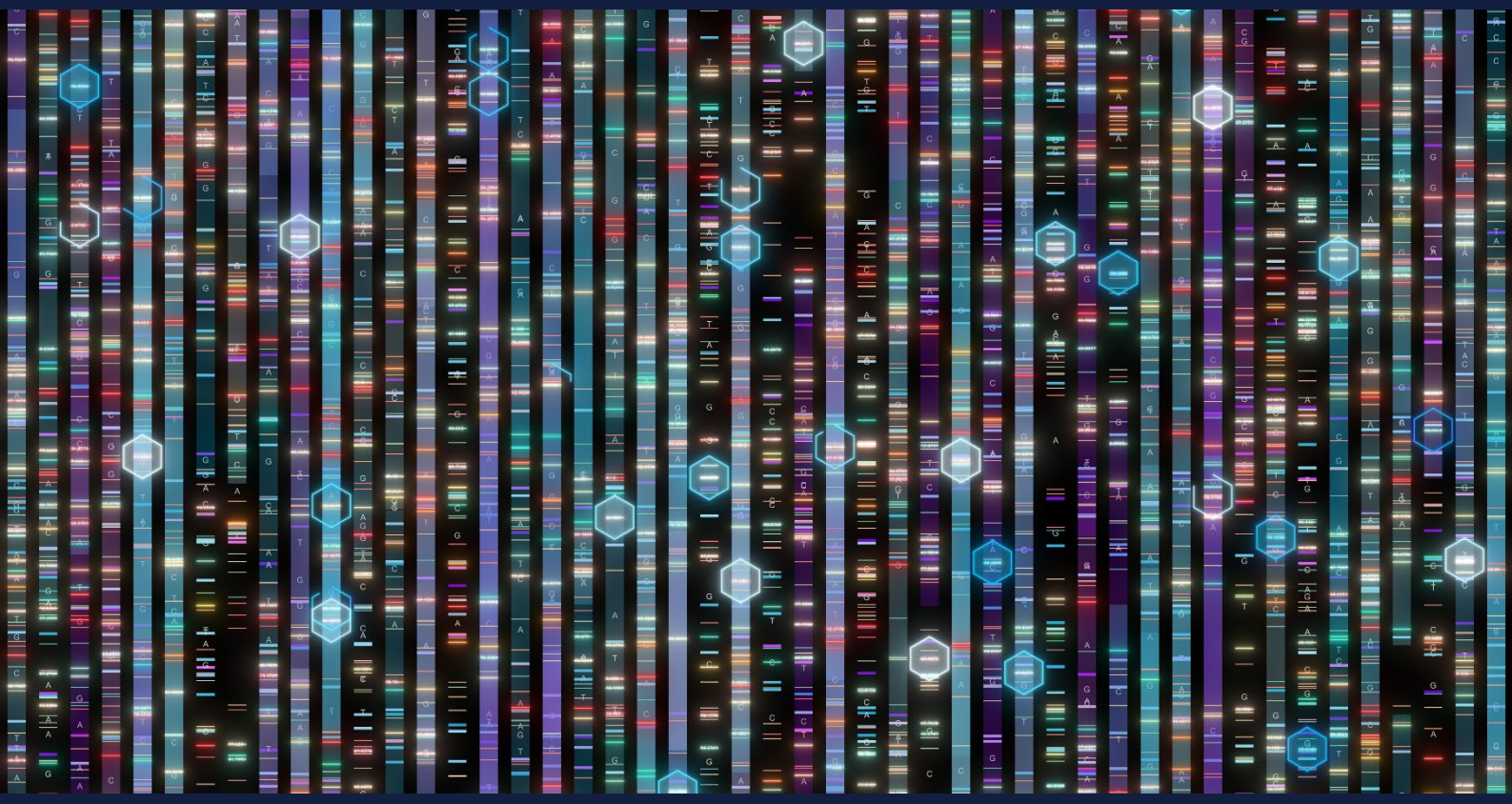
Investment Case for National Ovarian Cancer Precision Medicine Research Program

January 2022



OVARIAN CANCER RESEARCH FOUNDATION

ANZGOG

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Foreword

The *Ovarian Cancer - Investment Case for Future Funding* is a joint bid submitted by the Ovarian Cancer Research Foundation (OCRF) and the Australia New Zealand Gynaecological Oncology Group (ANZGOG), with complementary letters of endorsement provided by Ovarian Cancer Australia (OCA) and the Australian Gynaecological Cancer Foundation (AGCF).

The OCRF is the largest non-governmental funder of ovarian cancer research in Australia and the major funder overall of research into early detection and diagnosis. We fund research that will have the greatest impact on the greatest number of women with a strong focus on research into treatments, recurrence, early detection, and prevention.

ANZGOG is the peak national gynaecological cancer research organisation for Australia and New Zealand. Our purpose is to improve the outcomes and quality of life for women with gynecological cancers through conducting and promoting cooperative clinical trials and undertaking multidisciplinary research into causes, prevention, and treatments of gynaecological cancer.

This submission outlines the case for investment in a Precision Medicine in Ovarian Cancer Research Program that will deliver improved health outcomes and improved health system efficiencies and economic growth for the wider Australian community. It is in recognition of the need for urgent investment to lift the poor prognosis for women and girls diagnosed with this disease.

Ovarian cancer remains one of the most lethal and least understood gynaecological cancers affecting women in Australia and around the world. The five-year survival rate has stagnated at around 48 per cent and remains lower than the 5-year survival rates achieved back in 1975 for all cancers. This is a bleak picture for women diagnosed with ovarian cancer today.

The modern cancer era has shown that investment in cancer research translates into outstanding improvements in survival. The successes in survival outcomes have been realised through significant and sustained funding for high impact research since the 1970s. History shows that where communities, governments and industry come together, big improvements in survival can be realised and countless lives saved. While ovarian cancer has been left behind in the last 45 years of modern cancer research, with a similar focus and funding uplift, it can be the success story of the next generation.

Ovarian cancer will continue to kill women and girls in the prime of their lives. For almost half a century, these tragic outcomes have gone unchallenged. For our best shot at improving the chances of surviving this deadly disease, our collective challenge is to move the fight beyond researchers in the lab to more funding from government, corporates, and communities. The success of this investment bid is a big step forward in providing hope of significant survivability improvements for all women.

When funding into ovarian cancer research is neglected, women die. The next generation of women deserve better.

(Lucinda Nolan)

CEO, OCRF

OVARIAN CANCER RESEARCH FOUNDATION

(Alison Evans)

CEO, ANZGOG

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Executive Summary

This Investment Case for a National Precision Medicine in Ovarian Cancer Research Program outlines the case for increased investment in ovarian cancer treatments with specific investment recommendations as follows:

- **$73.9 million in molecular profiling for every woman diagnosed with ovarian cancer**
- **$1.5 in research to develop next generation precision medicine through functional profiling techniques**
- **$20 million in competitive funding to be made available each year over the four years of the program to support the attraction of precision medicine clinical trials and acceleration of precision medicine research in ovarian cancer.**

To successfully establish the program, the following activities will need to be developed and implemented:

- **Establish a governance model for the program, including the development of a National Precision Medicine Tumour Board**
- **Nominate national testing centres to undertake molecular profiling for the program to ensure quality and technical excellence in implementation as well as economies of scale**
- **Establish a competitive funding pool for clinical trials through MRFF to support access to next generation precision medicine therapies.**

Ovarian cancer is a complex, rare, low survival group of cancers with 5-year survival rates that still sit below the 5-year average survival rates for all cancers observed in 1975 and nearly half those observed for women diagnosed with breast cancer in Australia today.

The poor prognosis for ovarian cancer is a function of its complexity and rarity, which have served as disincentives for investment by industry and government alike.

In recognising the continued and significant challenges facing rare, low survival cancers like ovarian cancer, Australia's Senate Select Committee in 2017 called for a comprehensive, Australia-wide strategy to improve outcomes for low survival cancers to above 50 per cent by 2027.

Five years on from this recommendation, the Australian Government has provided some increased funding for ovarian cancer, but funding levels still fall short of the national strategy required. This stands in contrast to the approach and funding provided for other, similarly high risk and rare cancers, such as the ZERO Childhood Cancer project which has seen a systematic, national approach deliver significant improvements in treatment and health outcomes for children and young adults with similarly complex, high-risk cancers.

Significant breakthroughs in the molecular characterisation of ovarian cancer have opened up the possibility of a precision medicine approach to ovarian cancer, which, like childhood cancers, have been shown to improve treatment planning and health outcomes for women.

Despite the importance of precision medicine research and its adoption in clinical practice, Australia's current approach remains fragmented, inequitable, and underfunded. This leads to poor health outcomes for women, missed opportunities for Australian research, and potentially avoidable health system inefficiencies. The current patchwork of sub-scale research projects serves neither the women in need of treatment breakthroughs nor the

urgent research agenda for ovarian cancer. Moreover, available precision medicine programs are highly skewed to health literate women living in major capital cities.

This proposal puts forward the case for investment in a *Precision Medicine in Ovarian Cancer Research Program*, following the model adopted in childhood cancers. The proposed program would see all women in Australia undergo molecular profiling of their cancer. This would facilitate tumour-specific treatment and an increase in clinical trials available in Australia as a result of the creation of a pool of pre-screened women leading to lower costs of recruitment and more rapid recruitment timelines.

This approach will be expected to deliver improved health outcomes for women diagnosed with ovarian cancer and improved health system efficiencies and economic growth for the wider Australian community. Major benefits include:

- **Increased equity of access to health services**, with an additional 1,500 women with access to precision medicine each year on average and between 600 and 750 additional women enrolled in clinical trials over the course of the program
- **Significant improvements in survival and treatment of chemoresistance**, with early data showing progression free survival increasing by 50 per cent to 110 per cent through the use of next generation PARP inhibitor therapies, which equates to a rough doubling of progression free survival. These therapies have shown unprecedented potential, when used with a targeted approach, in a significant subset of women with high grade serous ovarian cancer, that combined, account for 35-45 per cent of all women diagnosed with ovarian cancer. Similarly, progression free survival has been doubled for low grade serous ovarian cancer, which accounts for a further five per cent of all women diagnosed with ovarian cancer, through a precision medicine approach
- **Health system efficiencies**, enabling scarce health dollars to go further, with economies of scale in testing, leading to $3.9 million in savings compared to status quo, lower costs of clinical trials recruitment delivering $1.0 million to $1.2 million in savings, and improved patient selection enabling savings on high-cost therapies in the order of $40.7 million to $81.4 million in avoided expenditure
- **Private sector investment**, with an additional six to eight clinical trials expected to be attracted to Australia in addition to 12-15 planned growth, leading to the attraction of between $8.4 million to $11.2 million in leveraged private sector investment
- **Skills development**, with an additional 4.2 clinical trial jobs created per additional trial attracted to Australia, leading to the creation of 63-84 additional clinical trial jobs over the program, and 80 additional highly skilled laboratory and researcher jobs; in total, over the four years of the program, more than 380 jobs would be created
- **Increased impact of Australian ovarian cancer research** globally, building on Australia's demonstrated leadership in precision medicine research through the International Cancer Genome Consortium and design and implementation of clinical trials through our many leadership positions in the Gynecological Cancer InterGroup (GCIG) (Chair-Elect).

Health and economic analysis show that the benefit cost ratio of the program – before taking into account any potential improvements in quality of life gained – is estimated to be between 0.7 and 1.3, depending on total benefits realisation. Moreover, breakeven analysis shows that the lower bound would increase to 1.0 if only 381 women, or 5.1 per cent of all women expected to be diagnosed with ovarian cancer, saw a one-year increase in survival as a result of the program.

In light of the early evidence, which shows that precision medicine can change diagnosis in more than five per cent of women and improve progression free survival by more than 50 to 110 per cent for more than 50 per cent of women, this suggests a high probability that the program would deliver a positive benefit cost ratio (BCR > 1.0) to the Australian community.

To establish the Precision Medicine in Ovarian Cancer Program, the following activities will need to be developed, following the model of the ZERO Childhood Cancer Medicine Program:

- Establish a governance model for the program, including the development of a National Ovarian Cancer Precision Medicine Tumour Board
- Nominate national testing centres to undertake molecular profiling for the program to ensure quality and technical excellence in implementation as well as economies of scale
- Establish a competitive funding pool for clinical trials through MRFF to support access to next generation precision medicine therapies.

In total, $75.4 million ($66.8 million in $NPV_{5\%}$ terms) in funding over the next four years is sought for the Precision Medicine in Ovarian Cancer Research Program. This comprises $73.9 million for molecular profiling of every woman diagnosed with cancer over that time period and $1.5 million in funding for next generation functional profiling research of ovarian cancer patients.

In addition to the Precision Medicine in Ovarian Cancer Research Program, an annual, competitive funding round of $20 million for precision medicine clinical trials and research, should be made available over the four years of the program to provide sustained support for next generation clinical trials and research in ovarian cancer. Importantly, based on historical funding trends, this would be expected to leverage additional industry funding at a ratio of 2.3:1. This would see up to $80 million in additional industry funding for clinical trials potentially leveraged into Australia. Funding for the next generation of precision medicine trials would be accessed on a competitive basis.

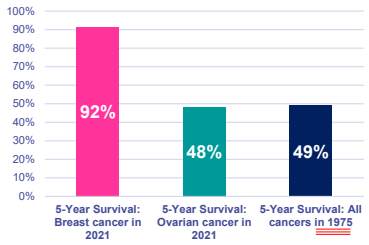
This would generate an unparalleled opportunity to generate an ovarian cancer dataset valuable way beyond our current grasp — molecular data, with associated clinical, genetic, pathology and other research data, allowing us to expand the benefits of Artificial Intelligence and other large data approaches — as for the first time our ovarian cancer data would be centralised. As Australian clinical and scientific ovarian cancer researchers standing on a global stage, we have the track record and the plan, we just need the backing.

The impact for the women of this decade and the next would be quite simply, transformative.

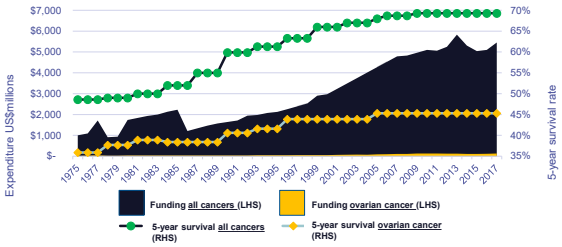
Investment Case: Plan on a Page

Ovarian cancer is a complex, rare, low survival cancer that requires a comprehensive, Australia-wide strategy

Poor survival outcomes…

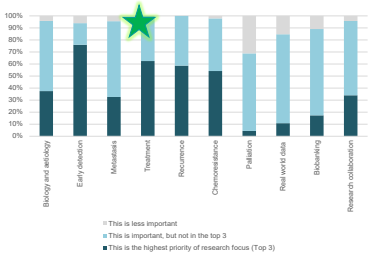


…persist due to poor funding and lack of strategic approach

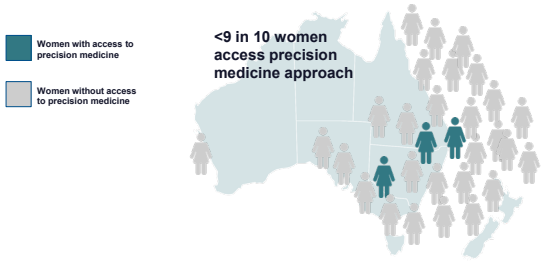


Precision medicine in ovarian cancer is one of the highest priorities to improve survival

Precision medicine is top priority…



…but Australia lacks national approach and funding



National Precision Medicine in Ovarian Cancer Research Program will deliver improvements in health outcomes and economic growth

Improved health outcomes…

Better health outcomes

- ✓ **Additional 1,550 women with access to precision medicine** each year on average
- ✓ **Additional 600-750 women enrolled in clinical trials over course of program**
- ✓ **Significant improvements in survival and treatment of chemoresistance**
- ✓ **Health system efficiencies**, enabling scarce health dollars to go further

Improved survival

- ✓ **Progression free survival increased by 50%-110%** in 50% of women with high grade serous ovarian cancer (35%-45% all women)
- ✓ **Progression free survival doubled** for low grade serous ovarian cancer (5% of all women)
- ✓ **Breakthroughs in treatment** of chemoresistance and women without current therapeutic options

Increased health system efficiency

- ✓ **Lower cost per testing** leading to $3.9 million in savings compared to status quo
- ✓ **Lower costs of clinical trials recruitment** $1.0 million-$1.2 million in savings
- ✓ **Improved use of systemic therapies**, avoided expenditure on ineffective therapies valued at $40.7 million - $81.4 million

…and economic growth

Economic growth

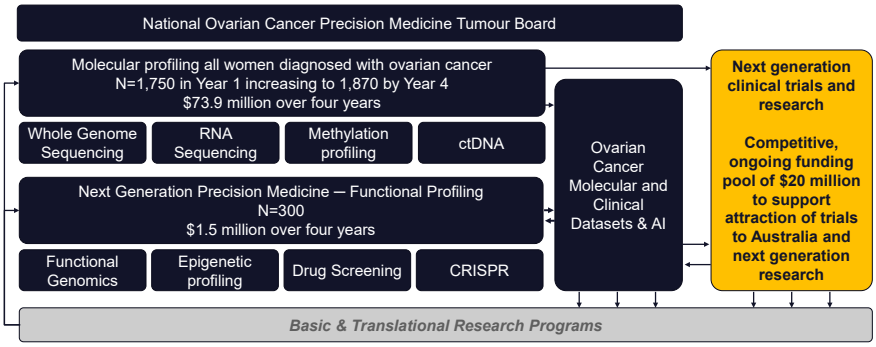
- ✓ **Private sector investment** – industry led trials
- ✓ **Skills development** – in clinical trials roles, advanced testing and laboratory research skills
- ✓ Increased **impact of ovarian cancer research** globally

Increased job and investment potential

- ✓ **Additional 6-8 clinical trials attracted to Australia** in addition to 12-15 planned growth
- ✓ **$8.4 million - $11.2 million leveraged private sector investment**
- ✓ **Additional 380-400 jobs created over next four years**
  - 4.2 jobs per trial (MTPConnect) leading to **63-84 additional clinical trial jobs over program**
  - **Additional 80 laboratory roles** created in national laboratory nodes, leading to 315 jobs created over four years

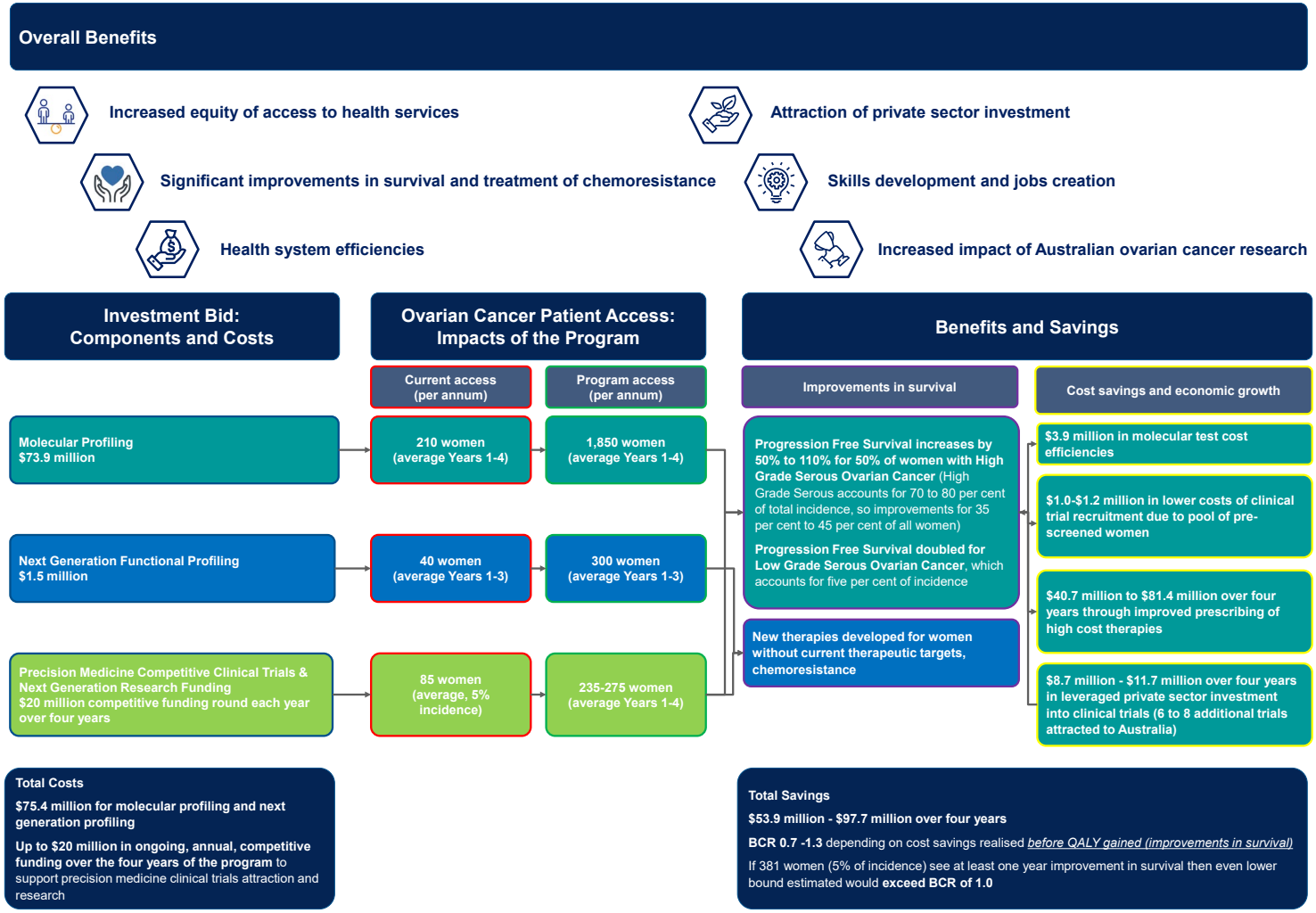
Funding of $75.4 million over four years needed to fund the program

To enable the comprehensive, Australia-wide approach recommended by Senate Select Committee



Outcome: Low Survival Target Reached, Ovarian Cancer 5-Year Survival to Increase >50 per cent

National Precision Medicine in Ovarian Cancer Research Program: Cost Benefits Map



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Chapter 1

Ovarian Cancer: A Low Survival Cancer with Limited Research Funding

While many cancers have seen significant improvements in survival, 5-year relative survival rates for ovarian cancer remain low, falling below 50 per cent.

The persistent, poor prognosis for women diagnosed with ovarian cancer is a function of its relative complexity, rarity and historically low levels of funding for research. Critically, funding for ovarian cancer research has been limited due to its relative rarity, which mutes commercial incentives for investment compared to other cancers.

While the Australian Government has taken initial steps to address market barriers to research investment for ovarian cancer, crucial gaps remain. One of the most significant gaps in funding for ovarian cancer research is the development of a precision medicine approach to treatment. Recent research breakthroughs have shown that more than 50 per cent of women have therapeutic targets that could be treated with novel agents delivering significant improvements in survival. The development of precision medicine in ovarian cancer represents one of the highest priorities for research, offering the potential to improve outcomes for women diagnosed with ovarian cancer today and into the future.

In spite of the importance of precision medicine research, Australia's current approach to research in this domain is fragmented, inequitable, and underfunded. This leads to poor health outcomes for women, missed opportunities for Australian research, and avoidable health system inefficiencies. The current patchwork of sub-scale research projects serves neither the women in need of treatment breakthroughs nor the urgent research agenda for ovarian cancer.

This section provides an overview of the policy problem and need for investment in precision medicine for ovarian cancer.

1.1 Ovarian cancer is a rare, complex, low survival cancer

Ovarian cancer is one of the most lethal and least understood cancers affecting women in Australia and around the world.

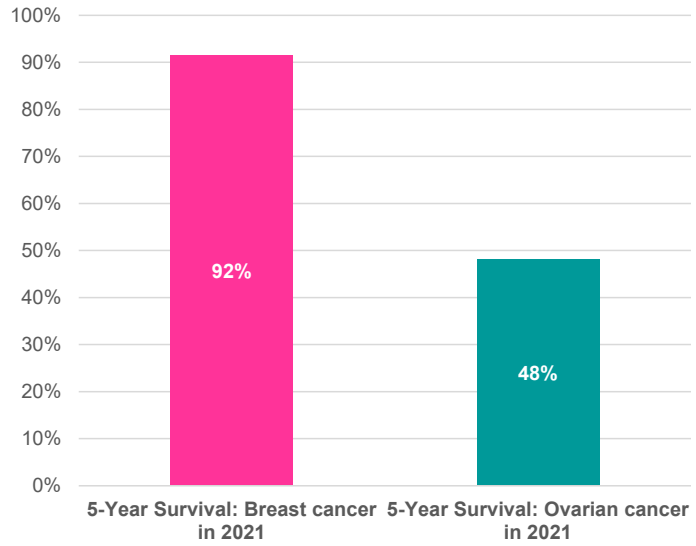
Women diagnosed with ovarian cancer face a challenging outlook, with 5-year relative survival rates of only 48 per cent today.[1] Sadly, the survival rate for ovarian cancer today is lower than the average 5-year survival rate for all cancers in 1975, when the modern cancer research era began (49 per cent).[2]

[1] Australian Institute of Health and Welfare, 2021, Cancer data in Australia, 5-year relative survival for ovarian cancer and serous carcinomas of the fallopian tube, accessed at: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-survival-data-visualisation.

[2] OCRF, 2020, State of the Nation in Ovarian Cancer: Research Audit, accessed at: https://www.ocrf.com.au/page/154/sotn. Data based on NCI Budget Factbook Archives 1975-2017, accessed at www.cancer.gov.au/about-nci/budget/factbook/archive. NCI SEER, 2016, Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent), https://seer.cancer.gov/archive/csr/1975_2016/results_merged/topic_survival.pdf.

Ovarian cancer comprises a range of complex sub-types of rare cancers, each distinct, with different cells of origin, biology and requiring different approaches to treatments and then to drug resistance. In aggregate, the Australian Institute of Health and Welfare estimated that 1,720 cases of ovarian cancer (including fallopian tube cancer) would be diagnosed in Australia in 2021. Notably, this is less than 10 per cent of the number of cases of breast cancer (20,030 cases in 2021), and women diagnosed with breast cancer, have five-year survival rate of greater than 90 per cent. (Figure 1.1).[3]

Figure 1.1: Percentage of persons alive five years from diagnosis – breast cancer compared to ovarian cancer



Source: Australian Institute of Health and Welfare, 2021, Cancer data in Australia, 5-year relative survival for ovarian cancer and serous carcinomas of the fallopian tube, accessed at: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-survival-data-visualisation.

As a result of the poor survival outlook for women diagnosed with ovarian cancer, it is estimated more than 14,000 Australian women will lose their lives to ovarian cancer over the next 10 years alone. Worldwide, mortality from ovarian cancer is expected to exceed **2.2 million women** between 2020 and 2030.[4]

1.2 Ovarian cancer's low survival is a function of historically low funding for research

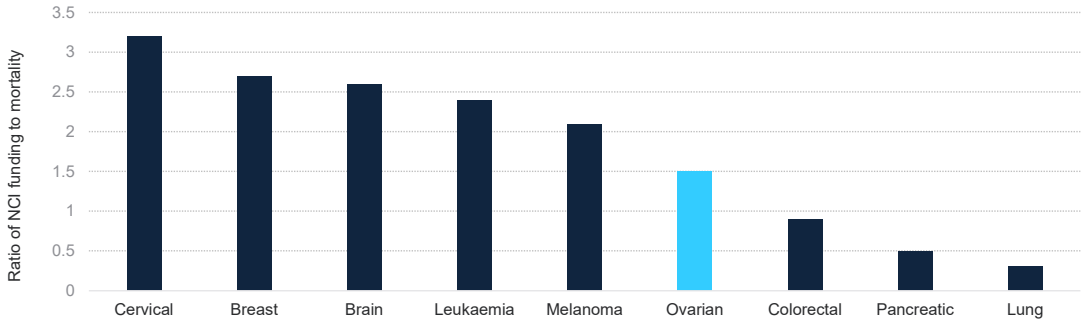
Unquestionably, investment in cancer research translates into significant improvements in survival. Survival rates across all cancers improved by 44 per cent between 1975 and 2015; these advances have been realised through significant and sustained funding for high-impact research since the 1970s.

Funding for ovarian cancer research, by contrast, has lagged behind other cancers with higher rates of incidence. This is a product of its relative rarity and complexity which has limited commercial and government incentives for investment in research and development compared to other cancers. For example, analysis of NCI funding highlighted the challenges related to underfunding of some cancers given their poor survival outcomes (Figure 1.2). Research into breast cancer, for example, has received NCI/NIH funding at seven times the rate of research into ovarian cancer since 1992. Given the significant volume of community giving alongside government funding, as well as commercial incentives to develop products

[3] Australian Institute of Health and Welfare, 2021, Cancer data in Australia, 5-year relative survival for ovarian cancer and serous carcinomas of the fallopian tube, accessed at: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-survival-data-visualisation.
[4] OCRF, 2020, State of the Nation in Ovarian Cancer: Research Audit, accessed at: https://www.ocrf.com.au/page/154/sotn.

for larger patient markets, it is likely this substantially underestimates the difference in funding levels observed.

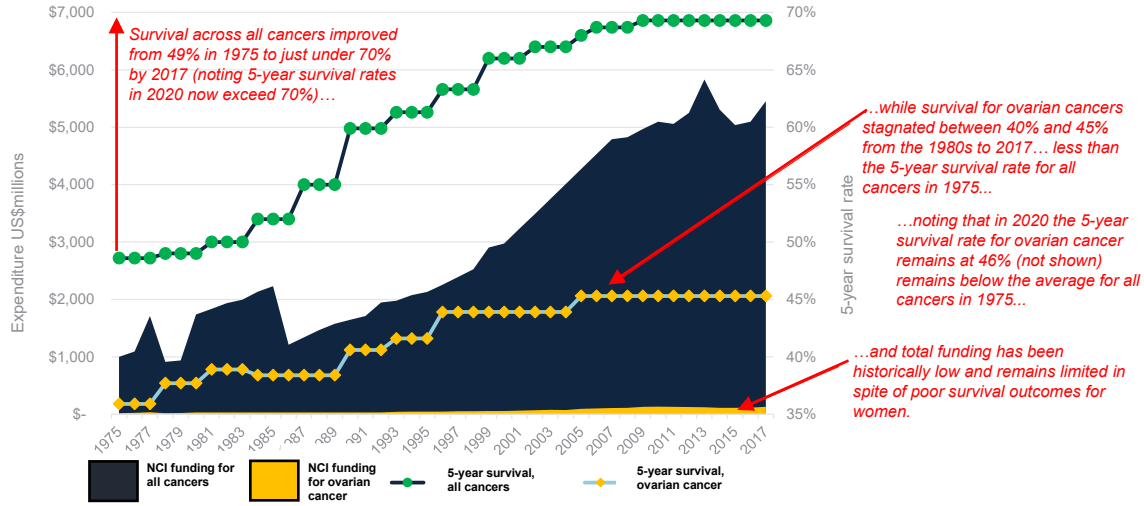
Figure 1.2: NCI funding relative to mortality rates for selected cancers



Source: Carter, AJ, and Nguyen, CN, 2012, A comparison of cancer burden and research spending reveals discrepancies in the distribution of research funding, BMC public health, 12, 526. doi: 10.1186/1471-2458-12-526.

Historically low levels of funding for ovarian cancer research have contributed to the poor survival outlook for women diagnosed with ovarian cancer. While many cancers have seen survival rates substantially improve over the modern cancer research era, ovarian cancer has not (Figure 1.3).

Figure 1.3: Limited funding for ovarian cancer in the modern cancer era has stifled breakthroughs ($US)



Source: OCRF, 2020, State of the Nation in Ovarian Cancer: Research Audit, accessed at: https://www.ocrf.com.au/page/154/sotn. Data based on NCI Budget Factbook Archives 1975-2017, accessed at www.cancer.gov.au/about-nci/budget/factbook/archive. NCI SEER, 2016, Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent), https://seer.cancer.gov/archive/csr/1975_2016/results_merged/topic_survival.pdf.

1.3 Australian Government Target for Low Survival Cancers: Increase survival above 50 per cent by 2027

The need for increased research funding to address low survival cancers has been increasingly recognised by developed nation governments; for example:

- In the United States, for example, the Federal government passed legislation in 2012 mandating public investment in research to improve survival for so-called 'recalcitrant' cancers with a relative survival of less than 50 per cent.[5]

[5] See H.R.733 - Recalcitrant Cancer Research Act of 2012, available at: https://www.congress.gov/bill/112th-congress/house-bill/733

- **In 2017, Australia's Senate Select Committee similarly recommended that the Australian Government develop a comprehensive, Australia-wide strategy to address low-survival cancers, with the explicit goal of increasing the 5-year survival rates for those cancers to above 50 per cent by 2027.**[6]

The adoption of a comprehensive, Australia-wide strategy is an essential requirement to tackle complex, rare, high-risk cancers. While Australia has a high-quality health care system and a global reputation for excellence in oncology research, its federated health model robs researchers of the scale and statistical power needed to make breakthroughs in poor prognosis cancers.

The adoption of a comprehensive, Australia-wide approach has been highly successful in childhood cancers. In childhood cancer, research is the standard of care. Children are treated at a network of specialist centres across Australia, which are integrated into global research initiatives and see children consistently enrolled in clinical trials. This integrated, systematic approach has seen the overall 5-year survival rate for children's cancer increase from 10 per cent in 1975 to nearly 90 per cent in 2015.[7]

Despite this, it became clear that many children diagnosed with rarer and more complex cancers continued to face a poor prognosis. To tackle continued poor survival for these high risk, complex, rarer childhood cancers, the ZERO Childhood Cancer program was developed to deliver a comprehensive, Australia-wide, personalised medicine treatment approach. As a result of the Australia-wide, systematic molecular profiling of each patient, a new treatment option was identified based on the child's cancer's genetic makeup within nine weeks for 70 per cent of the children. To date, 30 per cent of patients treated through the program have seen their tumour either shrink or completely regress, while a further 40 per cent have seen their tumour stop growing or stabilise.[8]

There are many parallels between high risk, complex, rare childhood cancers and ovarian cancer, which is similarly a group of complex, rare cancers with poor mortality. **The systematic approach adopted in childhood cancer is needed and can be replicated in ovarian cancer; this is what the Senate Select Committee has recommended to meet the unmet needs for people diagnosed with low survival cancers.** Moreover, with a relative survival of 48 per cent today, ovarian cancer is perhaps the only low survival cancer that has the potential to meet the ambitious target set by the Senate Select Committee by 2027.[9]

1.4 Improving survival in ovarian cancer: research priorities

Improving survival for women diagnosed with ovarian cancer by 2027 will require investment in high impact areas of research and the rapid translation of recent breakthroughs into clinical practice.

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[6] Senate Select Committee, 2017*, Funding for Research into Cancers with Low Survival Rates*, available at: https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Funding_for_Research_into_Cancers/FundingResearchCancers/Report.

[7] NCI SEER, 2016, Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent), https://seer.cancer.gov/archive/csr/1975_2016/results_merged/topic_survival.pdf Cancer Institute NSW, 2019, A history of global cancer breakthroughs, https://www.cancer.nsw.gov.au/learn-about-cancer/cancer-breakthroughs; Unger, JM, Cook, E, Tai, E, and Bleyer, A, 2016, The Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence, and Strategies, ASCO Educational Book, accessed at: https://ascopubs.org/doi/full/10.1200/EDBK_156686

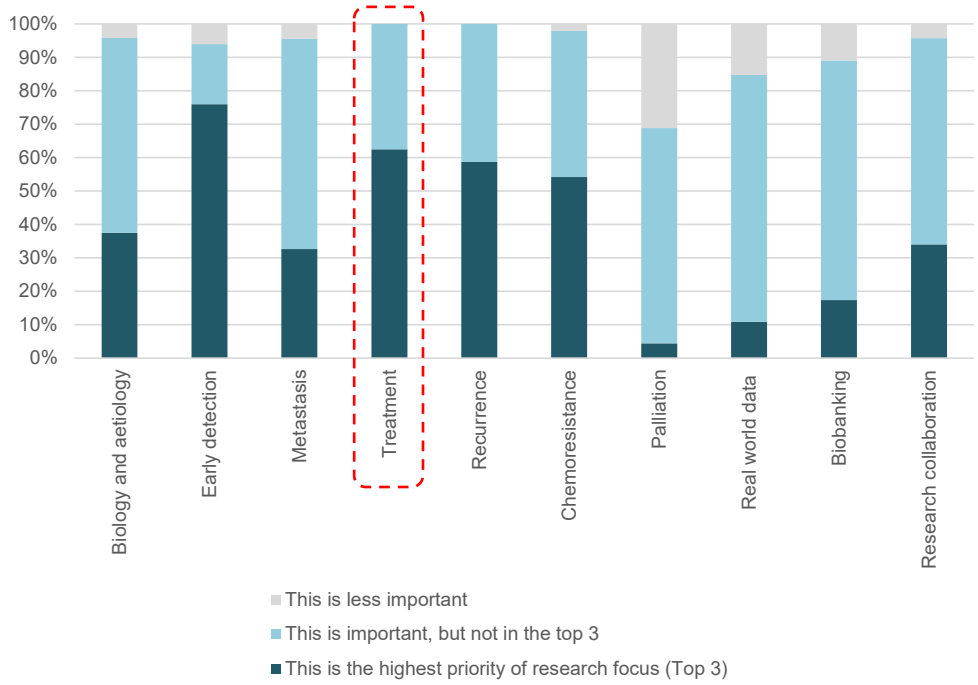
[8] Wong, M, Mayoh, C, Lau, LMS, et al. 2020, Whole genome, transcriptome and methylome profiling enhances actionable target discovery in high-risk pediatric cancer. Nat Med, 26, 1742–1753, doi: 10.1038/s41591-020-1072-4.

[9] Other low survival cancers have five-year survival rates that are substantially below 50 per cent, which are unlikely to be able to be improved above 50 per cent within a five-year horizon. For example, five-year relative survival rates in 2021 for other cancers include: liver cancer (19%), lung (22%), cancer of unknown primary (10%), pancreas (12%), stomach (32%), biliary (19%), oesophageal (23%), and mesothelioma (11%).

In 2020, the OCRF conducted a survey of ovarian cancer researchers and clinicians to identify priorities for research to improve survival. The most frequently identified top priorities for research included (Figure 1.4):

- Early detection
- Treatment
- Preventing Recurrence
- Preventing Chemoresistance.

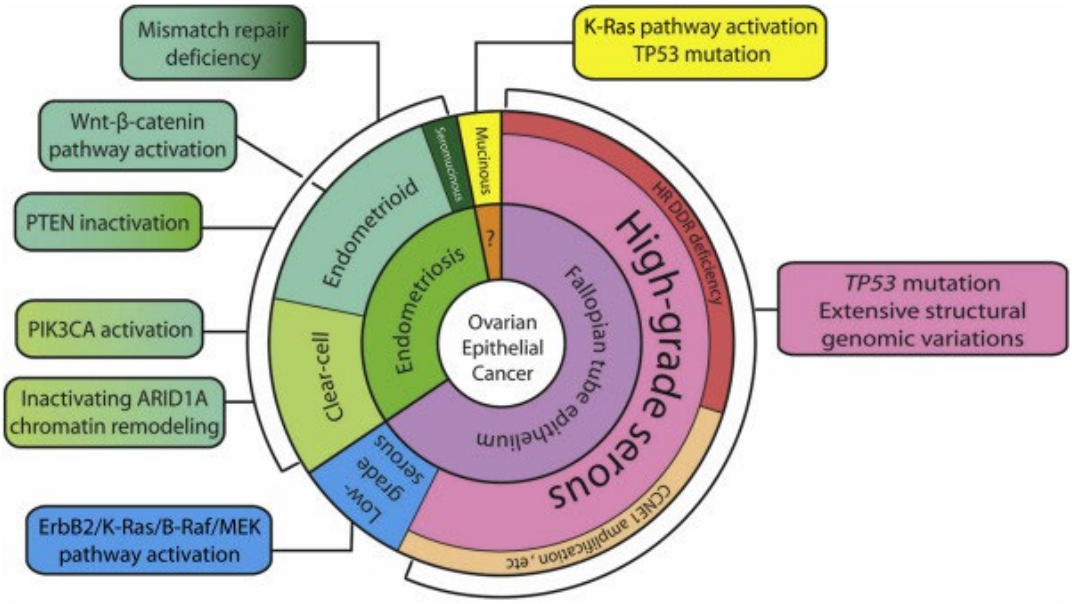
Figure 1.4: Highest priority areas of research to improve survival for women with ovarian cancer



Source: OCRF, 2020, State of the Nation in Ovarian Cancer: Research Audit, accessed at: https://www.ocrf.com.au/page/154/sotn.

The expanded use and accelerated development of novel treatments for ovarian cancer is a high priority in research because the molecular characterisation of ovarian cancer sub-types has made possible the evolution of treatment in ovarian cancer from an historical 'one size fits all' model of care, based on chemotherapy regimens to increasingly individualised treatment based on novel therapies targeted to a woman's specific tumour (Figure 1.5).

Figure 1.5: Tissue origins and major molecular pathway alterations for ovarian cancer



Source: Shih, I, Wang, Y, and Wang, T, 2020, The Origin of Ovarian Cancer Species and Precancerous Landscape, The American Journal of Pathology, doi: 10.1016/j.ajpath.2020.09.006

Given the long lead time to benefits realisation for other priority areas of ovarian cancer research, investment in treatment research represents one of the highest priorities to improve survival outcomes in the short term and meet the target for low survival cancers.

Over time, a systematic approach to precision medicine, combined with basic and translational research programs, has the potential to further deepen the understanding of ovarian cancer and deliver further improvements in survival for future generations as well.

1.5 Australia is a leader in ovarian cancer precision medicine research

Australia has proven itself to be a world leader in ovarian cancer research, generally, and in precision medicine research, specifically, including major contributions to the International Cancer Genome Consortium, as well as all important targeted therapeutic intervention clinical trials in ovarian cancer.[10] Members of ANZGOG hold leadership positions in the peak international gynaecologic international clinical trials group, Gynecological Cancer InterGroup (GCIG), including Assoc Professor Alison Brand AM as Chair-Elect.

1.6 Uplift in funding and a national approach to precision medicine is needed to meet the Australian Government Target for Low Survival Cancers

By working with Australia's ovarian cancer research community to develop the use of precision medicine technologies in ovarian cancer treatment, the Australian Government has the opportunity to implement the recommendations of the Senate Select Committee, and deliver on the target set, if it supports the comprehensive, Australia-wide strategy in ovarian cancer. Realising the goal of increasing 5-year relative survival above 50 per cent will not happen without:

[10] Further SciVal or Scopus citation analysis available on request. Supporting authors to this bid are second most highly rated authors globally in PARPi research. See also Patch et al, 2015, Whole genome characterisation of chemoresistant ovarian cancer, Nature, 521 (7553):489-94, doi: 10.1038/nature14410.

- A significant uplift in funding
- A new, national approach to precision medicine research.

Current funding does not support a comprehensive, Australia-wide strategy

While the Australian government has increased funding for ovarian cancer,[11] funding for precision medicine research, however, has been relatively limited.

Through the MRFF, the Australian government has allocated funding of just $7 million to precision medicine and drug repurposing in ovarian cancer since its establishment.[12] This funding has been targeted at smaller patient cohorts, including granulosa tumours and low grade serous ovarian cancers, which account for less than 10 per cent of all ovarian cancer diagnoses.

This approach falls short of the comprehensive, Australia-wide strategy called for by the Senate Select Committee. Consider, for example, that the Australian Government and Minderoo Foundation have recently invested a further $67 million in the ZERO Childhood Cancers research initiative;[13] this provides an indication of the order of magnitude of funding needed to deliver real improvements in outcomes.

Australia's approach to precision medicine is fragmented, sub-scale and inequitable

To diagnose a woman with ovarian cancer, the treating clinician may take a biopsy of the tumour before the woman undergoes surgical debulking and platinum and taxane-based chemotherapy (first line therapy for all women).

The biospy tissue confirms the diagnosis, but the analysis does not routinely include molecular profiling that could enable a precision medicine approach to a woman's treatment, except to confirm a *BRCA* mutation. Biopsy tissue is often 'stored and ignored' following diagnosis,[14] rather than being used to potentially inform a precision medicine approach to her treatment and care.

This means the full benefits of the biopsy or sample collection procedures is not always realised in practice.

In Australia today, there are only four programs which have been consistently available to enable a precision medicine approach to the treatment of women diagnosed with ovarian cancer; these programs are:

- The INOVATe (Individualised Ovarian Cancer Treatment Through Integration of Genomic Pathology into Multidisciplinary Care) program in NSW, which utilises a molecular profiling approach to guide individualised therapy for women following relapse from first line treatment. Since its inception in 2015, INOVATe has recruited approximately 600 women with funding to test roughly 100 women per annum. INOVATe uses a personalised medicine approach focused on identifying the most

[11] The Federal Government has been the major funder of ovarian cancer research, accounting for approximately 60 per cent of all Australian funding from 2010 to 2020. Since 2010, the Federal Government has funded an historical average of about $8 million per annum. Following the Australian Government, the OCRF and ANZGOG have been the next largest funders of ovarian cancer research in Australia. See: OCRF, 2020, State of the Nation in Ovarian Cancer: Research Audit, accessed at: https://www.ocrf.com.au/page/154/sotn.

[12] Grants have been awarded to ovarian cancer research projects in 2019 and 2020 through the MRFF program. See: https://www.health.gov.au/sites/default/files/documents/2021/08/medical-research-future-fund-mrff-grant-recipients-medical-research-future-fund-mrff-grant-recipients-as-at-11-august-2021.pdf

[13] Minderoo Foundation, 2020, First Results from the Zero Childhood Cancer Program show significant outcomes delivered for kids with aggressive cancers, Collaborate Against Cancer, 6 October 2020, accessed at: https://www.minderoo.org/collaborate-against-cancer/news/first-results-from-the-zero-childhood-cancer-program-show-significant-outcomes-delivered-for-kids-with-aggressive-cancers/.

[14] Any tissue remaining following diagnosis is normally stored in a tissue block that is kept in pathology archives for 10 years. Having said that, the biopsies are usually quite small, so there is huge value in ensuring that the tissue is used to obtain the maximum amount of information. Ascites (fluid) is often discarded.

suitable clinical trials available for each patient, based on the genetic alterations identified in the INOVATe testing panel.

- The WEHI-Stafford Fox Rare Cancer Program at the Walter and Eliza Hall Institute of Medical Research in Victoria, funded by philanthropy, leveraging additional funds from government, industry and philanthropy, which performs a range of molecular analyses for approximately 50 women per annum. The WEHI-Stafford Fox Rare Cancer Program at the Walter and Eliza Hall Institute of Medical Research provides national remote consenting and molecular profiling for a range of rare cancers, including rare ovarian cancer sub-types such as mucinous ovarian cancer, low grade serous ovarian cancer and high grade serous ovarian cancer beyond standard of care (for example primary refractory disease or post PARP inhibitor therapy). Molecular analyses delivered by the WEHI-Stafford Fox Rare Cancer Program includes panel testing (50 women) to Whole Exome Sequencing (20 women) to Whole Genome Sequencing (14 women) of different types of ovarian cancers per annum.
- The Precision Oncology Program in Victoria, which utilises an experimental functional drug screening approach to guide individualised therapy for women following relapse from first line treatment. Since its inception in 2019, the Precision Oncology Program has been used to guide a personalised medicine approach for up to 40 women per year; however, enrolment in the program was adversely impacted by COVID in 2020.
- The Genomic Cancer Medicine Program at the Garvan Cancer Medicine Program also offers molecular profiling to enable access to precision medicine through a range of basket trials for less common, high-mortality cancers, including ovarian cancers. The Genomic Cancer Medicine Program is estimated to screen a relatively limited number of women each year; it is estimated less than 20 women per year access this program.

This patchwork approach means that in practice only about 210 Australian women are able to access molecular profiling at diagnosis and a rapid precision medicine approach to their treatment in the event of relapse.

This means that nearly nine in 10 women diagnosed with ovarian cancer each year (approximately 1,600 women[15]) are not able to access a precision medicine approach to their treatment from diagnosis (Figure 1.4).[16]

Moreover, **access to these programs is highly skewed towards women in major capital cities**, in Australia's most populous states (Figure 1.6). Women have been reported to travel to NSW and Victoria from other states to seek access to precision medicine programs, and to try to access novel treatments, raising significant issues of equity for Australian women with ovarian cancer. Such a limited system also favors the medically literate, a further limitation, as described in a Rare Cancers Australia's *Rights and Roles of Australian Cancer Patients*:

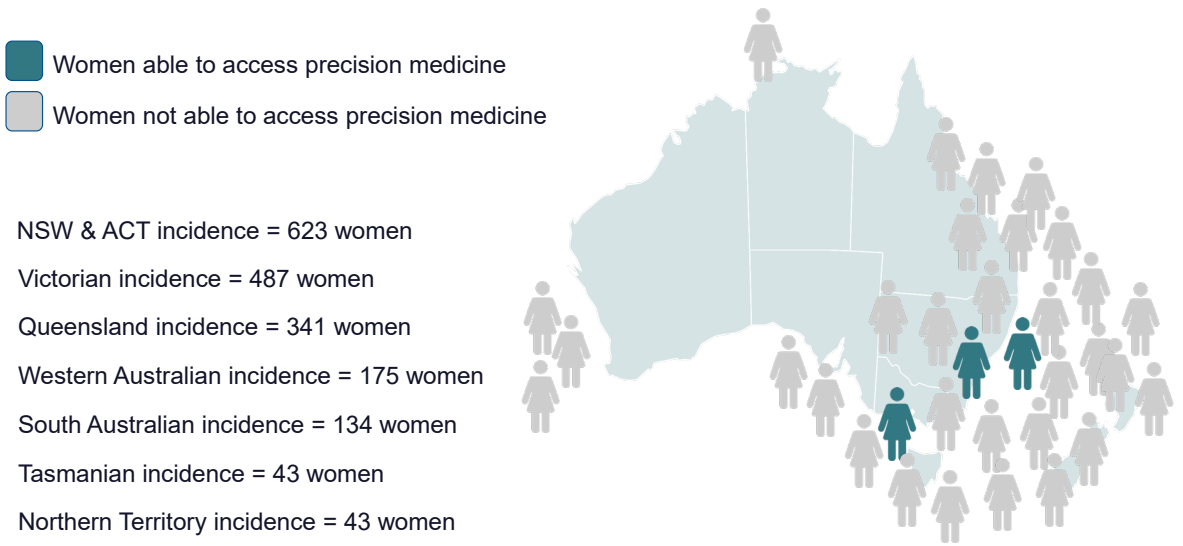
> *Since health literacy is a dynamic between the individual's capabilities and the demands of a healthcare system, interventions are likely needed both to assist patients with limited health*

[15] Calculated by subtracting the average enrolment in the major precision medicine programs identified above (e.g., the sum of INOVATe (100 women), Stafford-Fox (50 women), Hudson (40 women), and Genomic Cancer Medicine Program (20 women) enrolment, which sums to 210 women) from average incidence over the FY23-FY26 period (1,852 women). See Attachment 1.

[16] Australian Institute of Health and Welfare, 2021, Cancer data in Australia accessed at: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia.

literacy to participate in decision-making, as well as to support clinicians in engaging with patients.[17]

Figure 1.6: Limited and unequal access to precision medicine in ovarian cancer



For the 1,600 other women diagnosed with ovarian cancer without access to these programs, most of whom live outside a major metropolitan centre, they either:

- Seek to enroll in a clinical trial, or
- Proceed with standard second line therapies.

While many treating clinicians may investigate clinical trial options for women that have relapsed from first line treatment, many will not. For example, **ANZGOG data show that approximately only five per cent of women diagnosed with ovarian cancer go on to be screened for one of their clinical trials in Australia.**[18]

Even if a woman is screened for a trial, there is no guarantee there will be a trial available. Critically, the number of clinical trials available in Australia is hindered by the lack of a pool of pre-screened patients, which makes clinical trial recruitment more costly and inefficient. Because recruiting women to trials is so expensive and inefficient, fewer trials are available in Australia than might otherwise be the case if molecular profiling were part of routine practice. For example, in the first funding round for the INOVATe program, only 50 per cent of women screened through the program were identified to have a targetable mutation where a clinical trial was also available.[19]

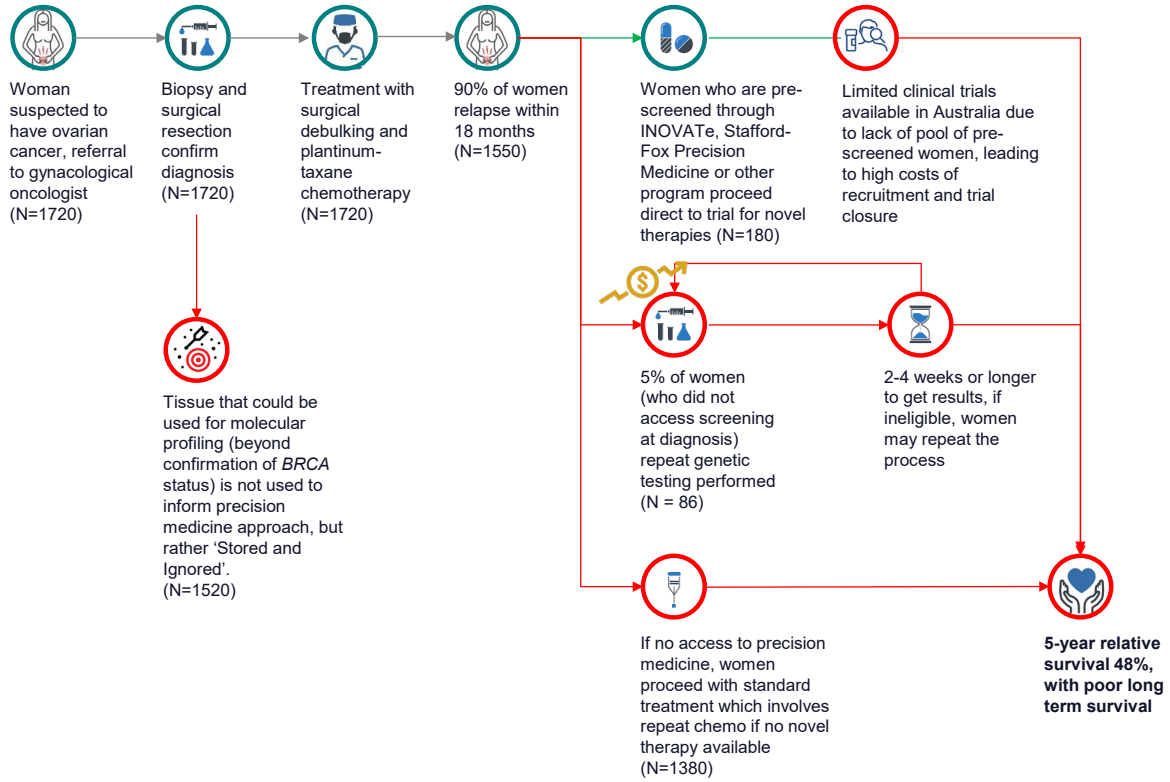
The process for determining access to trials for women following relapse is also fragmented and inefficient. **There is no single test to determine eligibility for available trials (as is the approach for the NSW and Victorian programs). Instead, women undergo a sequential series of duplicative and time-consuming tests to determine eligibility for each individual trial. This process can result in multiple tests, as well as weeks or months of delays in waiting for access to potentially life-extending treatments, as low testing volumes lead to laboratory inefficiencies and delays due to sample batching.** In practice, relapsed women can

[17] Rare Cancers Australia, 2021, Rights and Roles of Australian Cancer Patients, p 64.
[18] Based on analysis of OASIS clinical trials data.
[19] INOVATe data.

wait many weeks, at a time of rapid disease progression, to secure access to a novel therapy that may substantially extend their lives and time with loved ones.

Combined, the current approach fails women in need of novel approaches to treatment and misses significant opportunities to improve the economic output and impact of Australia's ovarian cancer research efforts (Figure 1.5).

Figure 1.5: Current treatment pathways for ovarian cancer

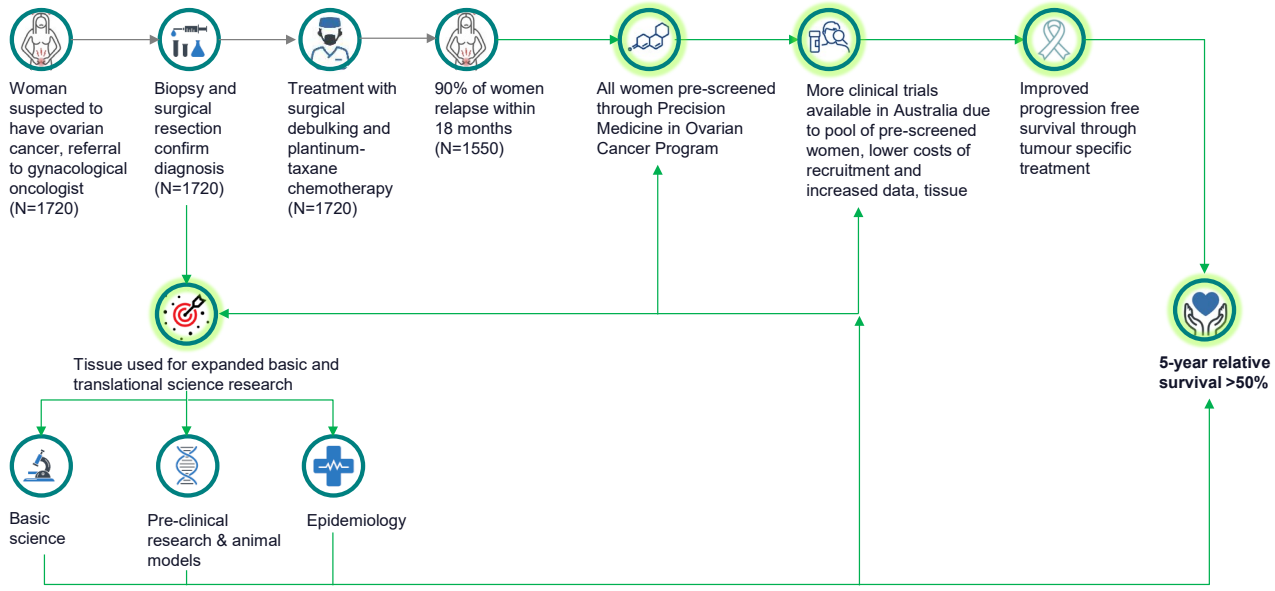


1.7 Precision Medicine in Ovarian Cancer can deliver on the Target for Low Survival Cancers

A nationally collaborative approach to Precision Medicine in Ovarian Cancer would see research incorporated into the standard of care for these women, and Australia's Target for Low Survival Cancers by 2027 realised for women with ovarian cancer (Figure 1.6).

In a Precision Medicine in Ovarian Cancer paradigm, the tissue that is already routinely obtained through biopsy and resection required for diagnosis, would not be wasted but would be evaluated through a national molecular profiling and drug screening program.

Figure 1.6: Precision Medicine in Ovarian Cancer treatment pathways



Women would still receive standard first line therapy but would be pre-screened for enrolment in available clinical trials in Australia so that in the event of relapse, or resistance to standard chemotherapy, they would receive novel agents individualised to their tumour, if available, approved and funded, or have the option of a suitable clinical trial. For the five per cent of women that would have otherwise navigated the clinical trials landscape following relapse, this would speed the time to treatment with a novel therapy. For women whose cancer does not have a molecular alteration, they would still gain access to a precision medicine approach through a functional drug screening approach, improving the effectiveness of their treatment, avoiding the side effects associated with ineffective treatment and improving cost efficiency of Australian health services through the avoidance of prescribing therapies that will not work.

This would unlock significant health and economic gains for women and the wider community (note that Chapter 2 explores evidence for these effects in detail):

- Improved health outcomes for women diagnosed with ovarian cancer as they more rapidly access novel treatments in the event of relapse, which occurs for 80 to 90 per cent of all women
- Cost efficiencies in molecular profiling through avoided duplication and increased scale as a result of a nationally coordinated approach in contrast to the current fragmented model
- A faster time to trial recruitment due to the creation of a pool of pre-screened women, lowering the costs of ovarian clinical trials in Australia
- Increased attraction of clinical trials to Australia resulting from more efficient and effective trial recruitment and linked data, expanding access to novel therapies for Australian women and increasing total investment in Australian medical research in Australia.

1.8 Alignment with Australian Government policy objectives

health system into the future and drive further medical innovation through the improved diagnosis and treatment of women with ovarian cancer.

The Program is aligned to the Patients theme identified within the MRFF 10-year plan,[20] as it would support:

- The development of innovative treatments
- Improvements in the efficiency and effectiveness of the health system
- Enhancements to the translation of research outputs to deliver impact, including through commercialization of research.
- The attraction of clinical trials
- Increased access advanced health care and medical technology for improved health outcomes.

These impacts are explored further in the next chapter.

[20] Department of Health, *Medical Research Future Fund 10-year plan*, 2019.

Chapter 2

Health and Economic Impacts of Precision Medicine Program

This chapter presents analysis of the net health and economic impacts of a Precision Medicine in Ovarian Cancer program as well as its alignment to Australian Government health research objectives and proposed measures of success.

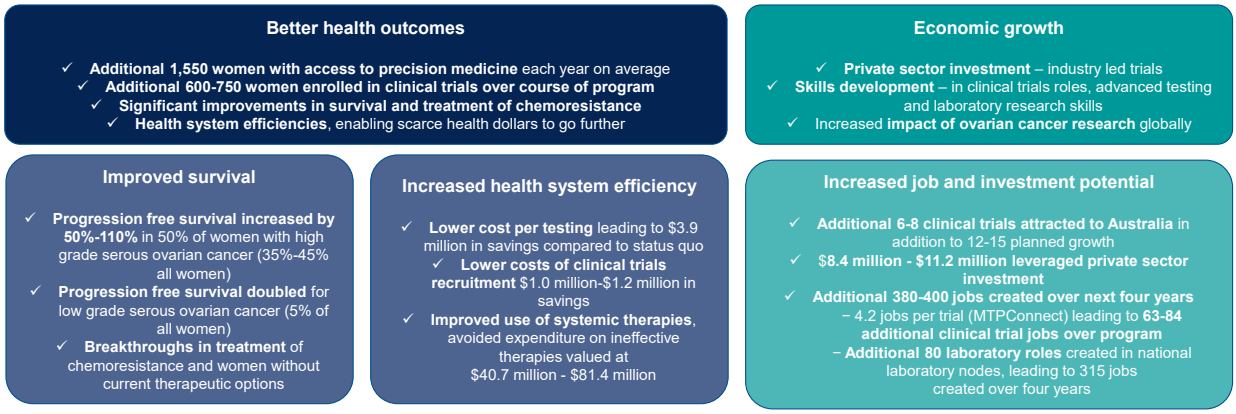
2.1 Overview of impacts

The vision for the Precision Medicine in Ovarian Cancer Program is to lift 5-year relative survival for women diagnosed with ovarian cancer above 50 per cent by 2027 through a comprehensive, national approach to the diagnosis and individualised treatment of women with ovarian cancer.

The Program will transform medical research and innovation in ovarian cancer, leading to (Figure 2.1):

- **Better health outcomes**, with improved survival and avoided side effects through an individualised approach to treatment
- **Health system efficiencies**, with comprehensive testing enabling the avoidance of test duplication and inappropriate treatment with high-cost therapies
- **Significant economic impacts**, with additional private sector funding to be leveraged into Australia through an increased number of clinical trials, as well as the creation of highly skilled jobs and the amplification of Australia's research impact globally.

Figure 2.1: Summary of health and economic impact potential of the Precision Medicine in Ovarian Cancer Research Program



The following sections present evidence of benefit against each of these criteria.

2.2 Better health outcomes

Comprehensive, national approaches to personalised medicine can deliver the breakthroughs needed for complex, low survival cancers.

As noted in Chapter 1, a comprehensive, Australia-wide strategy has delivered significant improvements in childhood cancer over the past three decades[21] and more recently through the ZERO Childhood Cancer program. The ZERO Childhood Cancer Program provides molecular profiling, including whole genome sequencing, whole transcriptome sequencing and methylation profiling, for every child and young adult diagnosed with high-risk cancer. The systematic molecular profiling of each patient has enabled significant improvements in the treatment of patients and health outcomes; early results published in Nature Medicine[22] showed that:

- 93.7 per cent of patients had at least one germline or somatic aberration
- Therapeutic targets were identified in 71.4 per cent of screened patients
- 5.2 per cent of patients had a change in diagnosis
- Among the patients that received a personalised medicine treatment, 31 per cent experienced clinical benefit, with their tumour either shrinking or experiencing complete regression
- In 40 per cent of cases the tumour stopped growing and stabilised.

This systematic approach adopted in childhood cancer can be replicated in ovarian cancer, which shares similar challenges to high-risk childhood cancers. Ovarian cancer is similarly a group of complex, rare cancers with poor mortality. Ovarian cancer research has also demonstrated early evidence of benefit from a precision medicine approach. For example, the ALLOCATE study[23] evaluated the clinical utility of real-time molecular profiling using whole genome sequencing and methylation and similarly found:

- 85 per cent of patients had at least one somatic genomic aberration or methylation events
- Therapeutic targets were identified in 60 per cent of all screened patients
- 25 per cent of grade 2 serous carcinomas had a change in diagnosis (reclassified from High Grade Serous to Low Grade Serous following identification of a *KRAS* mutation).

Similarly, a recent study found that the adoption of a precision medicine approach in breast and gynaecological cancers improved overall response rate, progression free survival and trends towards overall survival.[24]

Systematic molecular profiling of women enables access to novel treatment approaches with the potential to substantially improve 5-year survival above 50 per cent. To demonstrate the potential health benefits that could be realised, two case studies are explored:

[21] NCI SEER, 2016, Age-Adjusted SEER Incidence and U.S. Death Rates and 5-Year Relative Survival (Percent), https://seer.cancer.gov/archive/csr/1975_2016/results_merged/topic_survival.pdf Cancer Institute NSW, 2019, A history of global cancer breakthroughs, https://www.cancer.nsw.gov.au/learn-about-cancer/cancer-breakthroughs; Unger, JM, Cook, E, Tai, E, and Bleyer, A, 2016, The Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence, and Strategies, ASCO Educational Book, accessed at: https://ascopubs.org/doi/full/10.1200/EDBK_156686

[22] Wong, M, Mayoh, C, Lau, LMS, et al. 2020, Whole genome, transcriptome and methylome profiling enhances actionable target discovery in high-risk pediatric cancer. Nat Med, 26, 1742–1753, doi: 10.1038/s41591-020-1072-4.

[23] Kondrashova, O, Ho, G, Au-Yeung, G, Leas, L, et al, 2019, The Clinical Utility of Real-Time Targeted Molecular Profiling in the Clinical Management of Ovarian Cancer: The ALLOCATE Study, JCO Precision Oncology, 3, 1-18, doi: 10.1200/PO.19.00019.

[24] Charo, LM, Eskander, RN, Sicklick, J, Kim, KH, et al, 2022, Real-World Data from a Molecular Tumor Board: Improved Outcomes in Breast and Gynecologic Cancers Patients with Precision Medicine, JCO Precision Oncology, no. 6, doi: 10.1200/PO.20.00508

- The health benefits of access to next generation PARP inhibitors, potentially benefitting 50 per cent of women diagnosed with High Grade Serous Ovarian Cancer, and enabling focus on studying resistance to PARP inhibitor therapy, the next challenge for these women
- The health benefits of access to novel therapies for Low Grade Serous Ovarian Cancer, which affects a smaller number of women, often younger Australian women, for which there is limited benefit from standard platinum-based therapies.

The section concludes with a summary of cutting-edge research in development focused on women without molecular therapeutic targets or who experience chemoresistance.

Next generation PARP inhibitors for women with High Grade Serous Ovarian Cancer

PARP (poly[adenosine diphosphate–ribose] polymerase) inhibitor treatment was the first class of therapy specifically targeted to and approved for the treatment of ovarian cancer. PARP inhibitor therapy has shown unprecedented success, with three year longer median progression free survival compared with placebo, in the first line, after only two years of treatment. To date, only one PARP inhibitor is available in Australia, olaparib, but is subject to PBS Authority Restrictions, restricting it only to women whose ovarian cancer has a mutation in either *BRCA1/2* and is responding to platinum chemotherapy.

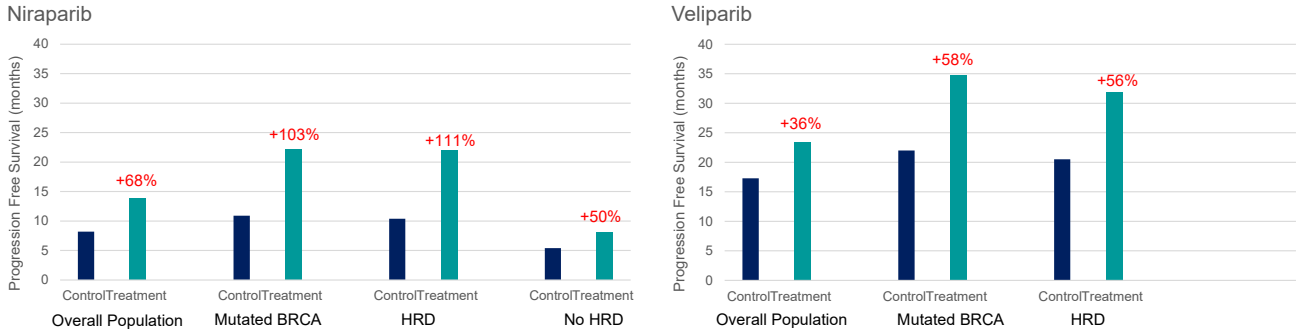
Following the early breakthroughs of olaparib, a series of next generation PARP inhibitors are also in development that similarly show significant promise: niraparib (TGA registered but not PBS listed, yet widely reimbursed in the UK, Europe, the US, India and elsewhere), veliparib (not TGA registered), and rucaparib (not TGA registered). Like olaparib, these PARP inhibitors have been shown to improve progression-free survival when used after first line treatment of surgical de-bulking and platinum–taxane doublets.

Early clinical trials have shown efficacy of these next generation therapies in three biologically distinct populations of patients to varying degrees, including:

- Patients with germline mutations in *BRCA1* or *BRCA2*
- Patients with high scores on the myChoice test (Myriad Genetics) for homologous-recombination deficiency (HRD), indicating an important loss of DNA repair function
- Patients with homologous-recombination proficiency (no HRD).

As shown in Figure 2.2, early data show progression free survival would be expected to improve for more than 50 per cent of women diagnosed with High Grade Serous Ovarian Cancer.

Figure 2.2: Improvement in Progression-Free survival with PARP inhibitors targeting genetic mutations



Source: Coleman RL, Fleming GF, Brady MF, Swisher EM, et al, 2019, Veliparib with First-Line Chemotherapy and as Maintenance Therapy in Ovarian Cancer. N Engl J Med. 2019 Dec 19;381(25):2403-2415. doi: 10.1056/NEJMoa1909707.; Mirza MR, Monk BJ, Herrstedt J, Oza AM, et al, 2016, ENGOT-OV16/NOVA Investigators. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016 Dec 1;375(22):2154-2164. doi: 10.1056/NEJMoa1611310. Epub 2016 Oct 7. PMID: 27717299; Longo, D, 2019, Personalised Medicine for Primary Treatment of Serous Ovarian Cancer, N Engl J Med 2019; 381:2471-2474, DOI: 10.1056/NEJMe1914488.

Critically, this will not happen in the current piecemeal, *ad hoc* approach where biopsies are being 'stored and ignored' – it will require the nationally collaborative, strategic approach where research is the standard of care for all women recommended by the Senate Select Committee and similarly implemented through the ZERO Childhood Cancer program.

In addition to health outcomes, PARP inhibitors can entail substantial monthly costs, in the order of US$114,000 to US$133,000 ($A157,000 to $A183,540).[25] As these therapies are increasingly used in clinical practice, molecular profiling testing is critical to better defining the appropriate prescribing of these therapies to individuals. Survival data will also help to clarify whether PARP maintenance therapy during the first remission is superior to PARP inhibitor administration later in the course of treatment.[26]

Novel targeted therapies in Low Grade Serous Ovarian Carcinomas

Low Grade Serous Ovarian Carcinomas, which are an extremely rare cancer, accounting for less than five per cent of all ovarian cancer incidence, have poor responses to chemotherapy.

Like women with High Grade Serous Ovarian Cancer, most patients present with advanced disease, and more than 70 per cent of women relapse following first line therapy.[27] Low Grade Serous Ovarian Carcinoma tends to occur in younger women, with the median age at diagnosis is 47-54 years old. Approximately 80 women are diagnosed each year, and it is estimated approximately 300 women are currently living with recurrent LGSC in Australia.

Low Grade Serous Ovarian Carcinomas has its own distinct molecular profile, with a number of alterations occurring along the MAPK pathway; in particular, *KRAS* mutations occur in approximately 30 per cent of LGSOCs, *BRAF* mutations occur in 10 per cent, and *NRAS* mutations occur in approximately 9 per cent.[28]

As with most rare tumor subtypes, few effective therapeutic options exist for women with LGSOC. Beyond chemotherapy, other options include endocrine therapy and bevacizumab, although the response to hormonal therapy remains limited (<15 per cent).[29]

MEK inhibitors are orally bioavailable, non-ATP competitive, small-molecule inhibitors of MEK1/2. Once MEK inhibitors became available for clinical development, it was logical to study them in LGSOC. Initial studies have produced mixed results,[30] with the most promising including the GOG 0281 trial, which saw progression free survival nearly double: median PFS of 13.0 months for trametinib and 7.2 months for PCC (physician's choice of standard chemotherapy) (HR, 0.48; P < .001). An initial phase II trial also examined selumetinib, which found an objective response rate (ORR) of 15 per cent, with 65 per cent of patients having stable disease, and median progression-free survival (PFS) was 11.0 months. Similarly, other studies comparing four different MEK inhibitors (trametinib, selumetinib, binimetinib, and refametinib) in novel LGSOC patient-derived cell lines found trametinib to have the greatest antiproliferative effects.[31]

These early trials have produced new questions to be answered, including the need to identify an optimal predictive biomarker for MEK inhibitor sensitivity. At the same time, these early trials also point to new opportunities to improve survival outcomes for women diagnosed with

[25] Longo, D, 2019, Personalised Medicine for Primary Treatment of Serous Ovarian Cancer, N Engl J Med 2019; 381:2471-2474, DOI: 10.1056/NEJMe1914488.
[26] Ibid.
[27] Gershenson, DM, Gourley, C, and Paul, J, 2020, MEK Inhibitors for the Treatment of Low-Grade Serous Ovarian Cancer: Expanding Therapeutic Options for a Rare Ovarian Cancer Subtype, Journal of Clinical Oncology 38, no. 32 (November 10, 2020) 3731-3734, doi: 10.1200/JCO.20.02190.
[28] Moujaber et al Endocrine-Related Cancer (2022) 29, R1-R16, doi.org/10.1530/ERC-21-0191
[29] ANZGOG
[30] Monk, BJ, Grisham, RN, Banerjee, S, Kalbacher, E, et al, 2020, MILO/ENGOT-ov11: Binimetinib Versus Physician's Choice Chemotherapy in Recurrent or Persistent Low-Grade Serous Carcinomas of the Ovary, Fallopian Tube, or Primary Peritoneum, Journal of Clinical Oncology, 38:32, 3753-3762; Gershenson, DM, Gourley, C, and Paul, J, 2020, MEK Inhibitors for the Treatment of Low-Grade Serous Ovarian Cancer: Expanding Therapeutic Options for a Rare Ovarian Cancer Subtype, Journal of Clinical Oncology 38, no. 32 (November 10, 2020) 3731-3734, doi: 10.1200/JCO.20.02190.
[31] Ibid.

Low Grade Serous Ovarian Carcinomas through precision medicine approaches that employ MEK inhibitor therapies.

Currently, there are no existing trials specifically for women with Low Grade Serous Ovarian Carcinomas in Australia. Through increasing consistent profiling of women for Low Grade Serous Ovarian Carcinomas, a critical mass of patients can be identified, enabling the attraction of next generation inhibitor trials to Australia and improving survival outcomes for up to 80 women per year.

Similarly, other key sub-types of ovarian cancer need this level of understanding and approach to improve the patient survival outcomes.

Next generation functional profiling for women without therapeutic targets today

While many therapeutic targets are available for women with different sub-types of ovarian cancer, there are still a number of women for whom molecular therapeutic targets have not yet been identified, leaving them without personalised treatment approaches today. Moreover, with repeated relapse and chemotherapy treatments, the cancer will change and will eventually become resistant to chemotherapy (chemoresistant). Chemoresistance is responsible for treatment failure and mortality for more than 90 per cent of patients with advanced stage cancer.[32] While different chemotherapy agents can be used, cancers will generally become resistant to all chemotherapy drugs. For women without molecular therapeutic targets and for those that see their cancer become chemoresistant, further research is needed beyond molecular profiling to identify novel biomarkers and treatment options.

To address this unmet need, researchers are increasingly exploring cutting edge research through next generation 'functional profiling' of patients, which uses a combination of genome sequencing, expression analyses, drug screening and patient-derived xenograph (PDX) generation, among other techniques, to develop patient 'avatars' or 'models' by which they can predict drug- and patient-specific responses to available treatments or combinations of treatments to determine the best treatment for a particular patient. These early-stage, experimental studies also seek to inform future drug development. For example, this is the approach that is currently being trialled through the Precision Medicine Oncology program at the Hudson Institute. With funding for only 40 patients per annum, however, the research program lacks scale and statistical power to make real insights into the potential of these novel precision medicine approaches to improve outcomes for women with ovarian cancer.

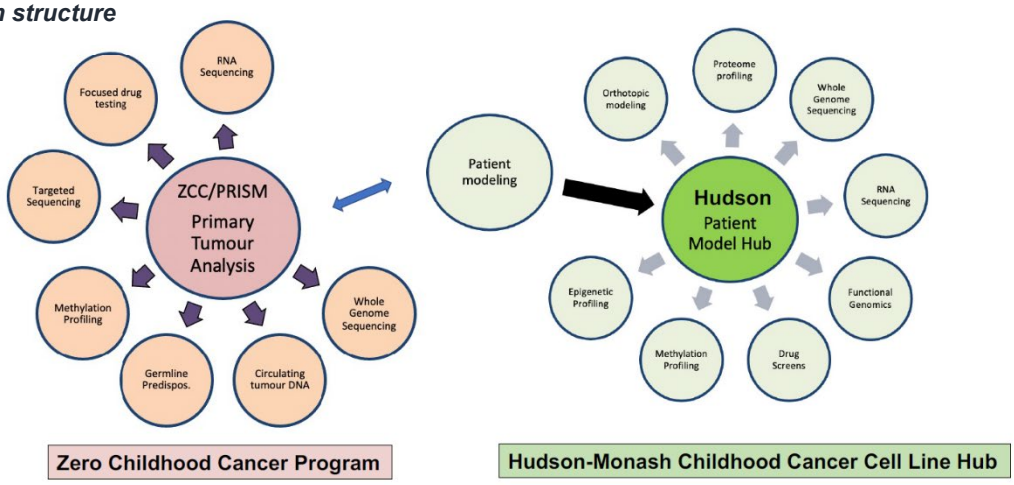
A far larger pilot program, with tissue samples from more than 250 patients collected, has been established through the Hudson-Monash Childhood Cancer Cell Line Hub, which is a functional profiling research program being run in partnership with the ZERO Childhood Cancer and PRISM programs (Figure 2.3).[33] Leveraging sample collection and molecular analysis through the ZERO Childhood Cancer Program, the Hudson-Monash Childhood Cancer Cell Line Hub develops patient models and performs 'four dimensional' (genomic, epigenomic, transcriptomic, and proteomic) analysis integrating molecular sequencing with high-throughput genetic screening (Cas9/CRISPR) and drug screens to identify new and existing therapeutic targets for a particular patient. The analysis is also used to identify novel biomarkers and inform future drug development.

[32] Brasseur, K., Gévry, N., & Asselin, E. (2017). Chemoresistance and targeted therapies in ovarian and endometrial cancers. Oncotarget, 8(3), 4008–4042. https://doi.org/10.18632/oncotarget.14021; Agarwal R, Kaye SB. Ovarian cancer: strategies for overcoming resistance to chemotherapy. Nature Reviews Cancer. 2003;3:502–16.

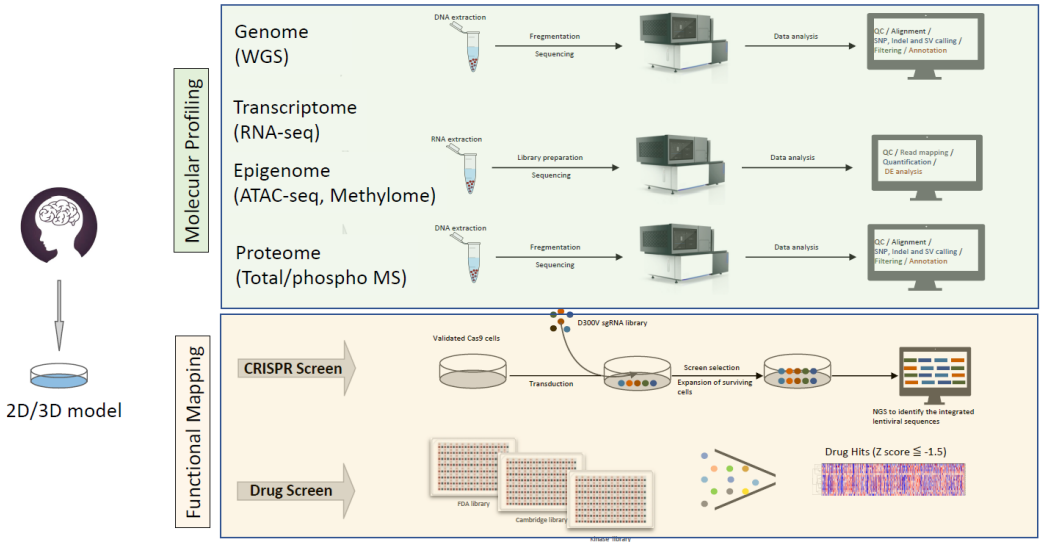
[33] See: Hudson Monash Paediatric Precision Medicine Program, accessed at: https://hudson.org.au/research-program/hudson-monash-paediatric-precision-medicine-program/

Figure 2.3: Next Generation Functional Profiling – the ZERO Childhood Cancer Program and Hudson-Monash Childhood Cancer Cell Line Hub program scope and pipeline

Program structure



Program pipeline



Source: Hudson-Monash Childhood Cancer Cell Line Hub, 2022, Flagship: Next-generation paediatric cancer precision oncology, pp 2 and 8.

Against the backdrop of unmet needs in ovarian cancer, adopting a similar approach to ovarian cancer, with the scale and statistical power made possible through a national approach, this could facilitate the development of therapies for women with ovarian cancer.

2.3 Health system efficiencies

Health system efficiencies would be expected to be realised in:

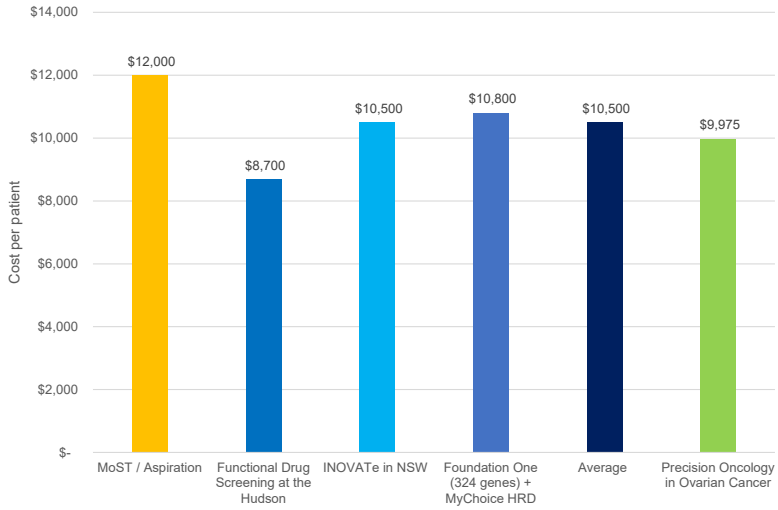
- Overall efficiencies in the testing approach, derived from avoided duplication and economies of scale compared to a counterfactual approach where each state developed its own approach
- The targeted use and avoided waste of high-cost therapies.

Avoided duplication and economies of scale in testing

In states where there is not an upfront approach to precision medicine, the current testing model is characterised by duplication, with women that do not access upfront molecular profiling being screened sequentially for clinical trial eligibility. Most women will likely not have time to be screened for more than one trial, due to the progression of her disease, but if a woman is not eligible for a particular trial, she could undergo testing multiple times. This results not only in unnecessary duplication in health services, but also can delay access by weeks when the cancer has recurred, often in a more aggressive form, adversely impacting her survival outlook even further.

There would also be some economies of scale realised through a national approach. It was estimated that **cost efficiencies from a more streamlined approach to ethics and governance as well as optimised batching would see efficiencies of five per cent on current industry averages (Figure 2.4). Compared to the status quo approach, this would deliver savings of $3.9 million in total over the FY23-F26 period ($3.4 million in $NPV_{5\%}$ terms).**

Figure 2.4: Benchmarking testing costs per patient



Source: Genomic Cancer Medicine Program Aspiration Program Costs, Precision Medicine Program, INOVATe, commercial testing rates for Foundation One and MyChoice.

Avoided inappropriate treatment with high-cost therapies

A national approach to precision medicine in ovarian cancer will also enable scarce health resources to be allocated to the highest, best uses.

For example, it has been estimated that nearly 50 per cent of women diagnosed with HGSOC ovarian cancer are potential candidates for treatment with PARP inhibitors given the frequency of germline *BRCA1/2* mutations, somatic *BRCA1/2* mutations, and homologous recombination deficiency among women with ovarian cancer.[34] Established and emerging PARP inhibitors, such as olaparib (which has PBS Authority Listing), niraparib (TGA registered but not PBS listed), rucaparib (not TGA registered) and veliparib (not TGA registered), have been shown to significantly improve progression free survival compared to the standard of care (see above), but they also present high costs to the wider health system as well as risks of Grade 3 and 4 adverse events.[35] It is reported the expected cost of treatment for olapraib, niraparib, and

[34] Wolford JE, Bai J, Moore KN, Kristeleit R, Monk BJ, Tewari KS. Cost-effectiveness of niraparib, rucaparib, and olaparib for treatment of platinum-resistant, recurrent ovarian carcinoma. Gynecol Oncol. 2020 May;157(2):500-507. doi: 10.1016/j.ygyno.2020.02.030. Epub 2020 Mar 13. PMID: 32173049; PMCID: PMC7410501.
[35] Ibid; and Mirza MR, Monk BJ, Herrstedt J, Oza AM, Mahner S, Redondo A, Fabbro M, Ledermann JA, Lorusso D, Vergote I, Ben-Baruch NE, Marth C, Mądry R, Christensen RD, Berek JS, Dørum A, Tinker AV, du Bois A, González-Martín A, Follana P, Benigno B, Rosenberg P, Gilbert L, Rimel BJ, Buscema J, Balser JP, Agarwal S, Matulonis UA; ENGOT-OV16/NOVA Investigators.

rucaparib is US$114,289 per patient, US$132,790 per patient and $US133,096 per patient, respectively.[36] Research has shown that genetic testing for *BRCA* and HRD mutations provide an indication of potential benefit from treatment with PARP inhibitors, but there is variation in efficacy and these biomarkers alone may not always be sufficiently precise to predict which individual patients will derive benefit from PARP inhibitor treatment.[37]

The use of molecular profiling as part of a Precision Medicine in Ovarian Cancer research program will enable the avoidable prescribing of high-cost therapies to patients for whom benefit will be limited. Given the total magnitude of potential spend, the payoffs from more effective prescribing are hard to overstate. For example, if all women potentially eligible for PARP inhibitor therapy were to access these novel therapies, this would cost in the order of A$98.6 million in FY23, growing to A$105 million by FY26. **If only 10 per cent of this prescribing is inappropriate, this would prevent A$10.2 million in wasted health funding each year on average over the FY23 to FY26 period, or $40.7 million in total over FY23-FY26 ($36 million in $NPV_{5\%}$ terms). If the rate of inappropriate prescribing were to increase to 20 per cent, the risk of health system inefficiencies and waste rises to more than $20.4 million per annum, or $81.4 million in total over FY23-FY26 ($72.1 million in $NPV_{5\%}$ terms).**

Table 2.1: Health system efficiencies through improved patient selection for PARP inhibitors (FY23-FY26)

Key metric	FY2023	FY2024	FY2025	FY2026	Average	Total	$NPV_{5\%}$
Cost of treatment with PARP inhibitors in $A	$161,710	$166,561	$171,558	$176,705	$169,134		
Women potentially eligible for PARP inhibitor therapy	628	641	655	669	648	2,593	
Potential cost of PARP therapies	$98.6m	$100.7m	$102.8m	$105.0m	$101.8m	$407.1m	$360.4m
Prevention of inappropriate prescribing – 10%	**$9.9m**	**$10.1m**	**$10.3m**	**$10.5m**	**$10.2m**	**$40.7m**	**$36.0m**
Prevention of inappropriate prescribing – 20%	**$19.7m**	**$20.1m**	**$20.6m**	**$21.0m**	**$20.4m**	**$81.4m**	**$72.1m**

Source: AIHW, 2021, Cancer Data in Australia, OCRF, 2020, State of the Nation in Ovarian Cancer: Research Audit, Wolford JE, Bai J, Moore KN, Kristeleit R, Monk BJ, Tewari KS. Cost-effectiveness of niraparib, rucaparib, and olaparib for treatment of platinum-resistant, recurrent ovarian carcinoma. Gynecol Oncol. 2020 May;157(2):500-507. doi: 10.1016/j.ygyno.2020.02.030; EviQ costs for Olaparib, accessed at: https://www.eviq.org.au/medical-oncology/gynaecological/ovarian/3737-advanced-metastatic-or-recurrent-olaparib#indications-and-patient-population-ovarian-advan

2.4 Economic growth

The Precision Medicine in Ovarian Cancer Program would not only improve more rapid access to novel therapies and health system efficiencies but would further expand economic activity in Australia through increased clinical trials attraction, leveraged private sector investment and jobs creation.

Increased trials activity and leveraged private sector investment

Australia's ovarian cancer community enjoys an excellent reputation for high quality science and to that end has succeeded in attracting a range of clinical trials with strong philanthropic and pharmaceutical industry investment historically, both of which represent new investment to

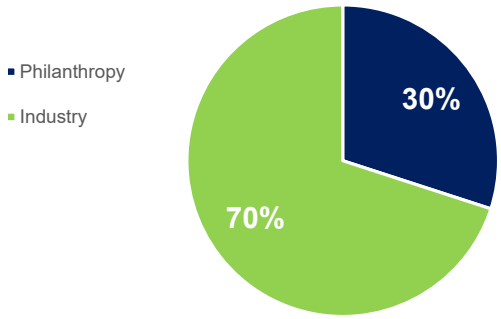
Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016 Dec 1;375(22):2154-2164. doi: 10.1056/NEJMoa1611310. Epub 2016 Oct 7. PMID: 27717299.

[36] Wolford JE, Bai J, Moore KN, Kristeleit R, Monk BJ, Tewari KS. Cost-effectiveness of niraparib, rucaparib, and olaparib for treatment of platinum-resistant, recurrent ovarian carcinoma. Gynecol Oncol. 2020 May;157(2):500-507. doi: 10.1016/j.ygyno.2020.02.030.

[37] Ibid.

the economy which might not have otherwise occurred. The high rate of industry investment is significant and underlines the quality of Australian ovarian cancer research; for example, **ANZGOG data shows that for every philanthropic dollar invested, industry has invested $2.30** (Figure 2.5).

Figure 2.5: Private sector funding opportunities – historical industry funding contributions for ANZGOG trials



Source: ANZGOG OASIS trials funding data.

At the same time, Australia's fragmented approach to molecular profiling and clinical trials nationally leads to high costs of recruitment, low enrolment in trials, long times to trial launch, and excess risks of trials closing due to a lack of enrolment. For example, ANZGOG reports that due to the uncoordinated and *ad hoc* nature of screening programs in hospitals across the country, they can struggle to achieve recruitment for rarer ovarian cancers in their trials with women missing out on these opportunities for targeted therapies. Notably, this challenge is not observed in NSW, where a statewide approach sees demand for molecular profiling exceed capacity. INOVATe noted it met patient recruitment expectations even within COVID lockdown periods. Similarly, in Victoria a highly efficient approach to molecular screening within the state sees high demand for the Stafford-Fox and Precision Oncology programs.

This drag on the establishment of clinical trials is unnecessary and holds Australian research back to the detriment of the economy.

ANZGOG data show a Phase II trial requires investment of $2.5 million on average in Australia.[38] ANZGOG estimates that if research was adopted as the standard of care, underpinned by a national approach to screening through the Precision Medicine in Ovarian Cancer model, that **the costs and time to recruit patients would drop by more than 25 per cent as a result of a pre-screened pool of women,[39] facilitating the attraction of between 6 to 8 additional clinical trials** to Australia compared to what would otherwise have been the case over the next five years. **Conservatively valued at an estimated $2 million per trial, the attraction of 6 to 8 clinical trials to Australia would see an additional $12 million to $16 million ($10.6 million to $14.2 million in clinical trials investment in Australia in $NPV_{5\%}$ terms), of which $8.4 million to $11.2 million ($7.4 million to $9.9 million in clinical trials investment in Australia in $NPV_{5\%}$ terms) could be leveraged from industry based on historical average funding trends.**

Skills development and jobs creation

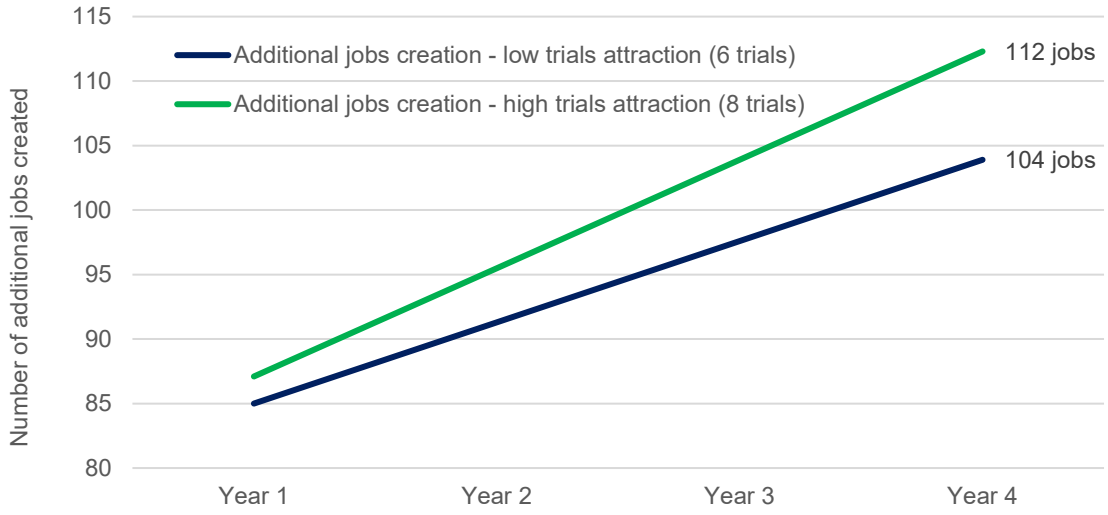
The Precision Medicine in Ovarian Cancer Research Program would create jobs as a result of the increased volume of molecular profiling and research, as well as the attraction of additional clinical trials to Australia.

[38] ANZGOG trials data 2010-2021.
[39] Note the total costs of recruitment ($250,000) would decline, not the total cost of the trial.

- *Additional laboratory and research jobs and skills development* — The INOVATe program employs 5.9 FTE laboratory and research professionals to conduct molecular profiling for 100 women per annum and associated research for the program. Based on this labour to test requirement, and factoring in an efficiency gain arising from scale of 20 per cent, **it was estimated that the national program would create 80 additional highly skilled jobs, enabling the upskilling of Australians in cutting edge molecular profiling and next generation functional profiling technologies**.
- *Additional clinical trials jobs* — MTPConnect estimates that 4.2 highly skilled jobs are created for every new clinical trial nationally.[40] If an additional six to eight trials were attracted to Australia as a result of the more cost-efficient recruitment process enabled by a national approach to screening, **this would create between an additional 25 and 34 new jobs by year 4 of the program, or 63 to 84 additional jobs over the course of the first five years of the program.**

In total, depending on the number of additional clinical trials attracted to Australia, the total number of jobs created by year 4 of the program would be expected to increase to 104 jobs to 112 jobs (Figure 2.6). Over the course of the four years of the program, between 380 and 400 additional jobs would be created.

Figure 2.6: Cumulative jobs creation as additional trials attracted to Australia



2.5 Net economic impact and measures of success

The Precision Medicine in Ovarian Cancer has the potential to deliver significant net health and economic impacts for women diagnosed with ovarian cancer, as well as benefits to the wider Australian health system and community.

Key costs include the additional molecular profiling and next generation functional profiling feasibility pilot for women who miss out on precision medicine approaches today. This would be expected to cost in the order of $19 million per annum on average over the four years of the program, or $75.4 million over Years 1-4. In $NPV_{5\%}$ terms the cost of the program would cost $66.8 million.

Offsetting these costs would be benefits from economies of scale in testing, lower costs of clinical trials recruitment, more efficient prescribing practices, and the attraction of new clinical

[40] MTPConnect, 2021, Australia's Clinical Trials Sector: Advancing innovative healthcare and powering economic growth, accessed at: https://www.mtpconnect.org.au/images/V7_MTPC11_Clinical%20trials%20report%20(web%20version).pdf, p4.

trials to Australia, which historically have involved a high private sector investment component, accounting for 70 per cent of the funding for new investigator led clinical trials.

In $NPV_{5\%}$ terms over the first four years of the program, economic benefits would be realised in the form of:

- **$3.4 million in molecular test cost efficiencies**
- **$0.9 to $1.1 million in lower costs of clinical trials recruitment, due to pre-screened pool of women nationally**
- **$36 million to $72.1 million in improved use of high-cost medicines**
- **$7.4 million to $9.8 million in leveraged private sector investment into Australia.**

In total, between $47.8 million and $86.5 million in benefits could be realised in $NPV_{5\%}$ terms – *before* accounting for improvements in health outcomes (quality adjusted life years (QALYs) gained). This suggests a benefit cost ratio for the proposed program of between 0.7 (low benefit realisation) to 1.3 (high benefits realisation) before potential improvements in survival are factored in.

To have a benefit cost ratio exceeding 1.0 for the low range of assumptions for economic benefits, an additional year of life would need to be gained for 381 women diagnosed over the four-year horizon of the program (5.1 per cent of all women expected to be diagnosed with ovarian cancer over the four-year program horizon), based on a willingness to pay of $50,000 per QALY. Given the available, albeit early data, which shows significant potential improvements in survival for High Grade Serous and Low Grade Serous sub-types alone, it would be expected that the Precision Medicine in Ovarian Cancer Program would deliver a net health and economic return to the Australian community measured in a BCR exceeding 1.0.

Most importantly, such an approach would enable Australia to achieve the target of greater than 50 per cent relative survival by 2027 for a previously low survival cancer. Investment in novel precision medicine approaches such as functional profiling will further progress therapeutic options for women without known targets today.

Figure 2.7: Measures of success over five years (Years 1-4)

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Chapter 3
Implementation & funding requirements

This chapter outlines implementation considerations and funding requirements for the Precision Medicine in Ovarian Cancer Research Program.

3.1 Proposed project structure and funding requirements

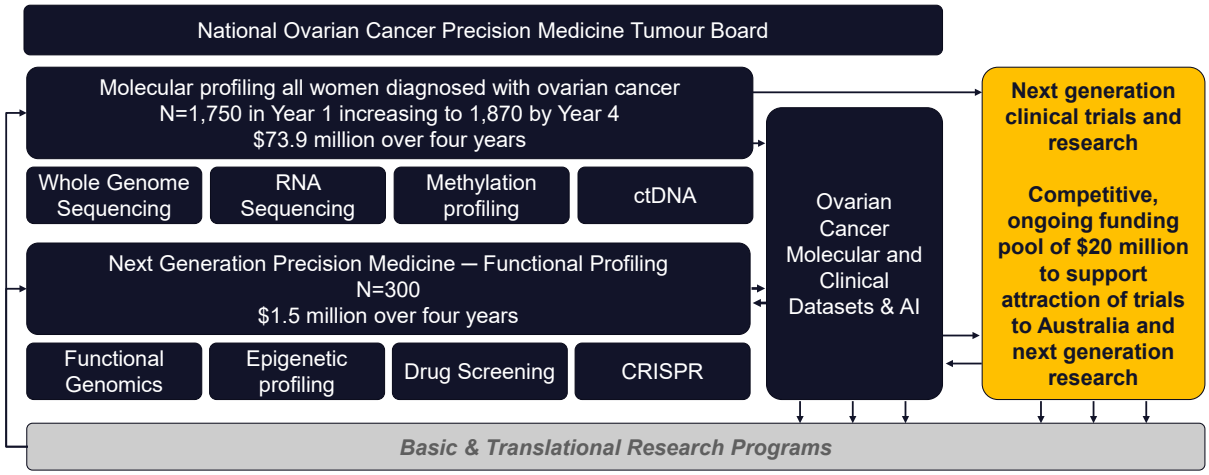
The ovarian cancer community is seeking funding for a national approach to Precision Medicine in Ovarian Cancer through molecular profiling for every woman diagnosed with ovarian cancers. A secondary goal is funding for experimental approaches to drug development where no molecular therapeutic target is identified.

Following the model established through the ZERO Childhood Cancer Medicine program, the Program would be delivered as a national collaborative, with testing centres established across Australia, reporting into a National Ovarian Cancer Precision Medicine Tumour Board.

Through the program, all women would undergo molecular profiling of tumours, with the results to be reviewed by the National Ovarian Cancer Precision Medicine Tumour Board and reported into a national ovarian cancer molecular and clinical dataset. Functional profiling would further be undertaken for a subset of women for whom therapeutic targets are not available to identify next generation biomarkers and therapeutic targets.

Funding for the Precision Medicine in Ovarian Cancer Research Program is sought for four years. This is comprised of $73.9 million for molecular profiling of every woman diagnosed with cancer over the next four years and $1.5 million in funding for next generation functional profiling of ovarian cancer patients. In total, $75.4 million ($66.8 million in $NPV_{5\%}$ terms) in funding is sought.

Figure 3.1: Proposed structure and funding requirements of the National Precision Medicine in Ovarian Cancer Research Program



In addition to the $75.4 million for the Precision Medicine in Ovarian Cancer Research Program, an annual, competitive funding round of $20 million should be established to provide sustained support for next generation clinical trials and research in ovarian cancer. Importantly, based on historical funding trends, this would be expected to leverage additional industry funding at a ratio of 2.3:1. This would see up to $80 million in additional industry funding for clinical trials potentially leveraged into Australia. Funding for the next generation of precision medicine trials would be accessed on a competitive basis.

3.2 Implementation considerations

To establish the Precision Medicine in Ovarian Cancer Program the following activities will need to be developed, following the model of the ZERO Childhood Cancer Medicine Program

- Establish a governance model for the program, including the development of a National Ovarian Cancer Precision Medicine Tumour Board
- Nominate national testing centres to undertake molecular profiling for the program to ensure quality and technical excellence in implementation as well as economies of scale
- Establish a competitive funding pool for clinical trials through MRFF to support access to next generation precision medicine therapies.

Attachment 1

Key assumptions and calculations

		2023	2024	2025	2026	Source, notes:	Average	Total	NPV5%
Incidence of ovarian cancer - no. of women	No. of women	1,794	1,832	1,871	1,911	AIHW, State of the Nation in Ovarian Cancer	1,852	7,409	
Current clinical practice in ovarian cancer									
Precision screening today	No. of women	210	210	210	210	INOVATe (100), Hudson (40), SFRCP (50), MoST (20)	210	840	
Clinical trial enrolment	No. of women	90	92	94	96	5% incidence, ANZGOG trials dat	93	370	
Cost of molecular profiling and functional drug screening today	$10,800	$2,268,000	$2,268,000	$2,268,000	$2,268,000	Average INOVATE, Precision Medicine, ASPIRATION	$2,268,000	$9,072,000	$8,042,216
Cost of panel screening for trials	$2,000	$179,409	$183,232	$187,136	$191,124	ANZGOG	$185,225	$740,901	$655,956
Cost to molecularly profile every woman based on current approach	$10,500	$18,837,911	$19,239,344	$19,649,330	$20,068,054	Average INOVATE, Precision Medicine, ASPIRATION	$19,448,660	$77,794,639	$68,875,387
Precision Medicine in Ovarian Cancer Program Research Program costs									
Cost of molecular profiling through national approach	$9,975	$17,896,016	$18,277,376	$18,666,864	$19,064,651	INOVATE, Hudson ZERO Program, ANZGOG	$18,476,227	$73,904,907	$65,431,618
Cost of next generation functional profiling	$5,000	$500,000	$500,000	$500,000		Hudson Patient Modelling Program for Zero Childhood Cancer Program	$500,000	$1,500,000	$1,361,624
Total cost of the program including functional profiling		$18,396,016	$18,777,376	$19,166,864	$19,064,651		$19,002,964	$75,404,907	$66,793,242
Total benefits of Precision Medicine in Ovarian Cancer Program Research Program									
Benefits of the program excluding potential QALY gains - low		$13,124,589	$13,361,696	$13,603,917	$13,851,361		$13,485,391	$53,941,563	$47,766,185
Benefits of the program excluding potential QALY gains - high		$23,744,950	$24,194,071	$24,652,840	$25,121,465		$24,428,332	$97,713,328	$86,522,517
Additional number of women gaining access to precision medicine approach		1,494	1,531	1,568	1,606		1,550	6,199	
Cost efficiencies compared to current approach	-5%	$941,896	$961,967	$982,467	$1,003,403	INOVATE, Hudson ZERO Program, ANZGOG	972,433	$3,889,732	$3,443,769
Efficiencies in patient selection									
Cost of treatment with PARP inhibitors in $A	$157,000	$161,710	$166,561	$171,558	$176,705	Wolford JE, 2020 and EviQ data for olaparib	169,134	$676,534	
Women potentially eligible for PARP inhibitor therapy		628	641	655	669	50% of HGSOC incidence, which is 70% of total ovarian cancer incidence	648	2,593	
Total cost to treat HGSOC with PARP inhibitors		$98,585,069	$100,685,898	$102,831,495	$105,022,814		101,781,319	$407,125,276	$360,447,860
Prevention of inappropriate prescribing - 10 per cent		$9,858,507	$10,068,590	$10,283,149	$10,502,281		10,178,132	$40,712,528	$36,044,786
Prevention of inappropriate prescribing - 20 per cent		$19,717,014	$20,137,180	$20,566,299	$21,004,563		20,356,264	$81,425,055	$72,089,572
Additional trials - private sector investment and jobs creation									
Increased number of trials - low	6	1.50	1.50	1.50	1.50	ANZGOG		6	
Increased number of trials - high	8	2.00	2.00	2.00	2.00	ANZGOG		8	
Value of additional trials - low	$2,000,000	$3,000,000	$3,000,000	$3,000,000	$3,000,000	ANZGOG, based on average for Phase I, Phase II		$12,000,000	$10,637,852
Value of additional trials - high	$2,000,000	$4,000,000	$4,000,000	$4,000,000	$4,000,000	ANZGOG, based on average for Phase I, Phase II		$16,000,000	$14,183,802
Leveraged private sector investment	70%	$2,092,437	$2,092,437	$2,092,437	$2,092,437			$8,369,748	$7,419,678
Leveraged private sector investment	70%	$2,789,916	$2,789,916	$2,789,916	$2,789,916			$11,159,664	$9,892,904
Additional jobs creation - low trials attraction (6 trials)	4.2	6	13	19	25	MTP Connect, 2021, 8000 employees per 1880 trials, Australia's clinical trials sector see https://		63	
Additional jobs creation - high trials attraction (8 trials)	4.2	8	17	25	34	MTP Connect, 2021		84	
Total number of trials in Australia - low estimate (12+6)	18	3.6	3.6	3.6	3.6				
Total number of trials in Australia - high estimate (15+8)	23	4.6	4.6	4.6	4.6				
Additional laboratory and research personnel	0.04	79	79	79	79	5.6 lab technicians per 100 women, with 5% efficiency gain - INOVATE	79	315	
Efficiencies in clinical trials recruitment									
Cost of clinical trials recruitment - status quo	$250,000	$257,500	$265,225	$273,182	$281,377	ANZGOG			
Cost of clinical trials recruitment - status quo, low estimate of trials		$927,000	$954,810	$983,454	$1,012,958			$3,878,222	$3,431,806
Cost of clinical trials recruitment - status quo, high estimate of trials		$1,184,500	$1,220,035	$1,256,636	$1,294,335			$4,955,506	$4,385,085
Cost of clinical trials recruitment - efficiences through pre-screened pool of women	$187,500	$193,125	$198,919	$204,886	$211,033	ANZGOG			
Cost of clinical trials recruitment - status quo, low estimate of trials		$695,250	$716,108	$737,591	$759,718			$2,908,667	$2,573,854
Cost of clinical trials recruitment - status quo, high estimate of trials		$888,375	$915,026	$942,477	$970,751			$3,716,630	$3,288,814
Savings - low		$231,750	$238,703	$245,864	$253,239			$969,556	$857,951
Savings - high		$296,125	$305,009	$314,159	$323,584			$1,238,877	$1,096,271

Attachment 2

Letters of endorsement

AUSTRALIAN GYNAECOLOGICAL CANCER FOUNDATION

3 January 2022

Support for a bid for a Precision medicine program for ovarian cancer

The Australian Gynaecological Cancer Foundation (AGCF) strongly supports the bid by the *Ovarian Cancer Research Foundation* and the *Australian and New Zealand Gynaecological Oncology Group* for funds to be made available for a National Precision Medicine in Ovarian Cancer Program. We believe that this is an opportune time to expect a cost-effective return from such an investment.

Ovarian cancer survival has languished around 40% since the 1980s, and it is only in the past decade that survival has slowly improved to 48%. This not surprising. Surgeons have been attempting to remove all gross disease in patients with advanced ovarian cancer for the past 20 years, so no further benefit can be expected from surgery. Chemotherapy has not changed for 30 years, with carboplatin and paclitaxel still the standard first-line approach. What has changed has been the recent introduction of targeted therapies, the development of which was facilitated by the completion of the Human Genome Project in 2003.

In relation to gynaecological cancer, the best known of the targeted therapies are drugs called PARP (poly adenosine diphosphate-ribose polymerase) inhibitors. They first entered clinical trials in 2013 and are effective against about 50% of patients with ovarian cancer. There are several other targeted therapies that have been developed, but these are effective against a much smaller cohort of patients. More such therapies will become available in the future.

When the correct drug is given to a patient who has a cancer with the corresponding genetic mutation, these drugs are very effective and significantly prolong good quality survival in patients with advanced and recurrent ovarian cancer. However the drugs are expensive, and access to them outside of major centres is currently limited.

Genetic profiling of an ovarian cancer is now relatively cheap and can be done in a matter of days. A national program to undertake molecular profiling and drug screening for every woman with ovarian cancer is a realistic aspiration. It would see rapid access to appropriate treatment for women from all parts of the country, increased clinical trial activity, and we believe it would see the 5-year survival for ovarian cancer increase to over 50% in the next 5 years. This would be consistent with the goals of the 2017 Senate Select Committee.

Kimberly Downes

Kimberly Downes

Acting CEO

Diane Langmack

Diane Langmack, OAM

Chair of the Board

24 January 2022

TO WHOM IT MAY CONCERN

Ovarian Cancer Australia is an independent national not-for-profit organisation, supporting women diagnosed with ovarian cancer. Our focus is to provide care and support for those affected by ovarian cancer; and represent them by leadingchange. Our vision is to *save lives and ensure no woman with ovarian cancer walks alone.*

Ovarian Cancer Australia united with the Australia New Zealand Gynaecological Oncology Group (ANZGOG) and Australian Society of Gynaecologic Oncologists (ASGO) to launch the Ovarian Cancer National Action Plan (NAP) 2020 – 2025.
Women diagnosed with ovarian cancer and their families are at the heart of thisplan.

The NAP sets out a roadmap to reduce the incidence, increase the survival rate and improve the quality of life of people diagnosed with ovarian cancer in Australia. It was developed over many months in partnership with women livingwith ovarian cancer and key organisations and leaders in ovarian cancer including researchers, policy makers and ovarian cancer health professionals.

The NAP's five core priorities are:

- Patient-and family-centred care.
- Diagnosis and treatment
- Early Detection
- Biology/aetiology
- Prevention.

The NAP highlights the importance of the development of Australia-wide genomic profiling for ovarian cancer as a critical step towards the development ofpersonalised medicine. In line with our NAP, Ovarian Cancer Australia wholeheartedly supports the proposal of the OCRF and ANZGOG for a Precision Medicine in Ovarian Cancer Research Program and a competitive funding pool of
$20 million for precision medicine trials to provide sustained support for next generation clinical trials in ovarian cancer research.

Understanding ovarian cancer as a diverse collection of diseases with differentcellular appearances and molecular characteristics, which simply share an anatomical location, is fundamental for furthering development of new diagnostic techniques and targeted treatments.

Timely access to emerging cancer therapies is a complex issue but one that affects women with ovarian cancer on a daily basis. The lives of women with

ovarian cancer depend on timely access to personalised treatment. Our recent consumer survey with women highlighted access to new treatments as one ofthe biggest priority areas for women living with ovarian cancer.

"Knowing the poor prognosis of surviving this lethal disease…one which gets little support or recognition as compared to breast cancer which has a far higher rateof survival, myself having experienced & living with both diseases, I feel Ovarian Cancer has robbed me from hope & joy for life knowing there are limited treatments & medication for this disease to provide me with quality of life or a future. Since being diagnosed with Ovarian Cancer I have been living with depression, fatigue, stomach bloating, bowel problems however the most troubling is the limitation of life expectancy this makes me sad."

We do hope that this initiative will be supported which has the potential togreatly improve outcomes for women with ovarian cancer.

Yours sincerely

Jane Hill

CEO

Ovarian Cancer Australia