Aotearoa: HPV vaccination and screening

Dr Elizabeth Goulding
MBBS, MPHTM, FRANZCOG, CGO
Gynaecological Oncologist
National Women's Health
Auckland City Hospital

Dr Tom De Greve
MD, OB/GYN (Ghent – Belgium)
Gynaecological Oncologist
National Women's Health
Auckland City Hospital

Success of the HPV vaccine

Cervix cancer is largely a preventable disease, with human papillomavirus (HPV) being the main cause of high-grade cervix abnormalities and cervix cancer. HPV types 16 and 18 are responsible for 50–60% of high-grade cervical abnormalities and 70% of all cervix cancers.[1,2] HPV types 6 and 11 are associated with 90% of anogenital warts.[3] HPV vaccination prevents cervix cancer and dysplasia in addition to anogenital and oropharyngeal cancers and genital warts.

A national HPV vaccination program commenced in Aotearoa in 2008, offering vaccination to women born in 1990 and 1991 (aged 17–18 years old) with the quadrivalent HPV vaccine (HPV4) in three doses. A catch-up program was offered in 2009 to all girls and young women aged 9–20 years. From 2017 a further extension of the program included a funded nonavalent HPV vaccination (HPV9) to all females and males aged between 9 and 26 years old. Currently the vaccination program is both primary care and primary school based (targeting all students in year 7 or 8) and more than 300,000 New Zealanders have been immunised against HPV.

In addition to the effect on the individuals immunised, herd immunity will likely have a positive impact to reduce the burden of cervix cancer in Aotearoa for women who are unwilling or unable to receive the vaccination; however, vaccination coverage should surpass 75% to achieve herd immunity. Currently vaccination rates have steadily increased from 39% for the 1990 cohort to 67% for the 2003 cohort,[4] but unfortunately still fall short of the herd immunity goal set out by the Ministry of Health. Encouragingly HPV vaccination uptake has been slightly higher and at an increasing yearly rate for at-risk populations including Māori and Pacific Islander wahine compared to other populations in Aotearoa.[4] Increasing vaccine uptake has been identified as one of the most effective strategies to reduce cervical cancer disparities and incidence and is a target in the New Zealand Cancer Action Plan 2019–2029. Strategies being explored include changing the HPV vaccination prescription classification to allow pharmacy vaccination, intensified catch-up and recall strategies.

Since the introduction of the HPV vaccine program in 2008, a significant reduction in HPV-vaccine preventable conditions have been seen. In Aotearoa an 83.4% reduction in genital warts was observed five years following the initiation of the program,[5] and a 31% reduction in cumulative incidence for high-grade cervix abnormalities was seen between 2011 and 2017.[6] This when coupled with the introduction of the HPV9 vaccine in 2017, anticipates a greater reduction of high-grade cervix abnormalities to be observed in Aotearoa.

The effect of the HPV vaccination program is not yet reflected in cervix cancer incidence due to the extended lag time between HPV infection and cancer development, with incidence showing a stable pattern of around 6 per 100,000 women in Aotearoa. International data however have shown a decrease in

population incidence of invasive cervix cancer due to vaccination,[7] and extrapolating from this, we expect this to translate into a reduction of cervix cancer incidence in Aotearoa.

HPV-based screening

In December 2017 the Australian National Cervical Screening Program was changed to encompass a five-yearly HrHPV primary screening test for women aged 25–74 years, making Australia one of many countries around the world who are performing cervical screening with HrHPV testing +/- reflex liquid based cytology (LBC) as opposed to traditional cervical cytology.

Screening with HrHPV testing has been shown to decrease the incidence and mortality of cervical cancer by 20% and 70% respectively, and a pooled analysis of four European randomised controlled trials of 176,464 women showed that high-risk HPV (HrHPV)-based screening provides a 60–70% greater protection against invasive cervical carcinomas compared with cytology for screening intervals up to five years.[8]

In regards to the efficacy of this screening test, HrHPV testing alone has a 100% sensitivity in detecting high-grade squamous intraepithelial lesion (HSIL), this is compared with a 68% sensitivity for conventional smears and 87% for LBC.[9] When considering whether to screen with HrHPV testing in isolation, or to combine it with LBC, a co-test, this question was answered by the ATHENA study (n=42 209), whereby HrHPV primary screening was as effective as hybrid screening, but required less screening tests to be done.[10]

The role of LBC comes into play in the triaging of HrHPV screening tests, as the high sensitivity of HrHPV testing comes at the expense of a lower specificity and positive predictive value (PPV) when compared with cytology and hence when used in isolation HrHPV testing increases the burden on colposcopy services. In HrHPV positive women, LBC has been shown to minimise overtreating and unnecessary follow up through increasing the tests specificity and PPV.

Another advantage of HrHPV screening is the increased screening interval of five years, which has been shown to be safe, due to its high negative predictive value (NPV), whereby the risk of HSIL at six years following a negative screening being been shown to be less than 1%.[11] Concerns have been raised regarding an increased screening age of 25 years. However, cancers are rare in this age group whereas HPV infections are common and therefore screening is likely to lead to overtreatment, and in addition to this, this cohort is likely to be vaccinated conferring them additional protection.

As such a move to screening with HrHPV testing is not only backed by robust evidence but will lead to higher detection of cancers with less overtreatment of women.

The current Aotearoa screening program

Currently in Aotearoa the National Cervical Screening Program (NCSP) comprises three-yearly smears after coitarche from the age of 25–69 years, with over 73% of eligible women having regular smear tests in recommended time frames.[13] Reflex HrHPV testing can then be used to triage women ≥30 with a low-grade squamous intraepithelial lesion (LSIL) or atypical squamous cells of undetermined significance (ASC-US) smear who have previously had a normal smear.

The NCSP has been hugely successful with the number of women dying from cervical cancer falling 60% since the NCSP began in 1990; however, this reduction has been inequitable with Māori wahine being less likely to be screened and being twice as likely to develop and die of cervical cancer than their pakeha counterparts.[13]

In line with Australia and robust international data, there is now a planned move to screening with HrHPV in July 2023, with the option of self-testing for all women being available. Studies undertaken in Aotearoa have suggested the option of self-testing is likely to increase participation and equitable outcomes by reducing barriers to screening and increasing access; with ongoing research being undertaken to assess the best way to invite wahine to participate in screening including GP-led opportunistic screening, telehealth and mail-out systems and invitation via Māori and Pacific health partners in community settings.

In line with Australia, it is hoped that this new screening approach will be both efficacious and acceptable to women. In addition to this, it is hoped that a culturally appropriate and acceptable approach to inviting women to participate in cervical screening, coupled with the option of HPV self-testing, may reduce the gap in outcomes and improve equity in Aotearoa wahine in the future.

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Update on gestational trophoblastic disease

Dr Jennifer Dean
MBChB, BSc Physiotherapy, DRANZCOG
Registrar, Obstetrics and Gynaecology
Royal Women's Hospital, Melbourne

Dr Orgad Rosenblat
MD, BMedSci, Obstetrics and Gynaecology
Consultant ISOG
Fellow, Gynaecological Oncology
Royal Women's Hospital, Melbourne

Dr Antonia Jones
MBBS, BMedSci, FRANZCOG, CGO
Department of Gynaecology Oncology
Royal Women's Hospital, Melbourne

Gestational trophoblastic disease (GTD) is a spectrum of disorders from benign to malignant, characterised by abnormal proliferation of trophoblastic tissue[1] and affects approximately 1/1000 pregnancies. Given the rarity of the condition, it can be a very confronting and surprising diagnosis for a woman experiencing pregnancy loss.[2] A number of internationally recognised guidelines now exist informing effective and patient-centred care, making this disease highly treatable.[1-3]

Benign GTD

Benign GTD can be divided into complete hydatidiform moles (CHM) or partial hydatidiform moles (PHM). Hydatidiform moles represent 90% of GTD.[3] At the time of normal conception, it is presumed that mitochondrial DNA is maternal and nuclear DNA is equal parts maternal and paternal, one set of chromosomes being derived from each parent.[4] A complete molar pregnancy is diploid and occurs when an empty ovum is fertilised by one sperm (~80%) or two sperm (~20%) leading to a karyotype of 46XX.[3-6] In keeping with an empty ovum and no maternal DNA, a placenta is formed but no fetal parts develop. A PHM occurs when two sperm fertilise a single ovum. The karyotyping is usually triploid and 69 XXX or 69 XXY. Fetal parts will develop and cardiac activity can be seen.[6,7]

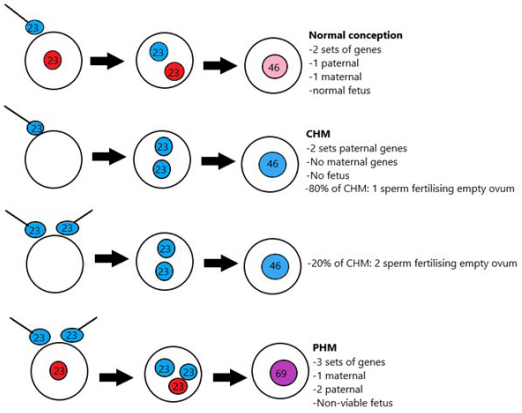

Figure 1. Molar pregnancy genetics.

Gestational trophoblastic neoplasia

Gestational trophoblastic neoplasia (GTN) includes the malignant GTD conditions of persistent trophoblastic disease, invasive mole, choriocarcinoma, placental site trophoblastic tumour (PSTT) and epithelioid trophoblastic tumour (ETT).[3] Overall, GTN affects fewer than 1/40,000 pregnancies and the latter two conditions are extremely rare, affecting at most 1/50,000 pregnancies.[3] GTN can be thought of as GTD that behaves in a malignant fashion, thus requiring further treatment in the form of chemotherapy and/or surgery when human Chorionic Gonadotrophin

(hCG) levels are persistent, rising or metastatic disease is detected. Whilst 60% of GTN originates from molar pregnancies, 30% arises from previous miscarriage, normal delivery or abortion and a further 10% from ectopic pregnancies.[3-6]

Presentation

Vaginal bleeding, which is the most common first presentation of GTD, will often trigger an ultrasonographic evaluation.[6,7] Classic ultrasound findings of CHM are an intrauterine snowstorm appearance and theca lutein cysts, but earlier and more advanced ultrasound assessment more commonly demonstrates a complex intra-uterine mass with no fetal parts and a cystic appearance of the placenta.[7] The findings with PHM are often more subtle and initially may be mistaken on ultrasound as a miscarriage although some sonographic features might raise the suspicion (e.g. thickened hydropic placenta with or without a 'Swiss cheese' appearance). In many cases the diagnosis is only made once histopathological examination has taken place. A diagnosis of GTD should be considered in patients with risk factors such as extremes of maternal age and previous molar pregnancies.[5,6]

Historically, patients with CHM presented with an enlarged uterus, hyperemesis gravidarium, hypertension before 20 weeks gestation and hyperthyroidism. The current trend for early ultrasound assessment means that these clinical findings are rare; therefore, whilst careful consideration should be given to medical manifestations of the disease, GTD is typically diagnosed post evacuation of uterine contents.[5,6]

CHM have a malignant potential of 20% and a 5% chance of distant metastatic spread.[1,6] PHM carry a malignant potential of 0.5–5%.[1,6] GTD management must therefore be timely and according to evidence-based guidelines. While recurrence rates for GTN are low at 0.6–2%, the risk of recurrence significantly increases without long-term follow up, supporting the need for ongoing care.[1]

Management

If GTD is suspected on ultrasound, serum hCG levels should be taken as well as patient blood type and a baseline full blood count. Liver function, thyroid function and coagulation profile can also be considered. If the diagnosis is suspected, suction curette should be undertaken by an experienced practitioner, preferably with ultrasound guidance to reduce the risk of perforation and leaving residual tissue. Clear communication with the operating team and anaesthetist is imperative due to high bleeding risk of patients with GTD. Consideration should be given for two units of packed red cells to be available and uterotonics such as ergometrine to be readily available in the operating theatre.[1,3,6] If oxytocics are required, they should be administered after evacuation.[2] Tissue should be sent for histopathology and ancillary testing (ploidy and p57 status) if GTD is suspected.[1] In a Rhesus negative patient, anti-D immunisation postoperatively is best practice.[2] If there are any clinical features suggestive of metastases, e.g. shortness of breath, a chest radiograph should be taken.[2] Likewise, if the index of suspicion is high pre-operatively, weekly HCG monitoring post evacuation should be considered, even before histopathological confirmation.

Following confirmation of a CHM or PHM, it is essential that the patient is informed and advised of the importance of follow up, risk of persistent

Histopathological features of GTD

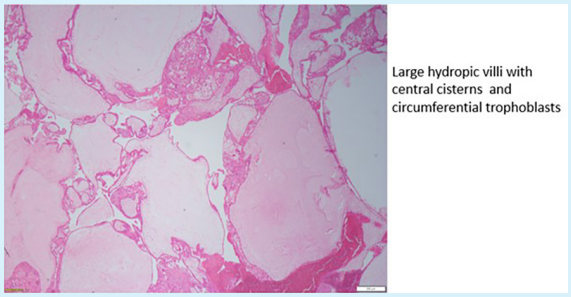

Figure 2a. Complete hydatidiform mole.

Figure 2b. Complete hydatidiform mole.

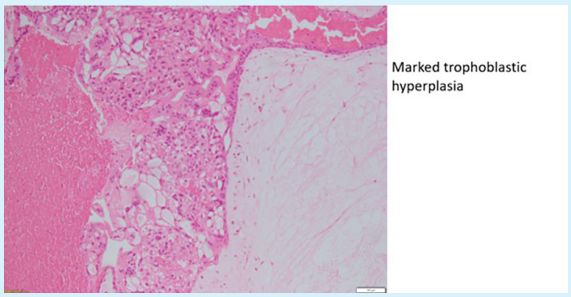

Figure 2c. Complete hydatidiform mole.

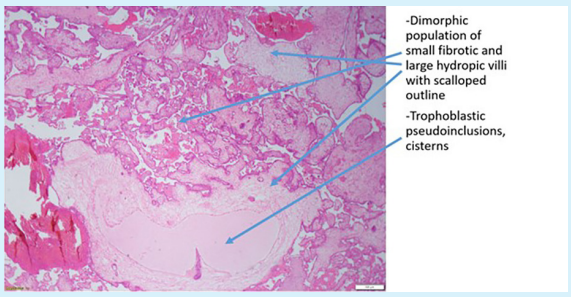

Figure 3a. Partial hydatidiform mole

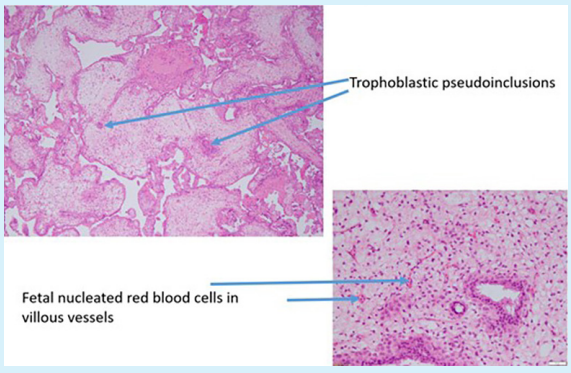

Figure 3b. Partial hydatidiform mole.

	Benign Gestational Trophoblastic Disease	
Type	**Complete Hydatidiform Mole**	**Partial Hydatidiform Mole**
Incidence	1/1500	1/750
Ploidy	Diploid	Usually triploid
Paternal DNA	1 set (80%): 23X, which then duplicates to 46 XX 2 sets (20%): 23X +/- 23X or 23Y	2 sets: • 10% 23X • 90% 23Y
Maternal DNA	No maternal DNA	1 set maternal DNA: 23X
Karyotype	46 XX (most common) 46 XY	69 XXY (most common) 69 XXX
Immunohistochemistry	P57 -	P57 +
Morphology (key examples)	Hydropic villi-diffuse Trophoblastic hyperplasia- diffuse	Partially cystic Trophoblastic hyperplasia- focal Villous scalloping Stromal trophoblastic inclusions
Fetal tissue	Absent	Partially present
Presentation	Huge uterus High hCG Medical complications: • Hypertension (before 20 weeks) • Hyperthyroidism • Hyperemesis gravidarium • Haematological issues: bleeding (common), anaemia and thrombi formation	Mistaken for miscarriage Often minimal symptoms Vaginal bleeding in early pregnancy
Diagnosis	Clinical or ultrasound diagnosis Post miscarriage histology (less common)	Post miscarriage
Ultrasound findings	Theca lutein cysts Snowstorm pattern Complex echogenic intrauterine mass	Swiss cheese pattern of placental tissue Formed fetus/ fetal parts Possible initial cardiac activity, followed by miscarriage
Malignancy/ post molar gestational trophoblastic neoplasm (GTN)	20% (majority local invasion) Distant mets in ~5%	0.5–5%

Table 1. Comparing molar pregnancies.

disease and the need to avoid further pregnancy until advised otherwise. In Australia there are two state based GTD registries in Victoria and Queensland.[2] Clinicians in these states are encouraged to register patients after which ongoing monitoring and advice to patients is provided by the registry multidisciplinary teams.[2] Outside of these states, care and follow up is provided by individual practitioners in accordance with RANZCOG guidelines. As well as registration, RANZCOG recommends following hCG levels in women weekly, commencing as soon as a diagnosis of a GTD is made. hCG levels are followed until three successive normal levels have been recorded. Following this, women with PHM can be discharged from follow up and those with CHM are recommended to have monthly levels for a further six months.[1-3,6] In order to ensure consistency, hCG levels should preferably be carried out by the same laboratory with the request specifying 'tumour' hCG to encompass all possible hCG forms and thus avoid false negatives.[2] Risk factors for post-molar GTN include initial hCG levels of >100,000, theca lutein cysts >6cm, an enlarged uterus and maternal age >40 years old.[3]

When to commence treatment
When the plateau of hCG lasts for four measurements over a period of three weeks or longer; that is, days 1, 7, 14, 21
When there is a rise in hCG for three consecutive weekly measurements over at least a period of two weeks or more; days 1, 7, 14
If there is a histologic diagnosis of choriocarcinoma

Table 2. FIGO criteria for treatment of GTN.

FIGO stage	Description
I	Gestational trophoblastic tumours strictly confined to the uterine corpus
II	Gestational trophoblastic tumours extending to the adnexa or to the vagina, but limited to the genital structures
III	Gestational trophoblastic tumours extending to the lungs, with or without genital tract involvement
IV	All other metastatic sites

Table 3. FIGO staging and classification for gestational trophoblastic neoplasia..

Staging of GTN

Once a diagnosis of GTN is made, the patient's disease is assigned a FIGO stage and the WHO prognostic factors recorded (see figure 2c).[1,2,6,8]

After diagnosis, a thorough history and examination, serum hCG, a pelvic US and chest x-ray should be performed. The chest x-ray results and patient's localising symptoms will guide further imaging requirements. If normal, no further imaging is required but if the possibility of metastases are raised, a CT chest should be arranged. Should this confirm chest metastases >1cm, an MRI brain with contrast as well as CT/MRI of the abdomen and pelvis is recommended.[1,6]

If the hCG is <5000 IU/L, and residual, non-myoinvasive, uterine confined disease is identified on ultrasound, a second curettage by an experienced practitioner can be considered. The patient should be counselled regarding risks of perforation, or brisk bleeding that might require further surgery (including hysterectomy) and that in up to 70% of cases, chemotherapy may still be required.[1,6,13]

For women who do not desire future fertility, a hysterectomy can reduce the need for chemotherapy by up to 80%.[10] The ovaries are normally preserved due to the rarity of ovarian involvement in GTN. If present, theca lutein cysts will generally resolve once hCG levels drop and their presence is not an indication for oophorectomy or cystectomy, irrespective of size, unless torsion is suspected. In cases of haemorrhagic bleeding and desire for fertility, uterine artery embolisation can be considered.[1] The rare conditions PSTT and ETT usually need to be managed surgically due to their relative chemo-resistance.[1,6,9,10]

Response to chemotherapy is excellent for the vast majority of patients and the decision to use low- or high-risk regimens is based on FIGO stage and WHO risk score.[1,6,9,10] In general, in FIGO stage I disease a low-risk regimen is sufficient, FIGO stage IV requires a high-risk regimen and Stage II or III disease regimen depends on the WHO risk score.

There is nearly a 100% cure rate for low-risk patients (WHO score <7) with single agent chemotherapy, in the form of multi dose methotrexate (MTX) or Actinomycin D. MTX should be administered with folinic acid on proceeding days. 10–30% of low-risk patients will develop resistance to single agent chemotherapy.[8] If hCG levels plateau or rise >10% over the course of two to four weeks of monitoring, resistance should be suspected. 15–20% of patients will require multi agent therapy. WHO Scores of 5–6 and/or choriocarcinoma may benefit from a higher risk regimen due to the higher risk of resistance to single agent chemotherapy.[1]

If the risk of recurrence is low (FIGO stage 1), MTX and Actinomycin D have equal efficacy and the choice of agent may be influenced by side effect profile and convenience/geography (four doses per fortnight in MTX versus a single Actinomycin dose fortnightly). Patients with stages II–III with a score of >7 or more and all stage IV are classified as having a high-risk disease recurrence and will require high-risk multiagent chemotherapy, the commonest regimen

is EMACO (Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide and Oncovin [Vincristine])[1,10] in conjunction with a medical oncologist, preferably through a multidisciplinary gynae oncology team. Higher doses of MTX or intrathecal MTX to facilitate blood-brain barrier transport may also be required in managing brain metastases.[1]

Given GTN is exquisitely sensitive to chemotherapy, consideration should be given to a diagnosis of non-gestational choriocarcinoma (where a non-pregnancy related malignancy has de-differentiated into choriocarcinoma) if the response to chemotherapy is not as expected. In addition, if a large disease burden exists at the start of treatment (i.e. 'ultra-high risk' WHO score ≥12, brain metastasis, large lung lesions, etc), a gentle approach to chemotherapy might be advised to reduce the risk of sudden tumour necrosis or significant bleeding with subsequent risk of early patient death.[1,2,6,10]

Currently there is emerging data that immunotherapy (i.e. anti PD-1/PDL-1 immune check point inhibitors) could be effective in recurrent high-risk disease such as choriocarcinoma or ETT/PSTT.[12]

The future

The majority of recurrences (>85%) in those with high-risk GTN, occur in the first year.[1,6] Patients should be counselled to avoid pregnancy for at least one year following any kind of GTN and treatment and support should be given to facilitate contraception choices. While the oral contraceptive pill was initially thought to slow the fall of hCG levels, the evidence for this is lacking and it is more important that women take a reliable form of contraceptive to prevent accidental pregnancy.

Once discharged from the registry after one year of follow up, 70% of women will go on to have a normal, term pregnancy. A woman can be reassured that the risk of GTD recurrence is only 1% in her subsequent pregnancy after a single molar pregnancy,[5,6] but is closer to 25% if she has had two complete molar pregnancies.[11] Women are therefore recommended to have an early ultrasound scan in any subsequent pregnancy to confirm a viable, non-molar pregnancy. A hCG level should be checked six weeks after every subsequent pregnancy, irrespective of outcome and consideration should be given to sending the placenta for histopathological evaluation.

Outcomes for patients with GTD have improved as a result of international consensus and evidence-based guidance.[1,9] Any clinician caring for a woman with GTD should be aware of this guidance and have a low threshold to contact an experienced GTD centre should they have any concerns.

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WHO risk factor scoring with FIGO staging	1	2	3	4
Age	<40	>40	–	–
Antecedant pregnancy	Mole	Abortion	Term	–
Interval from index pregnancy	<4 months	4–6 months	7–12 months	>12 months
Pre-treatment hCG mIU/mL	$<10^3$	$>10^3$–10^4	$>10^4$–10^5	$>10^5$
Largest tumour size including uterus	–	3–4cm	≥5cm	–
Site of metastases including uterus	Lung	Spleen, kidney	Gastrointestinal tract	Brain, liver
Number of metastases identified	–	1–4	5–8	>8
Previous failed chemotherapy	–	–	Single drug	Two or more drugs

Table 4. WHO scoring system based on prognostic factors.

Fertility preservation prior to cancer

Dr Devini Ameratunga
FRANZCOG, MBBS (Hons), MReproMed
CREI Fellow

Dr Ben Kroon
BHB MBChB FRANZCOG CREI

A/Prof Anusch Yazdani
MBChB, FRANZCOG, CREI

Cancer management has changed. In the last 20 years, despite an increase in cancer incidence in Australia, mortality rates have decreased while disease-free survival rates remain high.[1] Reproductive potential is a major determinant of quality of life in cancer survivors, and providers need to have an understanding of fertility preservation options with a pragmatic approach for accessing these services around the country.[2] As such, current clinical practice guidelines recommend that all reproductive-age patients with a cancer diagnosis be offered, and have documented, a fertility preservation discussion to allow autonomous decision making in a timely fashion to prevent any regret, remorse or medico-legal implications.[3,4]

Within the confines of the patient's reproductive potential, governed principally by their gender and age, chemo and radiotoxicity are determined by the choice of agent, the duration and intensity of the protocol. The Clinical Oncology Society of Australia outlines the impact of various protocols and provides clinical practice guidelines.[5] At the most fundamental level, discussions with cancer patients need to include options for fertility preservation such as oocyte cryopreservation, ovarian tissue preservation, semen freezing, testicular tissue cryopreservation, medical and surgical options to minimise damage during cancer treatment as well as third-party reproductive options such as gamete donation and surrogacy.

Patients and their families need to be made aware that there is no evidence that fertility treatment could diminish their chance of successful cancer treatment, nor increase recurrence, even in hormone-sensitive cancers. Conversely, fertility preservation will not guarantee reproductive success in the future.

Chemotherapy

In the female, chemotherapy exerts immediate effects through damage to the growing follicular pool. This effect may be temporary or more permanent depending on the resting ovarian cohort of primordial follicles. Ovarian function may recover subsequently, usually over six months, although there may be long-term effects on quality as well as the risk of premature ovarian insufficiency. The overall impact of chemotherapy on an individual's ovarian function will depend on their baseline ovarian reserve and age, the type of agents used (alkylating agents being more gonadotoxic), dose, duration, and frequency of administration.[6]

Radiation therapy

Radiotherapy, whether targeted abdominopelvic radiotherapy or total body irradiation may affect fertility by radiation-induced damage to the target organ, such as myometrial fibrosis, loss of elasticity, vascular damage and subsequent secondary hypoestrogenic effect. These changes may impact implantation, placentation and effect ongoing pregnancy, resulting in a higher risk of preterm birth, lower birthweight, uterine rupture, pre-eclampsia and stillbirth. Unfortunately, total treatment doses alone cannot accurately predict uterine damage or subsequent risk of complications and should be assessed prior to reproduction and childbearing.[7] Suitability for pregnancy should involve liaison with radiation oncologists, obstetric physicians and a high-risk pregnancy clinic. Assessment of uterine functionality may be performed with ultrasound and/or MRI to assess uterine volume, doppler and endometrial thickness, and consideration given to an

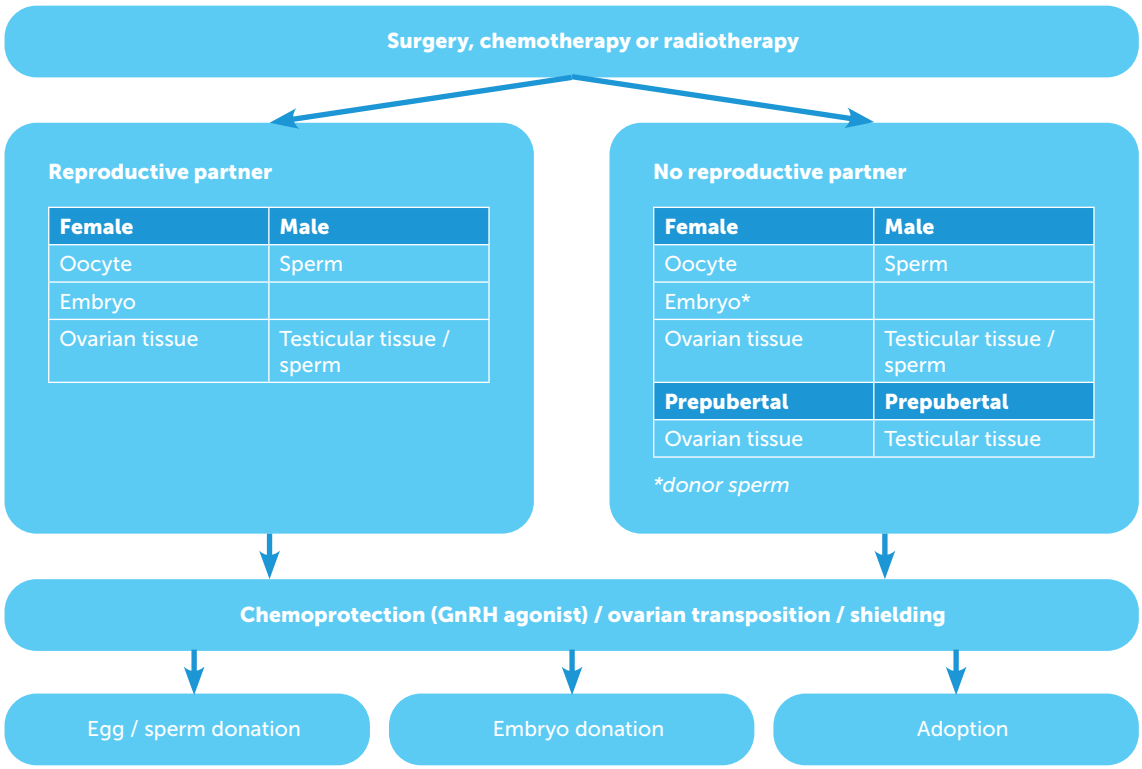

Figure 1. Patient communication aid

endometrial biopsy prior to an embryo transfer.[7] Similarly, radiation and chemotherapy have an immediate and direct effect on sperm function but may also damage germinal epithelium and spermatogonia. This translates into altered sperm production, sperm DNA damage, and, more rarely, altered endocrine function. While these damaged sperm will in time be ejaculated or undergo apoptosis, semen parameters themselves may take years to recover.[8]

Patient communication

Fertility preservation often occurs in an emergent setting in coordination with the patient, their partner, family and often a surgical and oncological team. The discussion of reproductive options in a person-centred setting must consider the patient, his or her reproductive intent and that of any given partner, the type of cancer and the planned intervention. Simple decision matrices may be used to facilitate this communication (Figure 1) at a time when patients can feel overwhelmed with the volume and complexity of information presented. Fertility preservation counselling should only be performed by specialists with experience or appropriate training in this field and patients should have clear answers to the important decision points (Figure 2).

Female fertility preservation options

In post-pubertal females, embryo or oocyte cryopreservation is an established practice. Recent evidence has confirmed the efficacy of the random start protocol, so that stimulation may commence at any time in the ovulatory cycle.[9] Medications such as letrozole can be added to the usual gonadotropin stimulation to reduce oestrogen levels in hormone-sensitive cancers, while GnRH triggers are utilised to reduce the risk of complications such as ovarian hyperstimulation syndrome. Oocyte cryopreservation has excellent survival rates, and although lower than non-cancer patients, comparable implantation and clinical pregnancy rates.[6]

In the pre-pubertal female, where oocyte or embryo cryopreservation is not possible, ovarian tissue cryopreservation has now transitioned from 'experimental' to a practice endorsed by the American Society of Reproductive Medicine and European Society of Human Reproduction and Embryology. This technique also offers an immediate fertility preservation option for post-pubertal females when cancer treatment is imminent. Once ovarian tissue has been removed, the cortex is prepared and then cryopreserved. When fertility is desired, this tissue is thawed and auto-transplanted into the

Important questions to be answered:

1. Will the fertility treatment delay my chemotherapy / radiotherapy / surgery?
2. Will the fertility treatment affect the success of my chemotherapy / radiotherapy / surgery?
3. What is the chance of loss of fertility with my chemotherapy / radiotherapy / surgery?
4. What is the chance of loss of ovarian function with my chemotherapy / radiotherapy / surgery?
5. What is the chance of success of the fertility therapy?
6. Will my chemotherapy / radiotherapy / surgery affect my ability to carry a pregnancy / give birth / breastfeed / care for a child?

Figure 2. Important questions to be answered

pelvis or into other areas of the body, after the tissue has been tested for the residual tumour or other biomarkers.[10,11] Re-introduction of malignant cells has not been reported in humans to date. Following transplantation, conception may occur unassisted or by IVF, with research into novel treatments continuing.

Ovarian transposition out of the radiation field and shielding can also reduce potential ovarian damage. In the post-pubertal female, GnRH analogs may have a role in chemoprophylaxis in certain cancers, such as the breast.[12] Proposed mechanisms for GnRH analogues in reducing the risk of damage to the ovary include simulation of the prepubertal hypogonadotrophic milieu, reduced ovarian perfusion and up-regulation of 'ovarian protecting' molecules.

Male fertility preservation options

Sperm cryopreservation is well-established in post-pubertal males (see Table 2). Depending on the sperm concentration, the ejaculate may be distilled into multiple vials, each allowing one attempt at natural conception (intrauterine insemination) or one cycle of IVF. For men unable to produce a semen sample, surgical sperm retrieval or, rarely, vibro-stimulation, provide established alternatives. In the absence of mature sperm production, pre-pubertal males present a challenge as the isolation of spermatogonial stem cells from testicular tissue is challenging. Currently, testicular tissue cryopreservation is considered experimental, and offered by limited units in Australia in the context of ethically approved research.[13]

Table 1. Options for female patients (adapted from COSA[5])

	Egg freezing	Embryo freezing	Ovarian tissue freezing
Partner or donor required	No	Yes	No
Time required	2 weeks	2 weeks	1 day
Pubertal status	Post-pubertal	Post-pubertal	Pre- or post-pubertal
Survival rates of tissue	60%	95%	Reasonable
Expectation of success	Good if enough eggs collected	Excellent if enough embryos	Low currently
Chemotherapy	GnRH agonists during chemotherapy		
Radiation	Ovarian transposition out of radiation field		
Third-party parenting options	Egg donation, embryo donation, surrogacy, adoption		

Table 2. Options for male patients

	Sperm cryopreservation	Testicular tissue cryopreservation
Pre- or post-pubertal	Post-pubertal	Pre-pubertal
Experimental	No	Yes
Survival rates of tissue	Good	Unsure
Partner required	No	No
Time frame	Immediate	1–2 days
Invasiveness	Nil	Minimal–moderate
Surgical shielding of testes		
Third-party parenting options	Sperm donation, surrogacy, adoption	

Access

Access to oncofertility services varies significantly across Australia and New Zealand. The nature of cryopreservation services has laid the onus onto the assisted reproductive technology (ART) sector, although specialised public hospital clinical departments that focus on oncofertility services have arisen more recently. A number of studies have shown that barriers to care include lack of insurance, financial burden, difficulties with referrals, lack of funding for research and lack of donated tissues.[14,15] Affordable access to fertility services thus remains location dependent, with limited public tertiary hospital fertility preservation services, despite referral pathways for patients in remote and rural areas. Many private fertility units provide oncofertility services with Medicare rebate with no, or minimal, cost to the patient. Sparce and geographically challenging service provisions can make integration of fertility and oncology services challenging. The establishment of dedicated, accessible oncofertility support and research services is invaluable for both clinical research and comprehensive fertility preservation and psychosocial support.[16]

Conclusion

Oncofertility has established itself as a significant discipline within our field, with emerging dedicated services in both the public and private sectors. With increasing rates of cancer diagnosis, improved treatment and cancer-free survival, it is imperative that we continue to strive towards efficient, accessible multidisciplinary services, irrespective of location or geographical challenges, that can be accessed by all.

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Use of biologic therapy in pregnancy

Dr Felicity Martin
Department of Medical Oncology,
Peter MacCallum Cancer Centre, Melbourne

Dr Wanyuan Cui
Sir Peter MacCallum Department of Oncology
The University of Melbourne

The incidence of cancer during pregnancy is estimated to be in 1 in 1000 pregnancies.[1] The delivery of anti-cancer therapies during pregnancy poses a number of physiological, safety and ethical challenges; one must balance best maternal care with safety to the fetus. There is established evidence that some chemotherapies can be safely delivered from the second trimester of pregnancy, for example, anthracycline-containing regimens platinum agents and taxanes used in breast and gynaecological cancers.[2] However, in the era of targeted and immunological treatments, optimal cancer care is no longer limited to chemotherapy-based regimens alone. Commonly used novel biologic agents for cancers that affect women of childbearing age, such as melanoma, breast cancer and lymphoma have limited safety data in pregnancy. Here, we review the current safety evidence for a number of commonly used agents (Table 1).

Monoclonal antibodies (mAbs)

Most therapeutic mAbs are IgG, which can be actively transported across the human placenta. Unlike chemotherapy, mAbs are generally considered to be safest during the first trimester of pregnancy because transplacental transport occurs in the second and third trimesters, following the development of placental transporting systems at approximately 14 weeks gestation.[3]

Rituximab is a mAb against the CD20 antigen and is commonly used in B-cell lymphomas and chronic lymphocytic leukaemia, as well as other immune-mediated conditions. In a meta-analysis of 102 pregnancies in which rituximab was used for multiple sclerosis or neuromyelitis optica spectrum disorders within six months of conception, 78 live births and 12 spontaneous abortions were reported. Myelosuppression and CD19+ lymphopenia occurred in 39% of neonates, all of which normalised within six months post-delivery.[4] The current recommendation for rituximab is to use with caution, preferably in the first and early second trimesters.[2,3]

Conversely, there are a number of mAbs that are contraindicated in pregnancy.[2,3] Anti-angiogenesis agents such as bevacizumab, which are commonly used in gynaecological and colorectal cancers, are absolutely contraindicated in pregnancy. Aside from the theoretical risk of pre-eclampsia due to concurrent risk of hypertension and proteinuria, there is evidence from animal models demonstrating their harmful effects on embryogenesis and placental development resulting in decreased fetal body weight and fetal death.[3] Likewise, human epidermal growth factor receptor 2 (HER2) targeted therapies, such as trastuzumab and pertuzumab (used predominately in breast and gastric cancers) can also be detrimental to embryonic development. Trastuzumab has been the most widely studied in pregnancy. A study of 18 cases demonstrated it carries a high risk of severe oligohydramnios, especially when given in the second or third trimester, with 73% of pregnancies thus affected.[5] However, a case series of 61 patients who continued pregnancy after prior exposure to trastuzumab (16 cases during and up to 3 months after trastuzumab exposure, and 45 cases >3 months after trastuzumab exposure) did not demonstrate adverse short-term fetal outcomes.[6] Therefore, HER2-targeted agents are contraindicated in pregnancy; however, women who become accidentally pregnant during trastuzumab administration can be counselled regarding the possibility of ceasing trastuzumab and continuing their pregnancy.[2,3]

Agent	Safety data in pregnancy	Recommendation in pregnancy
Rituximab	No teratogenic effects B-cell lymphopenia & cytopenias, recovered within 6 months	Use with caution
Bevacizumab	Teratogenicity & fetal skeletal abnormalities in animal models	Contraindicated
HER2 targeted agents	Oligohydramnios especially in 2nd/3rd trimester, prematurity	Contraindicated
Anti-PD-(L)1, CTLA4	Miscarriages, prematurity and intrauterine growth restriction reported; congenital hypothyroidism	Not recommended, especially in 2nd/3rd trimesters
BRAF/MEK inhibitors	Risk of teratogenicity in animals; growth restriction & prematurity in 2 cases & 2 healthy neonates	Avoid during pregnancy, limited data
EGFR inhibitors	Embryo death in animal models; limited number of uncomplicated pregnancies reported	Limited data, use with caution
ALK inhibitors	No fetal or developmental abnormalities in 5 reported cases	Limited data, use with caution
Imatinib	High rate of fetal malformations in 1st trimester; 5 healthy neonates in later pregnancy	Contraindicated in 1st trimester, use with caution in 2nd/3rd trimesters
Olaparib	Terotegenicity and embryo-fetal toxicity in animal studies	Contraindicated

Table 1. Biologic agents in pregnancy

Immune checkpoint inhibitors (ICIs)

ICIs have revolutionised the treatment of many malignancies over the last decade. Commonly used ICIs are immunoglobulin G4 (IgG4) antibodies which inhibit programmed death-1 (PD-1), PD-ligand 1 (PD-L1) and cytotoxic T-lymphocyte associated protein 4 (CTLA4). These play a key role in switching off inhibitory immune regulation, thereby activating the immune system. Immune regulation is imperative for maternal tolerance in pregnancy, and IgG4 antibodies can be transferred across the placenta. Thus, ICIs are likely to have an effect on pregnancy.[1,3]

A case series of seven women with metastatic melanoma who were administered ICI during pregnancy, reported increased pregnancy complications including miscarriages, prematurity (mean gestational age at delivery was 30.4 weeks) and lower birth weight (mean weight of neonates at delivery was 1267g).[1] Fetal immune-related adverse effects (such as congenital hypothyroidism) have also been observed due to maternal exposure to ICI.[1,3] Therefore, ICIs are currently not recommended in pregnancy.

Tyrosine kinase inhibitors (TKIs)

In contrast to mAbs, which require a transporting system for transplacental passage, TKIs are able to easily cross the placenta. The various molecular pathways that are targeted by many TKIs are often also implicated in physiological fetal development, and therefore use of TKIs in pregnancy may result in developmental abnormalities.

BRAF and MEK inhibitors, such as dabrafenib and trametinib, are used in BRAF V600E-mutated melanoma and other malignancies. The evidence for their use in pregnancy is limited to isolated case reports, two of which reported healthy neonates, one reported fetal growth restriction and emergency delivery at 30 weeks, and another resulted in early preterm delivery due to significant maternal adverse events.[3] As these agents have not been studied sufficiently to provide a clear recommendation, they are currently not recommended in pregnancy.[2,3]

EGFR inhibitors are standard of care for lung cancers with activating EGFR mutations. In animal models,

use of erlotinib resulted in embryo death. However, three cases of live birth with no fetal anomalies have been reported after use of erlotinib during pregnancy and two cases after use of gefitinib.[2] There have also been five reported cases of ALK inhibitors (alectinib, crioztinib and ceritinib) used in women with non-small cell lung cancer during pregnancy without any newborn malformations or developmental abnormalities (at 30 months of follow up).[7] However, as these agents have not been studied sufficiently during pregnancy , they are not currently recommended in pregnancy.[2]

Imatinib is a multitargeted TKI towards BCR-ABL, c-Kit and platelet-derived growth factor (PDGF) used in chronic myeloid leukaemia. When given in the first trimester, it has been associated with a high rate of complex fetal malformations (approximately 10% in a case series of 125 pregnancies).[8] However, a small study of seven women who ceased imatinib prior to conception then restarted after the first trimester resulted in only one spontaneous abortion.[9] Therefore, imatinib is contraindicated in the first trimester; there are limited data for its use after the first trimester.[2,3]

Olaparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, used in BRCA-mutated breast and ovarian cancers, has no human data in pregnancy. Animal studies of olaparib in pregnancy caused teratogenicity and embryo-fetal toxicity. It is therefore also contraindicated in pregnancy.

Conclusion

As standard-of-care cancer treatment continues to evolve to include novel biologic agents including mAbs, TKIs and ICIs, information about the safety of these agents during pregnancy is crucially needed. Use of biologic anti-cancer agents should be carefully considered with respect to both the safety and interest of the mother and child.

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A perfect partnership: women and medical professionals

Kath Mazzella OAM
Gynaecological-related Mental Health advocate

As a gynaecological cancer survivor, multiple award recipient, a gynaecological, sexual and associated mental health awareness campaigner and systemic advocate with 27 years of experience, it stills stuns me that women are too fearful to ask questions and lack the basic knowledge of women's anatomy, let alone the capacity to grasp the implications of gynaecological cancers. And I have been considering what it is about our health system that perpetuates this.

Many women over the years have shared with me their stories of suffering in silence, with some silence leading to death through lack of early diagnosis. Stories of attending appointments where they are seen briefly, given a diagnosis, handed a piece of paper and informed to follow the health treatment plan. Yet the moment they walk out that door, the details of the conversation swirl in their heads, they feel overwhelmed by the implications of their cancer diagnosis, all the questions they wanted to ask flood them and they know that they will not have access to their medical professional again without significant effort. Consequently, they often seek their information from unreliable sources like Dr Google and online support groups.

For some, their medical professional will never know what they are thinking because they paint a smile, nod their heads and pretend they understand what is being told to them because they don't want to appear ignorant. Yet internally, their world view is spinning, especially where the diagnosis relates to their female genital area or their future impacts on their sexual capacity.

As a medical professional, you are in the privileged position of holding information that can bring healing, or at least soften the blow. You are also intelligent, connected and able to command respect from others. People listen to what you have to say and generally, believe in your diagnosis. Juxtaposed next to this is a woman who is informed by her closest friends and family or Dr Google, is searching for answers to what can be very life-limiting conditions or even life ending and she is vulnerable, hurting and afraid. How then can the medical profession share power to create greater balance so that women play a greater role in their healing, which ultimately will reduce the pressure on the medical professional and the health system?

They say that knowledge is power. My tireless efforts in drawing attention to gynaecological health revolves around the concept that sharing information transforms the landscape for women.

Women are the threads that knit our communities together. They are constantly stressed through changing hats, working and caring for families and friends. When their anatomy is challenged, so are all these functional hats that they wear, and we lose threads from that fabric. When we consider the large volumes of women who are daily challenged in the workplace and home front because of gynaecological cancers, there is much to be done to keep our women healthy. One way we can do this is to empower them with knowledge and another is to show our support through participation.

Medical professionals can have a higher level of engagement with women without spending a lot more time in appointments by:

1. Recognising that there is stigma, embarrassment and shame that surrounds conversations relating to gynaecological, sexual and associated mental health conditions, especially cancers. Acknowledge that the woman may be embarrassed and validate their emotional experience. To you it may just be anatomy, but to them it may feel like their identity is being challenged.
2. Practice health literacy, where the onus is on the medical professional to ensure that any information given is understood by the patient. Give information about treatment plans in a written format that utilises plain English. A printed plan will allow them to reflect on the treatment after the shock wears off and to identify questions they need to ask. It will also allow them to share that information with the people that support them.

Before	Now	Future
• Women in the dark • Public shame and embarrassment • Protected from knowing what could happen • Incorrect terminology – vulva often called vagina	• Women seeing the importance of being vigilant • Don't need protecting • Need knowledge to protect themselves • Can cope with knowing • Women are smart	• Women with forthright, demanding better education, funding of research and support • Experiencing better outcomes • Working in partnerships with medical professionals

3. Refer them to support services if it is a diagnosis that will impact their day-to-day functioning. Emotional and practical support is essential to support the physical and mental wellbeing while journeying with their cancer diagnosis. Do not undervalue peer support services and the power of women sharing stories with people who have been through the same or similar situations.
4. Support community events, such as the International Gynaecological Awareness Day (Red Knickers Day Campaign 2022, 10 September), which is gaining global momentum. Play an active role, collaborate with community partners to create events that create awareness and reduce stigma. This in turn will create greater community interest to fund research and support services, a win/win.

Women and medical professionals as partners can achieve miracles, as saving and repairing bodies is heroic work.

More information available at kathmazzella.com or email kath.mazzella@bigpond.com or call 0402 605 603.

A community of cancer support

Jan Savage
Cancer Care Western NSW Inc

Cancer Care Western NSW is a community-run charity independent of health, containing a member cohort of professional and former professional members from many areas of life with appropriate skill bases set up to provide the much-needed funding and support for the now operational radiotherapy services at the new Orange Hospital.

The organisation was formed in late 2006 and formally registered in early 2007. We are independent of Health as an organisation. We provided the responsibility of raising funds to build Western Care Lodge, an accommodation facility for regional and remote patients undergoing lengthy cancer treatment at the hospital. The facility would provide the vital support required to enhance radiotherapy services that support the 300,000 people within the medical service catchment area of the hospital. Western Care Lodge opened in November 2011.

Situated on site, a short walk to the hospital, Western Care Lodge has been operational for more than ten years. It is maintained and upgraded as required by Cancer Care Western NSW. We rely on consistent funding from private, public, business organisations and grants to support any upgrades that are consistent and ongoing both internally and externally, as we are now entering our 11th year of operation.

The strength in our organisation is the consistency of leadership.

Our organisation raised the required $ 5.4 million dollars to build and fit out the Lodge. Funding was acquired through community engagement and participation of various clubs and organisations throughout the medical service catchment area, extending as far as Cobar, Lake Cargelligo, Coonabarabran and as far down as Young, and out to Mudgee and Lithgow.

A number of grants were also obtained over a few years, and connections of support were made through corporate entities, local and state government. Many individuals who grew up in the region and attended boarding school in metropolitan locations were also helpful in supporting funding. Our organisation held a few corporate functions – dinners, along with auctions, to support the funding. Personal visits and connections have also been ongoing

One country town held an Art Union and raised $75,000.

The continuity of support for the build and the service was contagious and our organisation is tasked with collating through our board the numerous donations and visitations. One businessman organised an annual car rally over ten years which covered most of the medical service catchment area and raised more than $600,000. This was a cohesive event also providing service and location information: the most cohesive and broad-spread marketing innovation.

It would be too onerous to list all the activity-based work and community engagement which over a few years took so many hours, days and months. It was an insight into the wonderful world of community, the outback and regional and remote NSW. The world of these cancer patients who have made the Lodge their home away from home for numerous weeks.

Our journey, and the that of the regional communities and private enterprises that have supported us, has opened our hearts more, so when we were approached to support the set up funding of Cancer Clinical Trials at the Health Service, again we responded, and raised over $330,000. This provided the seed funding for these trials that have provided additional treatment benefits for rural and remote patients. In addition, we supported the Virtual Reality Trials for regional and remote NSW at the trials unit to the amount of $50,000.

The comments and smiles from guests say it all for us at the Lodge, with some making ongoing friendships that endure when they leave, with the knowledge that their communities supported and helped shape their wonderful home away from home. The Lodge has 22 ensuite bedrooms, a large communal living area and kitchen, opening onto two outdoor areas for entertaining or relaxing, a library and wonderful outdoor garden spaces enhance the areas that are used for relaxation. We are situated on a campus that has heritage gardens throughout and adjacent to a club that runs bowls and golf and provides meals if required.

Our recent upgrades include over $30,000 spent on replacing our mattresses and combined bases, as well as providing planned updates to a rear perimeter fence to enclose additional garden space.

Care for our rural and remote guests; listening to stories, knowing how hard it has been for them to leave their homes and travel so far for treatment, but secure in the knowledge that their own communities paved the way for them to stay in what they have described as five-star luxury. Knowing that they are loved and supported, making new friends, and enjoying time and space to relax. One group make the return journey for a catch up laugh and a great luncheon annually. This brings so much joy to us.

What we have achieved as a community can be undertaken by all states, by all areas where the demographics are not favourable to health and socioeconomic outcomes. It is achievable by everyone working together, the amalgamation of forces that can provide the income to add to service delivery and the ability for unification of a strong and solid unit such as we have, with the ability to work the hours, take the chances and know that we have made a difference.

Our organisation has been able to continue to make changes, to unify and direct, because we engaged community, government, local government and business. We are a group of professional people and former professionals who donate their time and have done since early 2007. Most of all, we could not have provided what we have without communities engaging with us. We are indeed blessed to have undertaken this role and continue to do so, as needs change.

One of the huge advantages to regional and remote communities that formed support fundraising groups is that it unified the communities, provided support for cancer patients, grew pride, resilience and enduring friendships.

Further examples are evident throughout NSW of communities building accommodation to support those who are vulnerable to distance and acquiring support while undertaken vital health, and often life-saving treatments. All states could achieve these outcomes and in turn support the direction of vital service provision for rural and remote health. This support is invaluable to what we as Australians are committed to – the enduring growth and support of regional services that provide the responsible requirements of ensuring that regional and remote health issues are ongoing for those who are dislocated from service provision by geography.

Being independent of NSW Health also has been an advantage as we have total responsibility for the ongoing upgrades and operational area of our Lodge. While not reliant on capital funding from health. We do have support on campus as a service provider.

Preventing cancers through lifestyle choices

Dr Suzanne Dixon-Suen
BSc, BA, MEpi, PhD
Institute for Physical Activity and Nutrition,
School of Exercise and Nutrition Sciences,
Deakin University, Geelong, Victoria
Cancer Epidemiology Division,
Cancer Council Victoria, Melbourne, Victoria

Dr Brenton Baguley
APD, BHlthSci (Nut), MDietSt
Institute for Physical Activity and Nutrition,
School of Exercise and Nutrition Sciences,
Deakin University, Geelong, Victoria

Over six million cancers diagnosed worldwide each year may be preventable by avoiding known risk factors, such as maintaining healthy diet, avoiding excess weight gain, staying active, and avoiding alcohol and smoking.

High cancer burden in Australia/New Zealand and worldwide

Over 18 million cancers are diagnosed and nearly 10 million deaths worldwide each year (>166,000 cases and >57,000 deaths in Australia and New Zealand), excluding nonmelanoma skin cancers.[1] Each year Australians and New Zealanders lose over 880,000 and 127,000, respectively, years of healthy life due to cancer.[2,3] Economic cost is also high: for example in Australia >$6.3 billion in health system costs[4] and >$1.7 billion in productivity losses[5] annually, at least 0.5% of gross domestic product.[6]

Three to four in every ten of these cancer cases[7-9] and deaths[7] are preventable by avoiding known risk factors. These include lifestyle exposures, such as diet, physical activity, overweight and obesity, alcohol and smoking, which we will concentrate on in this article.

Eat a healthy diet

Relationships between specific nutrients and food groups and the risk of cancer have attracted significant research attention and public interest. The strength of the evidence in this field remains an ongoing debate, as most studies are observational and subject to similar biases (for instance, diet being hard to measure, and associated with other lifestyle factors), which meta-analysis does not overcome.[10,11] Nevertheless, the World Cancer Research Fund (WCRF)'s latest evidence summary and recommendations for cancer prevention (2018)[12] identified a number of dietary exposures as probable or convincing risk factors for individual tumour streams. Their interactive cancer matrix[13] is a useful resource for clinicians working in this space that outlines individual risk factors in relation to cancer risk. One key diet recommendation is that wholegrains, vegetables, fruit and legumes should form a major part of our diet. There is suggestive evidence that regular fruit and non-starchy vegetable intake (recommendation: at least five servings, or 400g/day) and adequate fibre intake (recommendation: 30g/day from food) may reduce risk of several gastrointestinal cancers and possibly others including breast cancer.[12] Red meat (whilst a good source of protein, iron and other nutrients) has consistent evidence of a link to increased colorectal cancer and so should be limited to three portions/week (350–500g cooked weight), cooked to avoid charring; processed meats, also strongly linked to elevated colorectal cancer risk, should be reduced or eliminated.[12] Dairy products and dietary calcium are probably protective against colorectal cancer[10,12] and possibly premenopausal breast cancer.[12] Fewer studies convincingly link dietary factors and gynaecological cancer, apart from consistent evidence indicating that coffee may decrease endometrial cancer risk while glycaemic load may increase risk.[12]

Recent movement towards evaluating dietary patterns (combinations of foods within a diet) has high clinical value, given food groups and nutrients are consumed in combination. Evidence from prospective studies shows high adherence to a Mediterranean diet (a largely plant-based diet with low levels of red meat)[14] is associated with decreased risk of many cancers including liver and gastric,[15] while a single trial suggested decreased breast cancer risk.[16] There is strong evidence that healthy or 'prudent' dietary patterns, also heavily weighted towards vegetables and wholegrains, may substantially reduce the risk of some cancers including colorectal and breast, with less evidence for gynaecological cancers.[17] Conversely, meta-analyses suggest Westernised dietary patterns (high

in processed foods, refined grains, added sugar, and low in fruits, vegetables and fibre) are associated with increased risk of cancers including colorectal, breast, and endometrial.[17-19]

There are many mechanisms likely to explain the associations between diet and cancer risk (including gut dysbiosis, inflammation, epigenetic changes, oxidative stress, insulin resistance and hormone metabolism),[20] but one key pathway involves the role of a healthy diet in helping to avoid overweight and obesity. Following the WCRF dietary recommendations noted above, and their additional recommendations to avoid sugar-sweetened beverages and reduce intake of 'fast' and other processed foods high in sugar, fat, and starch, will put you in good stead to achieve a healthy body weight.

Maintain a healthy body weight

The International Agency for Research on Cancer have determined that maintaining a healthy body weight (usually defined as body mass index [BMI] of 18.5–24.9 kg/m^2) is beneficial for reducing the risk of at least 13 cancer types,[21] with overweight/obesity the second biggest preventable cause of cancer.[8] Each 5kg/m2 increment in BMI is associated with a seven-fold increase in endometrial cancer, a nearly five-fold increase in oesophageal adenocarcinoma, and approximately 10% increases in postmenopausal breast cancer and ovarian cancer.[21] Mechanisms linking excess adiposity and cancer risk are likely to include metabolic dysfunction, chronic inflammation and sex hormones.[22]

Keep active: move more, sit less

Another daily choice that we can make to lower cancer risk, and a key WCRF cancer prevention recommendation, is staying active by doing regular physical activity and minimising time spent in sedentary activities (for example, computer use, driving or watching TV).[12] Physical activity is any movement needing more energy than resting, including aerobic activity, such as jogging or cycling, or anaerobic activity (resistance training) such as weightlifting. Exercise scientists often measure activity intensity by comparing oxygen uptake to resting rate, classifying activities as sedentary (sitting or reclining); light (standing or slow walking); moderate (e.g. brisk walking, with heart/breathing rates ~60–75% of maximum), and vigorous (e.g. running or team sports, with heart/breathing rates >75% of maximum). There is consistent evidence that vigorous activity reduces pre- and postmenopausal breast cancer, and that greater overall physical activity decreases risk of multiple cancers, especially oesophageal, colon, endometrial, and breast (particularly postmenopausal) cancer; risk reductions range up to 40% comparing most- and least-active people.[12,23] We know less about sedentary time, but evidence is accumulating that it probably increases risk of endometrial and other (perhaps colon, lung) cancers, independent of physical activity; however compounding by other unhealthy behaviours such as smoking remains an issue, and understanding interactive effects of physical activity and sedentary behaviour is an ongoing research effort.[22]

The WCRF cancer prevention recommendation is to meet or exceed national guidelines on activity. In Australia and New Zealand (in line with many other countries), adults are recommended to do >75 minutes of vigorous or >150 minutes of moderate aerobic physical activity (or a combination) every week, plus muscle-strengthening activities two days per week, and to limit and break up sedentary time.[24,25] Lifestyles which are physically active and lifestyles involving high levels of sedentary time are not mutually exclusive; for instance, people meeting physical activity guidelines may also have long continuous periods of screen time.[22] Therefore lifestyle modifications should consider both. People could consider active commuting and recreation, walking meetings, setting regular 'stand and stretch' reminders during sedentary activities, and using wearable activity trackers.

Being active and minimising sedentary time promote conditions less conducive to tumour initiation and growth; they may reduce cancer risk by helping to maintain a healthy weight (of strong relevance for endometrial cancer), but also more directly by reducing levels of sex hormones (e.g. of relevance for hormone-sensitive cancers including breast), improving metabolic function including insulin sensitivity, improving/preventing states of chronic inflammation including lowering adipokine levels, improving immunity, reducing oxidative stress, or reducing digestion time (likely of relevance for colorectal cancers).[22, 23]

Eliminate alcohol

Alcohol intake is classified by the International Agency for Research on Cancer as a confirmed carcinogen and is a key contributor to the global burden of cancer. Alcohol use is associated with >200 health conditions and causes over 3 million deaths annually worldwide, 0.4 million (13%) from cancers.[26] There is strong evidence that alcohol causes many cancers, including in the breast, liver, and multiple gastrointestinal tract sites, and building evidence suggests a causative role in others; risks range up to fivefold higher (oral, pharyngeal, oesophageal cancers; higher for women) for heavy drinkers versus nondrinkers.[12,27] There is no safe level of alcohol of any type from a cancer prevention perspective, so not drinking alcohol is another key WCRF prevention recommendation.[12] The International Agency for Research on Cancer curates a useful website, Cancers Attributable to Alcohol,[28] for further information. Explanatory mechanisms are still under active research and may include carcinogenicity of ethanol metabolites, epithelial damage in the upper digestive tract, immunosuppression, and increases in sex hormone levels.[27]

Avoid smoking

Tobacco smoke has long been classified a carcinogen with compelling evidence of carcinogenicity, and is the largest contributor to cancer incidence worldwide.[7,8,29] Tobacco use (smoked or smokeless) is a cause of many cancers, including most aerodigestive/gastrointestinal cancers particularly lungs and throat, bladder, kidney, liver and cervical cancer, and myeloid leukemia.[29] Over 80% of lung, 70% of larynx and 50% of oesophageal cancers are attributable to smoking;[8] all of these cancers have low survival rates. Smokers are at highest risk of lung cancer: current and ex-smokers have over eight- and four-fold, respectively, higher risk than never-smokers.[30] Quitting reduces risk by 30–50% after 10 years, relative to continued smokers.[29] Whilst Australia and New Zealand have seen a steady decline in smoking thanks to national public education campaigns and high taxes on tobacco products, 8–16% of young adults still smoke daily and rates continue to be higher in disadvantaged and regional areas.[31,32] The Royal Australian College of General Practitioners guidelines and New Zealand Ministry of Health guidelines for smoking cessation offer key

practical recommendations tailored to individual patient preferences, with nicotine replacement therapy plus behavioural support offering the most promising strategy.[33,34]

Conclusion

The burden of cancer in Australia and New Zealand is high, yet 30–40% of all cancers, and up to 80% of specific cancers, are preventable. Maintaining a healthy diet and weight, being physically active, and eliminating alcohol and smoking are the cornerstone cancer prevention recommendations from the WCRF (and will lower risk of many other chronic diseases). While addressing individual- and system-level barriers to adopting healthy lifestyles is required, implementing these recommendations as a collective may offer synergistic and multifaceted prevention strategies that are low cost and can reduce burden from a wide range of cancers. Active and timely referral to allied health professionals (i.e. nutrition, exercise, and psychological expertise) to support behavioural change along with continual education and awareness-raising around these modifiable lifestyle risk factors will help reduce the burden of cancer in Australia and New Zealand.

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Managing uncertainty: the challenge of change

Dr Louise Stone
MBBS BA DipRACOG GDFamMed MPH MQHR MSHCT PhD FRACGP FACRRM FASPM
Australian National University

As GPs, gynaecologists and obstetricians, we are used to supporting our patients through important transitions like puberty, pregnancy and menopause. When our patients have cancer, there are also important transitions. At these times, it may be challenging for patients to adapt to a new reality where illness becomes a larger part of their lives.

Uncertainty can begin at the screening stage for patients at high risk of cancer where complex surveillance regimes can lead to chronic anxiety.[1,2] In the early stages of diagnosis, particularly when diagnoses are difficult to make, patients will often resent the lack of certainty, and may feel misunderstood, isolated and vulnerable.[3]

At diagnosis, a person's identity forcibly undergoes transformation[4] with some writers suggesting that the assumption of an identity as 'a cancer patient' is likely to be permanent, even with recovery.[5] The moment of diagnosis is 'marked by disorientation, a sense of loss and of loss of control, and a sense of uncertainty'. Many lose their social connections when friends and family are unable to cope with the world of illness and they can become profoundly isolated.[5]

During remission, patients regain their autonomy and agency, but are often unable to regain the sense of self they had before they were ill. There is a sense of 'relentless vigilance' as patients scan their bodies for recurrence.[6] The person they expected to be, and the life course they expected to follow are gone, and the new identities they have adopted are unfamiliar and often frightening. It can be difficult to re-engage with their home and work because the familiar can seem strange and social relationships can be uncomfortable.

Liminality is a useful concept for considering the lived experience of uncertainly in illnesses like cancer.[7,8] Liminality describes situations in which people find themselves 'betwixt and between' states of being (including categories of health and illness). The term liminality, adopted from anthropology[9] was originally used to describe a life stage in which we move from one phase to another, such as adolescence, pregnancy, and bereavement. Cancer has its own liminality. The time between a positive screening test and a definitive diagnosis, is a time of great uncertainty. The patient is not well, but not yet 'sick' and they are stuck in a no-man's-land in terms of their identity. The time of remission is similar. They are no longer 'sick' but they are not exactly 'well'. When these times cross over with other transitions, like developing cancer in pregnancy, or treating cancer with an oophorectomy that causes a surgical menopause, it can be particularly difficult to manage. Patients describe being in familiar situations but feeling out of place because they are profoundly changed.

Change is not always negative; many patients describe positive change following transitions. However, some patients need help coping with the identity shifts involved in navigating the changes that cancer requires.

Coping

At times of great uncertainty, patients may need help with managing the stress and anxiety. Coping strategies include four distinct categories, each with their own focus.[10] The following discusses common approaches to coping and is extracted from 'illness uncertainty and risk management for people with cancer'.[11]

Appraisal focuses on how a person perceives the threat posed by their illness and how they understand their capacity to cope. Different patients will appraise the same diagnosis differently: one patient may see breast cancer as inevitably fatal, another will see it as an acute illness with a painful but inevitable recovery. People also differ in their sense of their own capacity to cope. While one patient may be confident they have the financial, social, emotional and physical resources to manage their illness, another patient may be overwhelmed by the prospect, and feel completely unable to manage.

Appraisal strategies help patients to accurately and realistically understand the threat their illness poses, and their ability to cope, given the support they are likely to receive. These strategies involve education, with a clear description of the likely course of the disease and the treatment plan. Accurate appraisal is supported by written information, lived experience stories, peer support and time to ask questions with the relevant clinical team to address concerns. GPs may need to help their patients recognise their own strengths by reminding them of previous situations that they have managed well.

Problem-solving involves managing practical issues, such as appointments, financial concerns, work and the management of treatment regimes.

Problem-solving strategies include helping patients prioritise, coordinating care, supporting patients with their administrative needs, such as work certificates, and discussing potential solutions to personal needs, such as parenting responsibilities.

Emotion-focused coping includes managing the distress associated with uncertainty, fear, pain and disability.

Emotion-focused strategies include positive strategies, such as exercise, social support, empathic connection with an appropriate healthcare provider, peer support and physical therapies, such as massage. Negative strategies also need to be managed, and include substance misuse, including misuse of prescribed medication and other unhelpful behaviours.

Meaning-focused coping is used when appraisal, problem solving and emotion-focused coping strategies are exhausted or inappropriate. These strategies are used when patients are coping by just getting through the days, one at a time.

Meaning-focused strategies include:

- Distraction, such as visiting a pleasant place, watching a movie or going to a sporting event
- Connection, such as visiting friends or family, or attending a social or peer group
- Self-efficacy, such as participating in a work meeting, completing a piece of schoolwork or learning a new skill, such as a craft activity. Often, when a person is ill, they will have few opportunities to feel effective and productive. It is important that friends and family recognise this and find ways to support the person with cancer by finding opportunities to help them regain a sense of meaning and purpose.

Conclusion

Liminal times involve great uncertainty, particularly if there is developmental liminality, like puberty, pregnancy and menopause, at the same time. Patients who live with disadvantage are likely to experience greater uncertainty. Doctors can help by assisting patients to navigate complex health systems, explaining illness in ways that are culturally appropriate, and discussing the loneliness and disorientation of being between wellness and illness.

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A GP's perspective on palliative care

Dr Paul Hanson
BMedSc, MBBS, DRANZCOG, FRACGP, MFM
Partner, Newstead Medical, Tasmania

GPs, particularly rural GPs who undertake quality palliative care, consider it to be part and parcel of the job. As doctors we have the privileged position of being involved in the many life stages from birth till death.

I consider it to be an honour to be allowed to be involved in the final stages of their life's journey.

In some ways it's akin to the privileged position we as doctors involved in obstetrics are given. As a former procedural rural GP who has been involved in approximately 300 confinements, I have firsthand experience in the challenges and satisfaction of providing intrapartum care and also in palliative care.

Being involved in a deeply personal part of a patient's life either by helping them give birth or helping them in the final stages of their life in some ways have a lot of similarities. In both situations we as caring professionals are invited into a deeply significant part of the patient's journey.

With the subspecialisation of medicine over the last few decades, palliative care is now a specialty. In urban practice most GPs are becoming less involved in palliative care.[1] Only about 30% of GPs in Australia visit aged care facilities (ACF). In urban practice ACF is where GPs are mostly involved in palliative care. Many patients in the palliative phase of the illness would like to stay at home. The GP involved in the 'at home' palliative phase of their care requires teamwork. This involves community nursing, palliative care, and nurse specialist, palliative care physicians.[2]

Palliative care has generally been focused on the care of people who have about six months of life left to live and normally is associated with metastatic cancer. However, it can involve chronic neurological conditions such as motor neuron disease, Parkinson's disease, multiple CVAs or even cardiac failure.

A case study

Recently I have been involved in the care of a retired lawyer. A number of years ago I diagnosed him with having normal pressure hydrocephalus. He was appropriately treated with a ventricular peritoneal shunt and made a good recovery. This allowed him to return to his semiretirement roles on various boards. I was also the GP for his wife and children and grandchildren. He maintained normal health until unfortunately he developed a myelodysplastic disorder which required regular blood transfusions. He was under the care of a haematologist. His cognitive function remained sound although his physical condition slowly deteriorated. He developed repeated infections and required more frequent blood transfusions. He wished to be cared for as much as possible at home. I was involved in his ongoing care at home, along with the community nursing palliative care team and his haematologist.

Caring for his wife and family was another priority as his illness became more pronounced. The support of his family was critical. His ongoing care in the community was part of my concern.

Over several months his condition became such that he required admission to an ACF. Cognitively he was still normal; however, he required more intensive nursing care. A decision was made after a family conference including the patient to stop the blood transfusions. The haematologist at this point thought it wise that he should be transferred to a palliative care unit. The family were very supportive of the plan to remain within the ACF where he had become relatively comfortable and familiar with the nursing and support staff. As the GP involved in his palliative care I was mainly focusing on his physical and mental wellbeing and the care of his family. Fortunately, he had very minimal pain. He had a very low platelet count which increased his chances of catastrophic terminal haemorrhage. This was managed with tranexamic acid orally.[3] His increasing anaemia resulted in increasing dyspnoea and was managed mainly by giving small quantities of subcutaneous morphine 2mg PRN hourly. This was preferred to having an oxygen mask on his face for his final days

With his conditioning worsening the family were encouraged to say their farewells. I too had the rare opportunity to say farewell the day before he died. This was an emotional time but provided a degree of comfort for the family.

I still see his extended family in the practice.

Conclusion

Undertaking palliative care in general practice enhances the breadth of knowledge and skills required of a GP. It allows the GP to be invited into a privileged and very significant part of the patient and their families' lives. It gives greater satisfaction to our roles as medical professionals.

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Q&A

For the broader *O&G Magazine* readership, balanced answers to those curly-yet-common questions in obstetrics and gynaecology.

Dr Heather Waterfall
BApSci (Med Rad), MBBS (Hons), FRANZCOG

Dr Candice Houda
MRMed, BMedSci(Hons), MBBS

Q How do I return to work and still provide breastmilk for my baby?

A *Dr Heather Waterfall returned to her private O&G practice when her twins were eight weeks old and Dr Candice Houda returned to work as an AGES Fellow when her daughter was six months old. Between them they have pumped or fed babies through theatre cases, telehealth appointments and hospital and RANZCOG Council meetings.*

Many of us have combined becoming parents with return to work as an O&G; returning to work while breastfeeding (or the 'food lady' as Candice has been affectionately nicknamed in her house) adds another challenge. Performing well and contributing to the team are important, but so is providing breastmilk for our babies, and for most women this means pumping/expressing milk at work.

Why is pumping/expressing necessary for breastfeeding women when they return to work?

Breastmilk supply is reliant on frequent and effective breast emptying. Breastfeeding women need to express milk approximately every three hours for about 10–30min. Long gaps between pumping sessions and inadequate food and drink intake can lead to engorgement, discomfort, mastitis, a drop in milk supply and the risk of premature weaning.

Every three hours? How is that possible at work?

It is every employee's legal right to have a break to express breastmilk, and it is important that women are supported to pump in a place of their choosing. Tell your team you need to stop and express, and have a plan in place to make pump breaks happen. Don't be embarrassed to tell people you need to pump, most people will admire your determination. By expressing at work and talking about breastfeeding we are normalising it. By doing this we can make it easier for junior doctors and nurses who come after us, who may not feel as able to speak up and ask for pumping time.

Practical tips for pumping at work

Essential kit: a battery powered double pump (Heather uses a Spectra S1) with a pumping bra for handsfree pumping, or a wearable pump (though more expensive) can be a timesaver allowing multitasking, examples including Elvies, Willows, Spectra Wearable (Candice's preference) and Freemies. If possible, have two complete sets of flanges/valves in case you get called in and need a clean set of kit. It is also important to replace pump parts regularly, in particular if you find pump volumes have dropped.

Buy a cooler bag with an ice-brick (if you don't have access to a convenient fridge), store your pump parts in a Tupperwear container in the bag and they only need to be washed every 24 hours. After trying a few options, milk bags and hospital specimen pots make excellent storage if you forget bottles. A cloth is always handy in your pack, plus nipple cream, a water bottle and snacks to ensure you eat and drink with every pumping session.

Videos/photos of your baby can help with a let down. Don't think about how much (or how little!) milk you are making, put a cover over the bottles so you can't see how much milk is there and instead think about your baby, or alternatively multitask with letters/operation notes/email/social media. 'Hands on' pumping with breast compressions may help increase volumes whilst expressing.

Starting the day 'empty' helps build up supply, and pumping in the car on the way to work takes minimal effort. This requires a wearable pump or a large scarf over traditional flanges with a handsfree pumping bra.

In theatre: pump before every major, even if it's a 'short one'. A wise urologist suggests 'if in doubt, pump.' Whilst not for everyone, it is possible to

scrub in for major cases with wearable pumps in (although you can resemble Dolly Parton). Let the team know discreetly when you turn them on, start pumping at skin closure or during the check cystoscopy to save time. If a wearable pump isn't suitable then a private place to pump between cases is necessary – a private office with a lockable door ideally, but a shower cubicle in the change rooms might be the most practical option. It is not acceptable to be told to pump in a toilet, nor should you have to use a pumping room on the other side of the hospital.

In clinic: If you can, block out time in your clinic to pump – make an appointment with your baby. Or block out time for phone appointments and pump and talk at the same time.

Useful resources
Dr Milk Facebook group
MAMMTB Lactation Interest Facebook group for any doctor regardless of gender
Work. Pump. Repeat. Jessica Shortal
World Health Organization articles and guidelines www.who.int/health-topics/breastfeeding
World Breastfeeding Week 2021 waba.org.my/wbw
Women in Surgery www.surgeons.org/en/Resources/interest-groups-sections/women-in-surgery
Tips for breastfeeding at work education www.possumsonline.com/blog/breastfeeding-and-returning-work
AAFP policy for medical trainees on lactation www.aafp.org/about/policies/all/breastfeeding-lactation-medical-trainees

Pumping on call: O&G can be unpredictable, if you get called in and will miss a feed, ideally you need to pump around the time of the missed feed. Pump in the car on the way in, or while waiting for theatre or writing the delivery note. Better to pump earlier than a usual feed time otherwise you risk missing the feed/pump entirely, with resultant engorgement and potential trigger for decreased supply.

All day training/meetings: almost all meetings now have the ability to join via Zoom/Teams. You can leave a face-to-face meeting and then join online while you are pumping, then return to the meeting face-to-face.

If you are caught out at work without pumping equipment, obstetric hospitals have hospital grade pumps available for patients to use, and often will let staff use them if needed in an emergency. It is even possible to use Uber parcel delivery to have your forgotten pump delivered to work.

When can you stop pumping at work?

After baby turns one and is reliably on solids, breastmilk intake will likely drop, and as supply = demand, breastmilk supply will likely drop as feeds become less frequent. The frequency of pumping can therefore be slowly decreased, though many women still choose to continue a lunchtime pump for comfort and to maintain supply if their baby would normally feed at this time. If you are away from baby for more than 12 hours, pumping remains necessary to maintain supply and not risk mastitis. The WHO recommends breastfeeding until two years of age, though there can be societal pressure to stop feeding or pumping earlier than this. As doctors we can normalise breastfeeding by talking about it and continuing to pump at work as needed, and supporting others to do the same.

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The Bali AOFOG YGA journey

Dr Debjyoti Karmakar
MBBS(Hons), MD, MRCOG, FRANZCOG

We boarded the flight from Melbourne on 19 May 2022, a bit nervous as this was our first overseas flight in two years. The flight was pleasant, but the queues in the airport for infection control were extremely long. Indonesia had some of the most stringent travel rules, and they were only slowly getting relaxed.

While there was excitement, there was a bit of nervous anticipation around the post-pandemic dive into this Community Fellowship Program (CFP) and the AOFOG Congress experience in Bali. The 10 Young Gynaecologist Awardees (YGAs) from the Asia Oceania region had already had an interactive Zoom call (yes, the lifesaver of the Covid-19 pandemic!), so it was apparent that it was an enthusiastic cohort.

On exit from the Bali airport gates, we were pleasantly overwhelmed by the warm welcome from the organisers at the gates. We were taken to our hotel, and it was obvious Bali was back in business with tourism with billboards about the upcoming G20 summit and the local government's emphasis on 'Rebuilding Together.' We were already witnessing their trademark hospitality.

On 20 May, we had our first social event where we were invited for an introduction to the organising committee and the AOFOG secretariat. This event also included ice-breaking activities for the participants to mingle and share initial thoughts. Dr Kania Praharsini was our liaison doctor throughout the CFP, and Dr Dian Tjahyadi was responsible for the overall CFP organisation. Their passion and hospitality made this a genuinely enjoyable experience.

We witnessed traditional dance, live music, and local cuisine, and it felt like the start of a new friendship with global colleagues. What struck me most was the natural keenness we had to talk about experiences in our countries and the barriers to equitable women's health, even in this informal setting. The CFP was intended to be a platform for sharing ideas between O&Gs in 10 countries of Asia Oceania to identify problems and collaborate to improve women's health locally and globally. The commitment to this platform was on a firm footing from all the participants.

On 21 May, the CFP formally started. We went on a field trip to an integrated primary health centre, 'Posyandu', in South Kuta and witnessed medical appointments carried out alongside an educational program on reproductive health for adolescents. On our return to our convention venue, in continuation of the theme from the morning, we were provided with an overview of the World Health Organization (WHO) Millennium Development Goals transitioning now to Sustainable Development Goals.[1] We focused on Asia Oceania and especially on the impact of PPH in accounting for the lives of women in developing and underdeveloped settings.

We were then provided with the Indonesian collaboration context to reduce maternal death. In Australia, the maternal death rates are extremely low,[2] so it led to an eye-opening and exciting exchange of ideas, experience and a drive to try and be an advocate for equitable access to quality healthcare for women across the region as a whole. On 22 May, we had a moving virtual premiere of 'Voices from the field',[3] which reminded me of my time in India dealing with PPH and the disparity between developed countries where I work now and underdeveloped countries where I have had opportunities to work in the past.[4]

These were followed by plenary sessions on reducing maternal and neonatal deaths on an interactive platform with sharing ideas across the table. That evening we were taken to the Uluwatu temple. We attended the 'Kecak Dance', followed by dinner by the bay, which provided the perfect opportunity to soak in the local culture in a relaxed environment and reflect on the learnings thus far.

On 23 May, we prepared our group resolution on conceptualising pathways to reduce maternal death and improve women's health globally, focusing on the Asia Oceania region.

The main emphasis of our report was the decentralisation of tertiary care and the involvement of young O&Gs to bridge the gap and iron out inequity. We also thought building platforms for communications within countries and across the Asia Oceania regions was crucial. We presented that this needed the active support of national O&G societies and not-for-profit organisations.

Young Gynaecologist Awardees at the local Posyandu, an integrated primary health centre, in South Kuta

Team-building games and activities followed this as the CFP ended. We practised a local Indonesian dance on the CFP days. Some of us were natural dancers, and some were shy, but by the end of the rehearsal, we were all thoroughly enjoying each other's presence in the dance performance. We presented it to the dignitaries at Presidents night on 23 May with a brief introduction to our country of representation and our thoughts on the fellowship program.

During the President's social night, I was fortunate enough to have some of the most stimulating conversations with Prof Mary Ann Lumsden, Chief Executive of FIGO, and Dr Eddie Morris, President of RCOG UK. The theme from all the O&G leaders seemed to emphasise harvesting young O&Gs' energy in shaping global women's health.

The AOFOG congress covered the length and breadth of updates in O&G, from essential interventions to cutting-edge innovation. It provided an opportunity to hear from the experts and upcoming researchers. In the free communication session, I presented my research on 'risk reduction salpingectomy'. I found the FIGO session at the congress most informative, reminding us of the critical global needs in women's health. I was fortunate to interact with RANZCOG President Dr Benjamin Bopp, and we discussed the CFP experience. Dr Bopp echoed the sentiment around the vital role of young O&Gs.

I am happy and very proud of my attendance, and the experience gained therein. I was also able to provide an Australian perspective to many discussions. It energised my commitment to work in global health and ideas that can be implemented at local or international levels. I also learned about disruptive innovation that could prevent maternal deaths at a fraction of current costs.

The networking experience was very beneficial and has provided all CFP attendees with a platform to share ideas, and we are all in touch via social media. I am delighted that I could represent RANZCOG and Australia and look forward to more such opportunities.

Dr Debjyoti Karmakar participated in the 2022 AOFOG Congress and Community Fellowship Program courtesy of the RANZCOG Shan S Ratnam Young Gynaecologist Award, as supported by the RANZCOG Women's Health Foundation.

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Letters to the Editor

It's time to prioritise iron optimisation in pregnancy

Iron optimisation in women working group:

Dr Lisa Clarke
Transfusion Policy and Education, Australian Red Cross Lifeblood, NSW, Australia
Haematology, Sydney Adventist Hospital, NSW, Australia

Dr Kylie King
Department of Haematology, Wollongong Hospital, NSW, Australia
Graduate School of Medicine University of Wollongong, NSW, Australia

Dr Catherine Tang
Department of Haematology, Gosford Hospital, NSW, Australia
School of Medicine and Public Health, University of Newcastle, NSW Australia

Dr Lynn Townsend
Ultrasound Care Australia
School of Women's and Children's Health, UNSW Medicine & Health, NSW, Australia

Dr Talat Uppal
Women's Health Road, NSW, Australia
Department of Obstetrics and Gynaecology, Northern Beaches Hospital, NSW, Australia

Dr Nada Hamad
Department of Haematology, St Vincent's Hospital Sydney, Australia
School of Clinical Medicine, UNSW Medicine & Health, NSW, Australia
School of Medicine, University of Notre Dame, NSW, Australia

Dear Editor,

We read with great concern Dr Barton Smith's article in *O&G Magazine,* 2022, vol.24, no. 1. 'Normal serum-ferritin in pregnancy: less is more'. We wish to dispute some alarming claims made by the author thus highlighting the importance of correcting obstetric iron deficiency for both mother and baby.

Dr Smith argues that the development of iron deficiency, which he mislabels hypoferritinaemia, 'serves two logical protective purposes' namely protection against sepsis and miscarriage. Dr Smith fails to acknowledge the complex interplay between iron and immunity negating to mention the important role iron plays in humoral immunity including neutrophil, macrophage, and T cell function.[1] Secondly, whilst we agree that obstetric complications are increased in iron overloaded states, it cannot be extrapolated that the correction of iron deficiency is harmful. This is analogous to tolerating maternal hypothyroidism due to the well-recognised adverse obstetric outcomes associated with hyperthyroidism.

The article makes no mention of the breadth of evidence supporting the negative effects of obstetric iron deficiency. Iron plays an essential role in cellular respiration and mitochondrial function and is a cofactor for the synthesis of the neurotransmitters dopamine and serotonin.[2] These non-erythropoietic roles explain why individuals with iron deficiency can be symptomatic even in the absence of anaemia with manifestations including fatigue, poor cognition, reduced physical performance and mood disturbances.[3,4] Small randomised trials have shown that correction of iron deficiency improves the ability to perform simple and complex cognitive tasks whereas correction of anaemia merely improves the speed in which these tasks are performed.[3] Specific to the obstetric population is iron's impact on maternal infant interactions and link to postpartum depression.[5,6]

Whilst studies on the correction of obstetric iron deficiency fail to prioritise quality of life scores as outcome measures, objective measures of anaemia at birth and risk of blood transfusion are reduced,[7] and whilst some may take the decision to transfuse lightly, it is not without risk including a 10% risk of alloimmunisation[8] which may negatively impact future pregnancies in regards to the risk of haemolytic disease of the fetus and newborn (HDFN).

There is evidence to support that neonates born to iron deficient mothers can develop iron deficiency with or without anaemia,[9] and in observational studies this has been linked to inferior neurocognitive performance at five and 10 years namely in areas of language ability and fine-motor skills.[10] Additionally, lasting behavioural issues have been seen at five years despite correction of this iron deficiency in infancy.[11]

Finally, whilst we acknowledge the concern in the obstetric community about the use of intravenous (IV) iron, we believe that ignoring the issue is not the solution; rather, we advocate for a proactive approach to iron optimisation in obstetrics with early identification of iron deficiency prior to the onset of anaemia. This also facilitates the greater use of oral iron through smaller doses or alternate day dosing thereby reducing the reliance on IV iron. Waiting for the woman to ask for iron replacement, as Dr Smith states, is unacceptable.

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Right of reply

Dr Barton L Smith
BSc (hons), PhD, MBBS, FRANZCOG
Obstetrics and Gynaecology Department
Joondalup Obstetrics and Gynaecology Group
Joondalup Hospital, Shenton Ave, Perth, WA

Dear Editor,

Thank you for inviting me to reply to 'It's time to take iron optimisation in pregnancy seriously'.

Dr Clarke et al assert a failure to acknowledge 'the important role iron plays in humoral immunity including neutrophil, macrophage and T-cell function'. In doing so, they incorrectly state T-cell function is a component of humoral immunity, when it is in fact cellular. More importantly, there is no evidence that intracellular immunity is deficient in iron in response to the normal pregnancy iron debt, or that gestational iron enhances immunity. There is, however, evidence that intravenous (IV) iron therapy worsens infections,[1] which is one reason the statement 'it cannot be extrapolated that the correction of iron deficiency is harmful' is incorrect. Other harms of gestational iron therapy include permanent staining,[2] hypophosphataemia,[3-5] financial cost,[6] myalgia,[7] fishbane reaction,[7] anaphylaxis,[8] death,[8] bloating, constipation, haemorrhoids, and anal fissures.

'Normal serum-ferritin during pregnancy' clearly stated that severe anaemia is uncommon in Australia, and specifically targeted the over-investigation and unnecessary treatment of non-pathological pregnancies with IV iron, not appropriate treatment of severe anaemia. The claim that 'neonates born to iron deficient mothers can develop iron deficiency with or without anaemia' refers to a cohort study of high-risk American adolescents prone to IDA prior to pregnancy whose babies had cord haemoglobin <130g/L in 24% of cases.[9] The majority of literature is in overwhelming agreement that neonates are not born anaemic unless maternal anaemia is severe (<90g/L).[10-19] McCarthy et al[20] found cord-ferritin assays <76ug/L in 8% of neonates but did not find any association between this and any cognitive, neurological or behavioural outcomes in their whole-data analysis. The only positive findings were an increase in childhood behavioural difficulties amongst children born via caesarean section with low cord-ferritin (positive at two and five years of age), and in those born with low cord-ferritin and to obese mothers at five years of age, but not earlier. The authors stressed caution regarding low numbers and extensive adjustments to their modelling, and the paper made no comment on maternal anaemia, iron parameters or iron therapy. Cord-ferritin as a gauge of fetal iron deficiency is inconsistent (Figure 1), and unless maternal anaemia is severe, most studies have found it is independent of maternal haemoglobin, maternal ferritin, fetal haemoglobin, or iron therapy.[21-38]

'...the breadth of evidence supporting the negative effects of obstetric iron deficiency', cites a small study in support of improved quality of life (QOL) measures amongst anaemic women after randomisation to iron therapy,[39] yet these women were not pregnant. This oversight is made worse by ignoring placebo-controlled RCT data that shows iron therapy does not improve fatigue or general wellbeing in non-anaemic iron bereft subjects.[40] Further, a study that focused on QOL outcomes specific to pregnancy comparing IV versus oral iron found that many positive QOL indicators, whilst initially improved with IV iron, failed to persist at

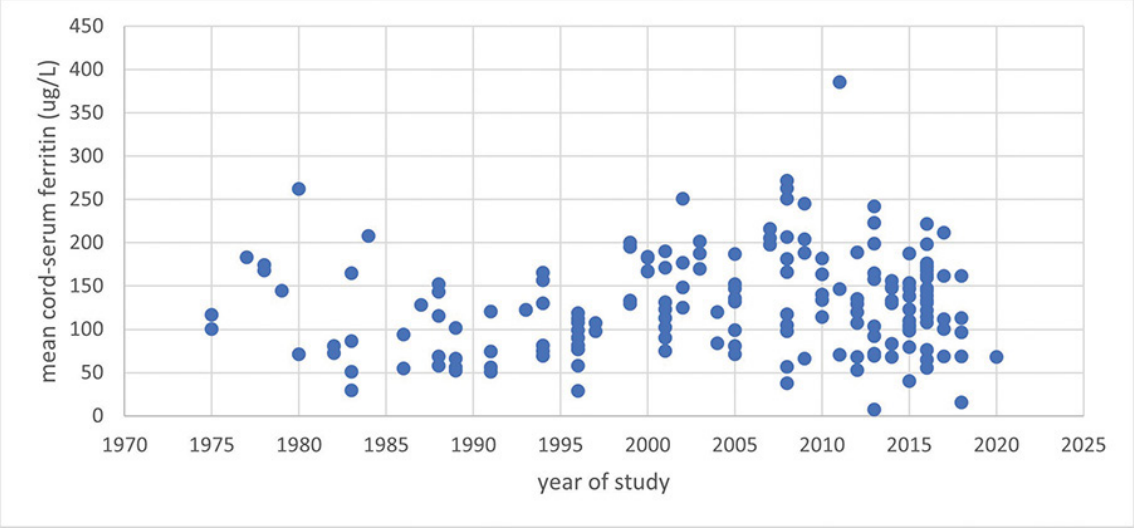

Figure 1. Mean cord-ferritin assays from >100 studies reported in the literature between 1975–2020.
(adapted from data presented in Delaney et al and Zhang et al)[21,22]

delivery or postpartum, despite patients being loaded with supraphysiological doses of iron.[41] Placebo aside, an improvement in physical QOL indicators immediately after IV iron may be attributed to an immediate inflammatory reaction rather than iron providing cellular energy. IV iron also has the propensity to decrease energy due to well-known side effect of hypophosphataemia – phosphate is a key component of the Krebs cycle.

Logically, if haemoglobin is used as a trigger to transfuse blood, then iron therapy should decrease the number of transfusions in the event of haemorrhage, and proportionally more benefits should be realised in populations with a higher incidence of anaemia, but this has not been realised in practice.[42-44] Dr Clarke et al have ignored these landmark trials, and instead appealed to a multi-interventional study which reported a decrease in the number of postpartum transfusions administered to women with Hb 70–100g/L, but not <70g/L, having instigated the following interventions: 1) increased education regarding the clinical threshold to transfuse, 2) encouraging single unit blood transfusions, and 3) increased antenatal screening with serum-ferritin and use of oral iron.[45] It is not possible to determine how much of the reported decrease in blood transfusions may have been due to the latter. Screening for iron deficiency with a serum ferritin cut off of 30ug/L renders an inordinate number of pregnant women pathological, and in settings with a low prevalence of anaemia and a low postpartum haemorrhage rate, the number needed to treat is exorbitant.

Failing to treat 'iron deficiency' during pregnancy is not 'analogous to tolerating maternal hypothyroidism.' Failing to treat overt hypothyroidism is negligent. Treating hypoferremia in low-risk pregnant women with a healthy haemoglobin is of no proven benefit. Svanberg's ingenuous iron isotope experiments demonstrated that first trimester iron absorption is actively reduced compared to the non-pregnant state.[46] Early pregnancy prophylactic oral iron is often counterproductive because of this – unpleasant side-effects are largely due to poor absorption and excess gut iron. Women who are unnecessarily trialled on oral iron in early pregnancy often 'fail' therapy due to poor tolerance which creates an aversion to oral iron and predisposes women to avoidance of it later in pregnancy when it is readily absorbed and more likely to be of benefit if needed.

Both intolerance to oral iron and refractory serum-ferritin <30ug/L are common pregnancy scenarios, and many obstetricians revert to IV iron in these scenarios regardless of anaemia.[47] It is irrefutable that routine screening for iron deficiency and/or routine oral iron therapy has contributed to the increased use of IV iron during pregnancy. Whether this consequence is intended or not is irrelevant, and it is naïve to claim early prophylactic oral iron and/or more ferritin screening will reduce this trend. Pharmaceutical companies profit handsomely from routine treatment and universal screening, and have manipulated modern antenatal care into an iron protocol to take advantage of it. This contrasts with the targeted approach to high-risk antenatal anaemia currently recommended by RANZCOG – screening with a full blood count and judicious use of oral iron, which is logical, safe, and cost-effective. 'Normal serum ferritin in pregnancy' did not state that doctors should wait until patients ask for iron but expressed appropriate caution that IV iron should not be administered purely on maternal request, or for unsubstantiated reasons. The term 'hypoferritinaemia' does not exist in the article – the accusation it was used as an incorrect label is absurd.

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Does Sims' speculum need a different name?

Dr Michael O'Dowd
MD, PhD, FRCOG, FRCPI, FICOG (Hon), DCH, DA

Dear Editor,

A student article 'Lucy's Legacy: why Sims' speculum needs a different name' in *O&G Magazine*, 2021, Vol. 23 No. 4, declared that the nineteenth century attempts to surgically repair vaginal fistulae were 'abhorrent ... unethical, sexist, and racist ... [while] condoning the history of violence and abuse ... the brutality of his [Sims] actions.'

As is revealed in the 'Lucy's Legacy' article, the students named Dr Kameelah Phillips O&G New York, who is overtly critical of Sims and who initiated the 'Lucy speculum' idea.

Also, the article's citations depended on two staff writers, Zhang (The Atlantic) and Brynn (History), both also critical of Sims, which helped form the student's opinions. Those named staff writers perpetuated both facts and pseudo-history in their writings, based on opinions from G. J. Barker-Benfield, Harriet Washington, Deborah Kuhn McGregor, and Deirdre Cooper Owens.

Those four named academic authors were highly critical of the development of gynaecology, and of J. Marion Sims. Scrutiny of their texts shows factual cited material, combined with radical opinions (no citations) that are without historical basis.

Also, the students quoted Robinson who wrote in his article 'With Dr. Morton's tenacity ... John Collins Warren (1778–1856) made history on October 16, 1846 with the first successful surgical procedure performed with anaesthesia.' The use of anaesthesia, which was experimental at the time, was not adopted immediately and remained a controversial subject in America and Europe for several years thereafter.

The 'Lucy's Legacy' article included a reference to Wallace and Weisman's article 'Should a war criminal be rewarded with eponymous distinction?: The double life of Hans Reiter'. Surely war crimes are not applicable to the subject matter?

While it is clearly stated 'The statements and opinions expressed in articles, letters and advertisements in *O&G Magazine* are those of the authors and, unless specifically stated, are not necessarily the views of RANZCOG' it is most important to be aware that the article lacked historical context, failed to offer balance, and promoted untruths.

The President Dr Benjamin Bopp wrote of 'the importance of culturally appropriate and respectful language' which in my view was not present in the 'Lucy's Legacy' article.

Students are future leaders in the profession. Surely they must not now, nor in time to come, propagate versions of medical history that are incorrect.

Right of reply

Anna Shalit (Monash University)
Andrew Downie (Monash University)
Mansi Tiwary (University of New South Wales)
Kirsten Arnold (Monash University)
Mary Malek (Monash University)
Afreen Feroze Akbany (University of NSW)
Natasha Walker (University of Newcastle)
Yahan Xu (University of New South Wales)
Laura McDuff (University of Notre Dame)

Though confronting the past can be challenging, it is essential for progress in any field. It is for this reason that we chose to highlight the little-known origin story of the Sims speculum.

As this was an opinion piece, we used a combination of sources that referenced historical facts as well as expert opinion. Our article did not proclaim to be a historical retelling of events, but rather an exploration and contextualisation of a contemporary obstetric instrument.

We firmly maintain that the linguistic change we have suggested is indeed both culturally appropriate and respectful. In particular for women of colour, the change of name would be a shift towards just and historically informed practice.

Though it is a shame we have seemingly caused offense with our article, we are pleased to have sparked a conversation about the importance of sensitive nomenclature in medicine.

Obituaries

Dr Erica Kathleen Shellabear 1959–2022

It is with much sadness that we record the death of our dear friend and colleague Dr Erica Shellabear. After a short battle with illness, she peacefully slipped away on 3 March 2022 with her beloved daughter, Sarah, by her side.

Erica was born in Perth at King Edward Memorial Hospital. She was a child of country Australia having spent her formative years in Albany where she developed her adventurous spirit with a great love of sailing, swimming and horse riding.

After a stint in Melbourne, her family returned to the west where she finished her schooling at Methodist Ladies College in Perth in 1976. She then studied medicine and eventually specialised in O&G with her early training at the hospital where she was born. As a registrar, Erica's warmth and encouragement certainly helped fellow junior doctors settle quickly into the King Eddies team. She made firm enduring friendships with colleagues in that time, our Friday journal club gatherings transitioning to regular social events.

After her fellowship in the UK, she returned to Perth and started a very successful O&G career in Attadale in the South of Perth. Later, she decided to focus on gynaecology and relocated her practice to the Mount Hospital. This suited her well after her daughter was born.

A tragic turn of events changed Erica's life dramatically. Her husband Michael became ill and passed away, leaving widowed Erica to manage her career and bring up Sarah alone. This was an incredibly difficult time but in characteristic fashion, Erica devoted herself to being the best parent she could as well as building a successful career.

Erica ensured that her career was not going to lose momentum. She embraced recent advances in minimally invasive surgery by training with laparoscopic surgical pioneer, Dr Tony McCartney, to become an expert herself. Her surgical skills were greatly appreciated and coupled with her patient, kind manner, she became a much loved and highly successful surgeon, respected by all.

Erica was an incredibly dedicated mum. Along with successfully managing her busy career, Erica introduced her daughter to her passion of horse riding, and they became proud owners of a beautiful pony, Freddie. Freddie is still a much-loved family member along with their dynasty of Cavalier Spaniels.

Erica's style of practice was to always include her patients in treatment decisions and to treat everyone with dignity and respect. She has a strong sense of justice and would not shy away from advocating for those she felt were wronged. She loved learning of advancements in her field and marvelled at new techniques and treatment tips from colleagues in general practice and specialties alike.

Erica was a very caring daughter and sister to her two siblings. Erica had recently wound down her private practice to care for her aging father and planned retirement when she was hit with her terrible diagnosis of pancreatic cancer. As always, she faced this with incredible bravery and dignity. She was a wonderful person, truly selfless, and did so much for so many. She made a tremendous contribution to women's health in Western Australia. Erica has left a legacy of dedication to giving the highest quality of care and showing kindness to all. She will be remembered as an extraordinary woman – kind, powerful, compassionate, empathetic and smart. She is greatly missed.

Dr Lucy Williams and Dr Mini Zachariah, WA

Dr Graeme Ralph Sharp 1926–2022

Dr Graeme Sharp, visiting O&G at Wellington Hospital from 1967 to 1985, was farewelled at a private funeral in Waikanae recently. He was aged 95.
'Mr Sharp', as he was always known to the midwives, will be remembered as a calm, confident and distinguished specialist who made a significant contribution to the profession before leaving early to take up farming.

Graeme Ralph Sharp was born in 1926 to a medical family. His father, George, finished medical school early to serve in the first World War (which included time as a medical officer at Gallipoli). Later, George set up practice in Featherston where Graeme's mother Myrtle, (a former head of Wellington Children's Hospital) was his nurse.

The young Graeme attended Featherston Primary School and then Christ's College before heading to Otago University, where he embarked on a BSC, later moving into Medicine. In Dunedin he met Christine Macdonald, his wife of almost 70 years.
Graeme's first House Surgeon experience was at Wellington Hospital. Then in 1956, with a new baby, the young couple headed to London and Edinburgh for Graeme's five years specialist training. (St Mary's, Queen Charlotte's and Whittington Hospitals in London. Edinburgh Royal Infirmary.)

Returning to Wellington in 1961 with a Surgical and O&G degree, Graeme was surprised at how difficult it was to break into the Wellington medical establishment. It took three years for him to make it on to the Wellington Hospital staff. Meanwhile he developed a thriving private practice – dashing around in his bright orange MG sports car for another delivery at Bethany, St Helen's, or Calvary, forever ringing home from public phone boxes to check if he was needed elsewhere or could call it quits for the day.

Through his career Graeme showed entrepreneurial spirit. He was an early researcher of diabetes in pregnancy. With a colleague he brought the first laparoscope to New Zealand and hired it out to other

surgeons. One of his proudest achievements was to pioneer vaginal hysterectomies in New Zealand, having made the procedure a focus of his sabbatical study overseas.

In the early 1980s, with thoughts turning to farming, the Sharps purchased land at Te Horo and the first thing they installed was a telephone in an old box by a lamp post in the middle of a paddock where Graeme could be reached if a patient was in labour. The younger children were told to listen for the phone and when needed Graeme would roar back to town in his MG, all the while planning each step of the operation that lay ahead. He was known to be a meticulous planner and constantly in search of better ways to do things, both in medicine and at the farm.

Not long after the move to Te Horo, Graeme became a full-time farmer but continued to spend his evenings reading medical journals.
When asked whether he wished he had been a farmer from the outset Graeme would say no. He thoroughly enjoyed O&G and was stimulated by the stress of it. He liked non-routine operations and procedures as they kept him on his toes.

Graeme is survived by his wife, Chris, four children, 11 grandchildren and seven great grandchildren.

Shona Willis, NZ, journalist

Prof Ian Stewart Fraser 1942–2022

It is with great sadness that we acknowledge the passing of Prof Ian Stewart Fraser, 79, in Sydney on 28 June 2022.

Ian dedicated his professional career to improving the health of women worldwide by teaching, training, research and advocacy, and to developing and mentoring others, particularly those involved in O&G. He was an authority in the field of Reproductive Medicine, pursuing a broad clinical and research career with particular interests in understanding and treating the very common disturbances of menstruation, menstrual pain, menopause and endometriosis.

Ian was born in Carlisle, England to Dr Ellis and Dr Stewart Fraser, and trained in medicine and O&G at the Universities of Edinburgh and Oxford, before moving to the University of Sydney in 1975. He was the sixth generation to become a doctor in the Fraser family.

He was awarded his Doctorate of Science from Edinburgh University and was the only gynaecologist in Australia with this qualification. He also received an Honorary Doctorate of Science from the University of Sunderland.

Ian held a Personal Chair in Reproductive Medicine at the University of Sydney, and was Visiting Professor at Sunderland University and Conjoint professor (Reproductive Medicine) at the University of New South Wales. He was also Honorary Subspecialist in Reproductive Endocrinology and Infertility at the Royal Prince Alfred Hospital.

Ian was appointed an Officer in the Order of Australia in the 2002 Queen's Birthday Honours.

Ian worked extensively with organisations devoted to the improvement of women's health, holding high scientific advisory positions on contraception, abnormal uterine bleeding and endometriosis. He was Chairman of the World Health Organization Steering Committee on long-acting contraceptives, and a member of the United Nations Population Council's International Committee for Contraception Research. One of his colleagues noted 'women's health is better, worldwide, because of Ian.'

He was Honorary Secretary of the International Federation of Gynaecology and Obstetrics (FIGO), and chaired multiple committees that modernised the worldwide study and practice of O&G. One of his proudest achievements was his years-long work with other members of the FIGO Menstrual Disorders Working Group to address the confusing terminologies, definitions, and classifications of menstrual disorders. This work culminated in the simultaneous publication of key definitions in journals in different countries, which would lead to a uniform and clear understanding of the symptoms of menstrual disorders and of published research studies across the world.

Ian devoted great effort to raising the standards of women's healthcare in Australia and ensuring that the standards of practice of Australia's O&Gs are amongst the highest in the world. He was a founding Fellow and vice-president of the Royal Australian College of Obstetricians and Gynaecologists, before he served as Foundation President of the newly created RANZCOG. To mark his presidency, he donated to RANZCOG a set of surgical instruments owned by Joseph Lister.

As one RANZCOG Fellow noted, 'The College was very fortunate to have Prof Fraser's wisdom at the amalgamation of RACOG with RNZCOG to form RANZCOG in 1998.'

He also helped Taronga, Adelaide and Melbourne Zoos to raise the standards of healthcare for primates, by advising on and inserting contraceptive devices into orangutans, gorillas and chimpanzees.

He had a strong passion for teaching and nurturing the skills and experience of others. He supervised advanced training in reproductive medicine to gynaecologists across the world, and many of his former students and colleagues have paid tribute to his impact on them personally and their careers. A number commented that Ian saw something in them they didn't see themselves; he encouraged them to pursue new challenges and mentored them as they did.

Ian co-authored over 500 scientific publications in various fields of reproductive medicine, including more than 400 original research papers in peer-reviewed journals.

Ian was a keen birder, combining it with his love of travel. He and Dorothy shared a love of opera and Formula One motor racing.

Ian leaves behind his wife, Dorothy, his daughters, Lindsay, Gael and Rowan, his grandchildren, Dylan, Cristyn, Zenobia, Edwina, Alexander, Ian and Carson, and his great-granddaughter, Arabella.

Rowan Fox, NSW, Prof Fraser's daughter

Remembering Our Fellows

Our College acknowledges the life and career of Fellows that have passed away:

- **Dr Richard Allan Speed**, NZ
- **Dr Peter Alexander Scott**, ACT
- **Mr Graeme Ralph Sharpe**, NZ
- **Dr Christine Ann Ross**, Qld
- **Dr Neil Robert Johnstone**, Vic
- **Prof Ian Stewart Fraser**, NSW
- **Dr Peter Heath**, Vic
- **Dr Raymond Stanley Hyslop**, NSW

Dr Neil Robert Johnstone 1944–2022

Neil spent his childhood and adolescence in Canterbury and Box Hill. He attended Canterbury State School before completing his secondary education at Camberwell High where he gained his matriculation certificate in 1961. In 1962 he started his medical degree at the University of Melbourne and became a registered medical practitioner at the end of 1967. After a year's residency at the Alfred Hospital, he spent a year at The Royal Children's Hospital. He then moved to The Royal Women's Hospital, first as a resident, then as a registrar before joining the Professorial Unit as a second assistant. After gaining membership to the English College of Obstetricians and Gynaecologists, he spent two years in London, from 1974–76, as a senior registrar at West Middlesex Hospital. In 1976 he returned to Melbourne and started his private practice in O&G. He also gained employment at The Royal Women's Hospital in 1976 in various positions in O&G. He completed his Masters in O&G at The University of Melbourne and was awarded the Arthur Nyulasy Prize for 1976.

In 2000 he retired from private practice after many years of caring for women, a career he found very fulfilling. He continued to work in clinical sessional positions at the Royal Women's Hospital until 2008 when he resigned prior to the hospital's relocation from Carlton to Parkville.

After retirement, Neil's many interests and keenness to explore other fields kept him busy, teaching himself to write computer programs, of which he wrote many, exploring astronomy as well as continuing to read medical journals and books to broaden his general medical knowledge.

To the outside world he was a quiet, private person who shunned the limelight, but to his family and very close friends he was kind, gentle and funny. He loved a good joke and delighted in cutting out silly little articles from the newspapers to show anyone who was interested, especially his children and their offspring.

He has left us all with very happy memories of a rather naughty but funny, irreverent person who was certainly not 'woke'.

He is survived by his wife, four children, nine grandchildren and three great grandchildren.

Jean Johnstone, VIC, Dr Johnstone's wife

Dr Thomas Guy Wright 1951–2022

It is with great sadness that we acknowledge the passing of Dr Thomas Wright, aged 70, in Cairns, Qld on 28 February 2022.

After moving from his birthplace of England to Australia with his family, Tom attended high school in Cairns, before attaining his medical degree at the University of Queensland. He completed his O&G training in Sydney, before returning to work in Queensland for his consultant career, initially in Mackay, and then since 1991, back in Cairns.

Tom was a much loved and respected member of the Cairns community, both within and outside his profession. Those of us who remember being trained by Tom as young PHOs and registrars, fondly recall his ever calm and patient attitude, regardless of the time of day or night. To his colleagues, both junior and senior, he was a profound role model and mentor, always demonstrating the utmost compassion and care for his patients, and a meticulous attitude to procedural work. He also played an instrumental role for many years in teaching James Cook University medical students, including the very first cohort of students in 2004.

To the many women for whom he cared during his lifetime of service in O&G in Cairns, he was a much loved and trusted professional, who was responsible for delivering babies across generations for many families in Cairns. The level of esteem in which he was held by his patients and their families was evidenced by the hundreds of loving and thankful messages posted on social media at the time of his passing.

Tom treated everyone with whom he came into contact with respect, from patients and their families, to medical students, medical colleagues, midwives, nursing staff and other hospital colleagues, and always made others feel valued and welcome.

He is also fondly remembered by all for his sometimes rather eccentric activities, such as bursting into a rendition of 'I'm a Little Teapot', with actions of course, or his ability to perform handstands for unnaturally prolonged periods of time.

One of Tom's well-known habits was to order breakfast for all of his postnatal women for the morning following their births. He always ordered a 'double serving' of bacon and eggs for each woman, so that when he went to see them the next day, he could avail himself of some of their breakfast whilst perching on their bed and having a chat.

Tom is survived by his beloved wife, Heike, his two sons Andrew and Simon, and their families. His absence leaves a gaping hole in the O&G community in Cairns, and the Cairns community at large. He will be sorely missed as both a colleague, and a friend to all.

Dr Samantha Scherman, QLD