A survey conducted by Ovarian Cancer Australia: A report summarising findings on a family history and genetic testing survey

Executive Summary

Introduction
Ovarian Cancer Australia (OCA) surveyed 183 women with ovarian cancer to explore their experiences with diagnosis, family history and genetic testing. Our survey captured a sample of women with ovarian cancer across all subtypes and stages. Currently, symptoms are important to diagnosis as there is no approved population screen for ovarian cancer. We wanted to better understand the nature of the symptoms felt by women and how this influenced their diagnosis. Family history is also important as up to 20% of ovarian cancer cases are thought to be inherited. Mutations in BRCA genes significantly increase a woman’s risk of developing ovarian cancer and current guidelines mean that most women with invasive ovarian cancer should be offered BRCA testing. We wanted to understand the extent to which these guidelines have been implemented and gain insight into women’s experiences and perspectives on genetic risk, counselling and testing, and to identify areas for improvement.

Diagnosis and Symptom Awareness
The study confirmed that ovarian cancer is not a “silent disease”. The majority of women responded that they experienced more than three identifiable symptoms, primarily abdominal bloating, pain and fatigue leading up to diagnosis. Symptom awareness is crucial to initiation of the diagnosis process:

- the majority of diagnoses (75%) were initiated by women’s concerns over their symptoms
- 93% of respondents experienced the common symptoms of ovarian cancer before diagnosis and of these, there was an average of 3.3x symptoms per respondent; only 3% of respondents felt no symptoms
- symptoms were felt across all stages of disease.

There is a need to improve women’s confidence in their abilities to know ovarian cancer, to recognise and act upon symptoms. It is vitally important to continue and expand a public awareness campaign.

Timely diagnosis is a critical area of need. Knowing ovarian cancer could improve time to diagnosis, reduce the number of GP visits and minimise hospital emergency presentations:

- 47% of diagnoses require two or more visits to the GP, 21% involved three or more visits, 18% were emergency room presentations
- higher numbers of GP visits correlated with lower satisfaction regarding care and outcomes.

Regardless of ovarian cancer subtype, timely diagnosis and an effective response to women presenting with symptoms is important to treat and reduce symptom burden.

Family History and Genetic Testing
Genetic testing and counselling is becoming increasingly more important for risk, diagnosis, prevention and treatment. Although most respondents reported numerous symptoms, only 25% of respondents were asked by their GP about family history before diagnosis. Women need to empower themselves with their family
history and discuss this with their GP. It is imperative that GPs take an in-depth family history and refer all presenting symptomatic women for genetic counselling and testing.

More women with ovarian cancer should be offered genetic testing and they should be offered earlier in the process, preferably at diagnosis. An increase in services is needed to meet the expected increase in demand. There is a case for offering genetic testing to all women diagnosed with ovarian cancer. The study found:

- The peak time for being offered and receiving genetic testing is after initial treatment, whereas sooner is preferred
- Not all women with ovarian cancer who are eligible are being offered testing – 36% gap
- There needs to be sufficient healthcare workforce and infrastructure to support the current guidelines for genetic testing and associated counselling
- More resources are required to enable faster testing for more women
- Testing cycles are too long (> two months for 52%) meaning that women may miss out on best treatment options.

Women are generally happy with testing and counselling though referral rates are low and the turnaround times are lengthy, suggesting more efficient approaches to testing and counselling are required. Only a minority of women declined genetic testing. Testing positive for BRCA mutations influenced treatment choices and enabled family members to consider their options such as genetic testing and preventative action (risk-reduction surgery). General community attitudes towards knowing family history, genetic testing and preventative surgery options were found to be positive.

More research is required on identifying genetic risk factors and developing tests that would identify at risk women and lead to improved prevention. There is a need to explore more efficient and cheaper ways of testing/counselling for greater accessibility. Greater accessibility to clinical trials is also required.

**Conclusion**
For every woman, best practice is timely diagnosis of ovarian cancer, efficient and professional counselling and testing for her benefit (treatment options) and for her family (prevention). Ovarian cancer is not a “silent disease”, there are symptoms. Awareness of these symptoms is important for women to seek medical help and importantly for GPs and health professionals to ensure timely diagnosis, initiation of treatment and best care to enable the best possible outcomes. Awareness of family history and the link between ovarian and breast cancer is important for women to make informed decisions in relation to risk management and prevention, and for GPs to identify women at risk earlier (prevention) or for when women present with symptoms (diagnosis and treatment).

Know the ovarian cancer symptoms:
- If more women are aware of symptoms, they will present to GPs earlier
- If more GPs are aware of symptoms, they can improve referrals to gynaecological oncologists.

Know the family history:
- If more women are aware of family history, they can provide better information for doctors to work with
- If more GPs are aware of family history, referrals to genetic counsellors can be made earlier, when they are needed.

*Ovarian Cancer Australia would like to thank the women who participated in this survey.*
Full Report

Introduction
Ovarian Cancer Australia launched this survey to better understand the experiences of women diagnosed with ovarian cancer. Our aim was to get a snapshot of women’s thoughts and experiences around diagnosis, family history and genetic testing.

The first section focused on experiences leading up to and including diagnosis. Our previous market research showed that many ovarian cancer symptoms are not well recognised by women in the general population and that nearly 50% of women were not aware that ovarian cancer was symptomatic.

We wanted to understand how important the known symptoms of ovarian cancer are to prompting a timely diagnosis and whether there is a need for increasing awareness in the general and medical community.

The second section explored women’s experiences in relation to family history, genetic testing and counselling. Up to 20% of ovarian cancers are thought to be hereditary and the most commonly known genetic risk factors are BRCA mutations, which significantly increases the lifetime risk of a woman developing ovarian cancer compared to the general population. Research identifying the high prevalence of BRCA mutations in women with ovarian cancer prompted changes to guidelines that now recommend that women with invasive ovarian cancer (> grade 2, or with a family history) should be offered BRCA testing. Information on BRCA status provides important information on prognosis, treatment options and for family members, who may also want to be tested so they can take preventative action if needed. Recent research has shown that eligible women want to be tested as soon as possible\(^1\).

We wanted to know if all eligible women were being offered testing, when they were offered the testing, who offered it, their experiences with counselling and how the results affected them.

This information is important to help us in our efforts in raising awareness of the symptoms of ovarian cancer and of the link between family history and ovarian cancer, and for understanding how referral pathways and guidelines for genetic testing might be improved.

Demographics
The survey was conducted over two weeks (April 2\(^{nd}\) - 17\(^{th}\) 2015) using Survey Monkey. We received a total of 183 responses from women diagnosed with ovarian cancer. 86% of the respondents were over 40, with 62% being over 50, which is typical of the age range for women with ovarian cancer (Figure 1A). Respondents covered the range of ovarian cancer types, although 17% did not know their type (Figure 1B). Approximately 50% of respondents were diagnosed since 2012 (Figure 1C). Nearly one quarter were early stage (Stage I), the majority being late stage (56%, Stage III/IV) (Figure 1D). Only 8% did not know the stage of disease. Importantly, 84% of high grade serous ovarian cancers were captured at a late stage, which is consistent with previous reports that it is very difficult to diagnose this aggressive subtype at an early stage.

Section 1: Know the symptoms of ovarian cancer

Our survey showed that the majority of diagnoses (75%) were initiated through symptom awareness; that is, visits to GPs were usually initiated through women’s concerns over their own symptoms. Only 3% of cases were picked up during a routine health check and 21% of cases were picked up through examinations or procedures for other purposes. **Symptom awareness is crucial to initiating diagnosis.**

Multiple visits to the GP were generally required before ovarian cancer was considered, with 47% of diagnoses requiring two or more visits and 21% requiring three or more visits (Figure 2). A significant proportion (18%) of respondents presented to emergency room with severe symptoms, with one third of these having previously made three or more GP visits over symptom concerns.

Figure 2: Frequency of visits to GP and presentations to emergency room

Nearly all respondents (93%) experienced the known symptoms of ovarian cancer, with an average of 3.3 symptoms per respondent. The most frequently felt symptoms were bloating, tiredness or fatigue, pain in
the gut or pelvis, urinary urgency and feeling full after only eating a small amount (Figure 3). Women commented that their worst symptoms were bloating and discomfort, then equally pain, bowel and urinary symptoms. 17% of respondents experienced other symptoms which related to menses (excessive bleeding and pain during menstruation, cessation of cycle, bleeding mid-cycle), nausea and breathlessness (due to ascites or lung problems). Only 7% of respondents experienced none of the common symptoms and 3% no symptoms at all.

**Figure 3: % of respondents experiencing symptoms**

Although there is a trend for a greater number of symptoms at a later stage, symptoms were experienced over all stages (Figure 4). There was also no significant differences in the number of symptoms across ovarian cancer subtypes.

The symptoms reported by women diagnosed with ovarian cancer reinforces our message for women to be aware of their body and to seek medical advice if there are unusual and persistent symptoms. This is important in the light of recent findings that only 47% of the general population are aware that ovarian cancer is symptomatic².

There is a need to improve women’s confidence in their abilities to recognise and act upon ovarian cancer symptoms and it is important to continue and expand our public awareness campaign.

**Figure 4: Number of symptoms by stage of ovarian cancer**

Our data indicated that higher numbers of GP visits correlated with lower satisfaction levels regarding care and outcomes and there is a need to reduce the number of GP visits and emergency room presentations to diagnosis. Other comments from respondents indicated a high level of frustration at long timeframes leading to diagnosis despite seeking regular medical assistance. A number of women reported that their symptoms were not initially recognised as relating to ovarian cancer and seeking a second opinion was a common theme.

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² Ovarian Cancer Australia survey, conducted by Wallis Social and Market Research, Jan, 2015
“I visited my GP more than 3 times but he kept on insisting that I had IBS. Went to another GP who discovered that I had an enlarged uterus. Ovarian cancer was never considered as a possibility”

“I had been regularly for 12 months with various symptoms which were put down to menopause.”

“I saw one doctor 4 times who just kept telling me to eat more fibre, not once did he examine me”

“GPs need to be trained in identifying the symptoms of ovarian cancer”

GPs who were aware and proactive enabled a fast diagnosis and short time to treatment.

“From me going to the doctors and being operated on was only 6 days. I was informed 3 days later that I had Stage I ovarian cancer

“I was very fortunate that my GP acted very quickly towards diagnosis and testing and counselling was carried out very efficiently and professionally. I do hope that one day Ovarian Cancer can be diagnosed in earlier stages.”

OCA aims to work with women, GPs and health professionals to ensure that a timely diagnosis of ovarian cancer is not just a matter of good fortune.

Research suggests that outcomes are better for ovarian cancer patients if they are referred to a specialist in gynaecological oncology. 56% respondents were referred to a gynaecological oncologist, while 41% were referred to a gynaecologist or obstetrician. 78% of respondents underwent a series of tests before being referred to a specialist. The most common tests were CT scans, Trans-Vaginal Ultrasounds and blood tests (often CA-125), which indicates that ovarian cancer might have been suspected in some of these cases. Women were also referred to a diverse range of specialists, depending on the most apparent presenting symptom. The comments detailed suggest that the referral pathways are potentially not clear for GPs. The specialists included gastro-enterologists, colorectal surgeons, hepatologists and respiratory physicians, however, the majority were referred to a gynaecologist first.

The pathway to diagnosis could be improved through increasing GP awareness of symptoms and appropriate referral pathways (supporting the need for a GP awareness/education campaign)

Section 2: Know family history and its relation to genetic testing

Family history
There is a need to increase awareness of the link between family history and the risk of developing ovarian and breast cancer in the general and medical communities.

44% of respondents knew of the general link between family history and the risk of breast and/or ovarian cancer before diagnosis, but they did not necessarily know of their own history. 23% of respondents had a
primary relative with breast cancer and 10% had a family history of ovarian cancer. Overall, 31% of respondents were at a higher risk than the general population through having a known family history (Figure 5). A number of women highlighted difficulties in finding out about their family history, whereby this information was either not known or women’s business was not openly discussed. Accessible registers may improve this in the future but the need for women to better understand their own family history is important for proactive risk assessment.

“My one regret is that I should have been more aware that there was a link between breast and ovarian cancer. I always had my annual mammogram test (my mother had breast cancer in her early 50’s). On reflection, I would have insisted on an annual ultrasound and CA125 marker test as well. Perhaps that is something that could be advertised more in the media.”

There was also an identified need for greater GP awareness. Only 25% of the respondents were asked about family history by their GP before their diagnosis, and 10% were never asked by their GP or specialist. Those who were asked, were asked an average of 1.8 times about family history from before diagnosis to recurrence with the peak time for being asked being after diagnosis but before treatment. The specialist, rather than the GP, was more likely to enquire about family history (nearly 2x more likely).

Based on these results, we believe that women presenting to their GP with symptoms of ovarian cancer should be asked about their family history so that their risk can be better assessed. In general, patients are increasingly asking their GP about a family history of cancer and its implications for their health and/or cancer treatment. It is important that GPs can evaluate a patient’s risk of a hereditary cancer accurately and refer on or monitor as appropriate. Research conducted in UK indicated that just 10% of GPs were aware that BRCA mutations can be inherited from the father’s side as well as the mother’s. Education on symptoms and risk factors as well as increased implementation of decision support tools are already available for GPs (Cancer Australia) that may increase their confidence in identifying women with potential ovarian cancer symptoms and those at risk.

Figure 5: the % of respondents having a family history

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2 Target Ovarian Cancer; [http://www.targetovariancancer.org.uk/](http://www.targetovariancancer.org.uk/)

Genetic testing

Introduction
BRCA mutations can be identified through genetic testing which provides key information about the risk of an individual developing ovarian or breast cancer and helps in prevention strategies, early detection and treatment choices in ovarian and breast cancer for those at risk. In addition, identification of a BRCA mutation allows for counselling and the testing of other family members with the potential to intervene with risk reduction strategies. Negative results can reduce anxiety and allow for more informed counselling of women from high-risk families.

Referrals and their timing
Genetic testing is least likely to be recommended by a GP (only 10%) and most likely to be offered by a specialist, such as a gynaecological oncologist (40%). In fact, self-referral (22%) is more common than referral by a GP. Women are most likely to be offered and receive testing after their initial treatment (Table I). Recent research indicates that women with ovarian cancer would prefer to be tested at initial diagnosis – the sooner the better – for the benefit of family members and themselves, to inform treatment and to understand their condition. Genetic testing should be offered earlier to women with ovarian cancer.

Table I: summary of results showing the stage at which women were offered genetic testing and when it was conducted

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Offered</th>
<th>Received</th>
</tr>
</thead>
<tbody>
<tr>
<td>How many?</td>
<td>54% (83/155)</td>
<td>46% (71/155)</td>
</tr>
<tr>
<td>After diagnosis</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>Before treatment</td>
<td>16%</td>
<td>4%</td>
</tr>
<tr>
<td>During treatment</td>
<td>22%</td>
<td>21%</td>
</tr>
<tr>
<td>After initial treatment</td>
<td>45%</td>
<td>51%</td>
</tr>
<tr>
<td>After recurrence</td>
<td>13%</td>
<td>17%</td>
</tr>
</tbody>
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In Australia, consideration of who should receive genetic testing for BRCA mutations depends on several factors including a personal or family history of breast and/or ovarian cancer, ancestry and whether a mutation has been identified in a relative. Guidelines have been developed that provide recommendations on who should be offered BRCA testing. These guidelines were updated in 2012 to expand the number of women with ovarian cancer eligible for testing, based on research that demonstrated more women with ovarian cancer had BRCA mutations than previously thought.

Our survey revealed that not enough women were being offered genetic testing for BRCA mutations. While 83/155 respondents were offered genetic testing or referred themselves, 14 of these were outside of eviQ guidelines. However, according to the information provided by respondents on type and stage of ovarian cancer and their family history, 109 women should have been offered genetic testing, whereas only 69 of these women were – a gap of 36% (Figure 6). Interestingly, there was no detectable increase in the percentage of women diagnosed with ovarian cancer being offered BRCA testing since 2012, when...

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7 EviQ: [www.eviq.org.au](http://www.eviq.org.au)
guidelines were updated. This may indicate a lag time at the stage of the offer, nevertheless, more women should be offered BRCA testing earlier.

**Turnaround times**

Turnaround times for genetic counselling and testing were in ranges. 32% of respondents waited 2-4 weeks for a genetic counselling appointment, 45% waited four weeks or more and 20% greater than two months. The turnaround time for receiving test results was generally greater than one month (~67%), with a significant proportion having to wait more than two months (30%). The total turnaround time averaged 8-13 weeks.

Based on the responses, the turnaround time for counselling and testing is greater than, or likely to be greater than eight weeks for 52% of respondents (37% definitely, 15% likely). Only 26% definitely occurred within eight weeks and 22% possibly within eight weeks (Figure 7). The timeframes were shorter in New South Wales and Victoria compared to Queensland.
Technology advances such as Next-Generation Sequencing may facilitate more rapid testing but the fact that some cycles can be less than one month indicates that the barriers to shortening testing cycles are not technology but resource issues.

There is a need to increase the efficiency of testing. Eligibility for maintenance therapy with PARP inhibitors (e.g. olaparib), requires knowledge of BRCA status within eight weeks of completing a second round of treatment. If testing is offered too late in the treatment cycle and testing times are too long, some women may miss out. **Turnaround times must be tightened through increased genetic counselling and diagnostic testing services.**

**Genetic counselling**

All women referred to genetic testing should also be offered genetic counselling to receive information, support and advice to help inform their choices about proceeding with testing, informing family members and other important issues. Also, counselling after testing is important for understanding the implications of results for family members, who may also benefit from testing and for informing treatment options.

We found that only 39% of women who were tested received genetic counselling before and after testing. 22% of respondents received no counselling before or after testing and 33% received pre-test counselling only.

Overall, the level of satisfaction with counselling was high. In relation to pre-test counselling, 94% of respondents felt comfortable or reasonably comfortable with having the BRCA test. On receiving test results, 92% of respondents felt satisfied with counselling received and felt adequately supported (78%) and informed (80%). In general, counselling through familial cancer centres and with geneticists was considered worthwhile and positive. For those that received counselling, the majority were satisfied that they received sufficient information to make an informed decision about having the test, that they understood the information and knew who to contact for further information.

In the majority of cases, the specialist (65%) rather than the GP (35%) discussed results with the patient. It was also noted that GPs do not have the time, expertise or information to effectively manage counselling or information around testing, supporting the need for specialised counselling around genetic testing.

“**They (Drs) do not have time for detailed counselling.”**

**Counselling services are high quality, but more people should have received counselling before and after testing**

**Effects of BRCA testing**

Of the 83 women who were tested, 25% were positive for BRCA mutations. Nearly half (44%) had a family history of breast or ovarian cancer, or other hereditary risks.

Women testing positive tended to discuss the results with family members. Family members of women who tested positive for BRCA mutations also underwent counselling (67%) and received genetic testing (63%). Some family members who also tested positive underwent preventative surgery.

“**Whilst it was too late for me, and it was hard to tell family members, I do believe it was the best and has given them the opportunity to make informed decisions about their**
health and future. My sister and cousin (both BRCA1) have both had their ovaries and tubes removed.”

“…both parents had BRCA mutations and ours was inherited from our father.”

44% also thought that having a BRCA mutation influenced their treatment choices. Testing negative also helped.

“I was relieved not to have the BRCA mutations as I have 3 sisters, one of whom is my identical twin. I was grateful that they know they do not have an increased genetic risk from the general population.”

Testing positive for BRCA enabled family members to get tested and take preventative action and influenced treatment choices.

Future directions in genetic testing
Exploring ways of enabling greater access to BRCA testing will be important for preventative strategies. Some experts are recommending that BRCA testing be available for all women over 30 based on the knowledge that a significant proportion of women with BRCA mutations do not have a family history. Indeed our survey found that 56% of the women with ovarian cancer who were found to have BRCA mutations did not appear to have a family history, which is broadly consistent with previous observations. So a broader BRCA screening strategy could help capture those cases. On the other hand, other key opinion leaders are concerned that our current health systems are not ready for this and that cost and the lifelong surveillance required would present significant capacity issues. Initiatives that are developing more efficient processes for BRCA testing include the Ovarian Cancer Dream Team in the USA developing a web-based approach to genetic testing and counselling and the Mainstreaming Cancer Genetics program in the UK which has reported a four-fold increase in throughput at one-quarter the cost of testing with traditional sequencing.

There needs to be sufficient healthcare workforce and infrastructure to support the current guidelines for genetic testing and associated counselling. It is also important to explore options for improving the efficiency and reducing costs of genetic testing and counselling for broader screening.

Nearly half (48%) of women who tested negative for BRCA mutations had a family history. This finding supports the need for more research into identifying and validating other genetic risk factors, and developing them into new tests or broader test panels. 89% of respondents thought that research into the identification of new genetic risk factors and their development into genetic tests should be a priority.

11 http://health.clevelandclinic.org/2015/03/should-all-women-be-screened-for-brca1-and-brca2/
13 Future of Genomic Medicine (FoGM) VII. March 6, 2015
"I strongly believe that there are other genetic links to ovarian cancer that are yet to be identified."

**Barriers to testing**

While most respondents who were offered testing proceeded, a significant minority declined (13/83, 16%). The main reasons for declining were that some women felt that they had enough to deal with at the time (42%), they wanted to complete treatment first (31%) or that there was no known family history (38%). This latter reason raises an important issue as an estimated 44% of women with aggressive ovarian cancer that are germline BRCA positive have no reported family history. Others were concerned with how the test might affect family members (31%).

"I have 2 daughters and am not sure what to say to them re genetic testing."

The possible effects of life insurance or private health insurance were not considered to be significant barriers to testing. Cost did not deter many women from actually having the test, however, it was still a consideration for 33% of women who had the test. Despite this, only 2% paid fully for the counselling and testing, while 82% paid nothing. Medicare contributed to the cost of testing in 53% of cases and private health in only 9%. We assume from this that familial cancer centres are covering the bulk of testing costs. Given the implications of BRCA testing for treatment and the potential for wider adoption for prevention, there is a case for BRCA testing to be covered by the Medicare Benefits Schedule to ensure equity of access for all eligible women regardless of their geographical location.

**Clinical trials and new treatments**

Clinical trials offer opportunities to access new targeted therapies and are known to improve outcomes. 68% of respondents were either never offered the opportunity to participate in a clinical trial, or were interested but this was never discussed with them. 12% of respondents who were offered to participate in a clinical trial were not eligible, while 18% of respondents have participated or are participating in clinical trials. The fact numbers of women on clinical trials is higher than some overseas counterparts is a testament to the high impact of Australian clinical research through the existence of a strong clinical network organisation (ANZGOG). Nevertheless, it is important to further increase access to new therapeutics under clinical trials. More clinical trials should be made available to Australian women with ovarian cancer.

**New Treatments**

In ovarian cancer, BRCA mutations have been associated with improved survival and increased responsiveness to chemotherapy treatment and to new targeted treatments such as PARP inhibitors. In Dec 2014, the BRCA mutation genetic test was approved by the US Food and Drug Administration for use as a companion diagnostic for olaparib (Lynparza®), a PARP inhibitor concurrently approved for treating ovarian cancer. Olaparib is also approved in Europe. 31% of respondents were aware of treatments under development targeting BRCA mutations. For those women that had previously declined or were unsure about BRCA testing, knowledge about potential new treatments under development for BRCA mutations may encourage further discussion about testing.

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15 Australia and New Zealand Gynaecological Oncology Group
treatment options based on the BRCA test would influence their decision in the majority of cases (93%). Respondents demonstrated support for more research on new treatments.

“Not enough money going into research. Not good enough to know that treatments have not much improved since 1970’s”

General community
In January 2015, Ovarian Cancer Australia commissioned market research\textsuperscript{16} across the general population (643 respondents) relating to genetic testing and ovarian cancer. 78.6% of respondents said they would have a genetic test if there was a family history of breast or ovarian cancer and if a family member tested positive for a BRCA mutation, 89.2% would want to know about it. If a respondent tested positive for BRCA, 87.4% would want other family members to know. The majority (82.2%) of the 415 female respondents would consider preventative surgery which involves removal of the ovaries and fallopian tubes in the event of testing positive for a BRCA mutation. This increased to 91.5% for women over 50. People in the general community are positively inclined towards knowing their family history, genetic testing and preventative surgery options.

\textsuperscript{16} Ovarian Cancer Australia survey, conducted by Wallis Social and Market Research, Jan 2015