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Webinar: Can we improve outcomes for women with ovarian cancer? Early results from the OPAL study

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Presenters: Professor Penny Webb, Associate Professor Vanessa Beesley

ANNA GORDON:

Good morning, everyone and welcome to Cancer Council Queensland's Health Professional Webinar. Can we improve outcomes for women with ovarian cancer? Early results from the OPAL study. My name is Anna Gordon, and I'll be your host this morning. I'd like to welcome all our participants this morning, in particular those of you who have dialled in from regional, rural and remote areas. Before we begin, I'd like to acknowledge the Traditional Owners of the land on which we work and live, and also, I'd like to pay my respect to Elders, past, present and emerging. This webinar will run for about an hour and we actually have two presenters today not one, Professor Penny Webb will be joined by Associate Professor Vanessa Beesley today. And our presenters will speak for about 45 minutes or so and we'll have some time for questions at the end, but please feel free to ask questions at any time during the webinar by typing them in your chat box. The session will be recorded and shortly, will be also made available on our website. So, if you have any colleagues who can't make it or if you want to re-watch it, you'll be able to do that.

Now I'd like to introduce our presenters, both Professor Penny Webb and Associate Professor Vanessa Beesley work at QIMR Berghofer Medical Research Institute, and Professor Webb is a cancer epidemiologist, specialising in women's cancers. She heads gynaecological cancers group at the QIMR Berghofer Institute and leads studies that attempt to identify factors that influence risk of and survival following ovarian and endometrial cancers. In 2012, Professor Webb established Ovarian Cancer Prognosis and Lifestyle study, to follow more than 900 women with ovarian cancer to assess whether potentially modifiable lifestyle factors might influence their quality of life and survival, and we'll hear more about this study today, and Associate Professor Beesley is a behavioural scientist, and she has dedicated over a decade working in the field of patient-reported outcomes in cancer research and is passionate about person-centred care based on these outcomes. She has published over 50 scientific articles and has had multiple contracts to provide recommendations to government about improving cancer care, and is also an executive member of the Queensland Collaborative for Cancer Survivorship. So, both our presenters this morning are really experienced and we're very excited to have you both as guests this morning. So now, I'll hand it over to Penny Webb, who will start our presentation this morning.

PENNY WEBB:
Thank you Anna, thank you for that introduction, and it's a pleasure for both of us to be here talking to you today , to give out some of the work that we've been doing for the last, I guess about seven years now, looking at whether we can improve outcomes for women with ovarian cancer. And just before we start, I'd like to reiterate Anna's comment, that we'll be very happy to take questions at the end of the presentation but if anything comes up while we're talking, we're very happy for you to send questions as we're going along and we'll do our best to answer them if we can.

So, just to start by giving you an overview of what we'll be covering today, I'll start out with telling you a bit, about why we're talking about ovarian cancer, why this is an area we're interested in. I'll tell you a bit about the OPAL study that Anna mentioned.

And then we'll get into discussing some of the early results from that study. I'll start out by talking a little bit about some of the issues faced by women when they're going through treatments, I'll then hand over to Vanessa, who's going to talk a bit about recovery, and particularly answering the question that women often want to know and when will I feel normal again. And then finally, we'll talk a bit about the new normal and what happens after women have finished their treatments. And trying to answer really the primary question that we set the study up for, what should I do now? And Vanessa will talk a bit about some of the work, we've been doing looking at coping styles, and mental health, and then she'll hand back to me, to talk about some of the stuff we've been doing, looking at whether a woman's lifestyle might influence her outcomes from that point onwards.

So first up, why are we interested in ovarian cancer in the first place? And this is an interesting graph, these are the latest data that I downloaded from the International... International Agency for Research on Cancer, sorry, mental blank there. And it's interesting how this figure has changed over time, this shows the numbers of new cases of cancer diagnosed in Australian women estimated for 2018. It's quite a busy slide, but you can see over on the right I marked with two red stars. Ovarian cancer is currently the 11th most common cancer in Australian women, accounts for about 2%, of all new cases of cancer diagnosed in women in Australia. And it's interesting because when I downloaded the slide a few years back, ovary actually was quite a bit higher up than this somewhere around six, seventh, eighth. So, it's actually been dropping down in recent years. So, it's only the 11th most common cancer in terms of new cases, but if we move to the next slide, and we look at where it ranks in terms of the number of deaths, we can see here, it's moved up to fifth place, and accounts of almost 5% of deaths in women with cancer in Australia. So, it's a relatively low survival cancer, only about 45% of women who are diagnosed with ovarian cancer will live for more than five years and this is really why we're interested in it because it is affecting so many women and causing so many deaths.

The good news in terms of ovarian cancer, if we look over time, is that the rates when we allow for age are falling, this graph here shows the trend of incidence rates from 1982 onwards, the last five or six points projecting out 2021. And the predictions are that the incidence rates, standardised for age will continue to fall. And the same is true for mortality. We can see we have more data here, but the rates have been consistently falling over time. But the flip side of that is ovarian cancer is a disease primarily of older women and we know that women are living longer now and also the population in Australia is increasing. And the result is that although these age-standardized rates are falling, which looks like a good thing, if we look at the numbers of cases diagnosed each year, they're increasing. The light blue line at the top shows the numbers of new cancers diagnosed each year, the darker blue line at the bottom shows the numbers of deaths occurring each year. And we can see that, although the rates are falling, the actual numbers of women affected are increasing quite dramatically.

So, it's an increasing problem and this is why we're particularly interested in it. The other reason that we're looking particularly to ovarian cancer and survival is this slide show some results from work that colleagues and I were involved with a few years back, where we tried to estimate the proportion of cases of cancer diagnosed in Australia that could be attributed to modifiable risk factors, and therefore, cases that could potentially be prevented, if we could change those risk factors. And what this graph shows at the top we have cancers like, cervical cancer, where if we could get rid of human papilloma virus infection, we could potentially prevent 100% of cervical cancers. We have lung cancer, where close to 80% of cases can be attributed to smoking. So again, if we could reduce smoking, we could prevent lung cancer. Similarly, high percentages for liver cancer, which is very strongly associated with things like alcohol consumption, melanoma, obviously associated with sun exposure. But when we look at ovarian cancer, it's way down towards the bottom of the graph and really, despite everything we know at the moment, potentially modifiable factors

really only account for about less than 6% of cases. So at the moment, there's not really a lot we can do to try to prevent ovarian cancer from occurring. So, therefore, our interest in, if it is occurring, what can we do to help women who are affected and try and improve their outcomes.

So, this is what really led to the OPAL study and the logo for the study has somehow disappeared from the slide, but blank white space at the top should have the OPAL study logo in it. We established the study in 2012 and the main reason for this was that, we've been doing a study a number of years earlier, and women in that study with ovarian cancer would ring me up and ask, what should I do? I've seen on the Internet, that sugar causes cancer, should I stop eating sugar? Or I've seen on the Internet that soy foods contain types of oestrogen, should I stop eating soy foods? And if so, how do I do that? Because just about everything has soy protein in it. And there are a lot of other websites in particular, that recommend that people with cancer do, do different things from eating enormous amounts of fruits and vegetables, from living on fruit juices, vegetable juices. And so I think women out there and not just those with ovarian cancer are left feeling, what should I really do, in order to help have the best possible outcome?

When I started looking at the evidence, there was really at that time in particular, very little real hard evidence as to what might make a difference. And so we decided to set up the OPAL study, which stands for Ovarian Cancer Prognosis and Lifestyle study, really to answer these questions that women were asking. Particularly what can, what can I do now? What should I do now? But also the question that women I think often ask, ask when they finish treatments is, when will I feel normal again? So, this was really a study prompted by these questions from women. And the main aims of the study, the primary aim really was to identify whether potentially modifiable aspects of lifestyle and by lifestyle, I mean, these things listed in blue at the bottom, things like diet, use of dietary supplements, smoking, alcohol, physical activity, sedentary behaviour, and use of common medications, whether any of these things could

actually improve women's quality of life and long term survival. The primary aim was really to look at the effects of lifestyle after women finished treatments and outcomes. But we were also interested in looking at whether, what women actually did while they were going through treatment might affect the levels of side effects, they experience, their physical and emotional well being, and then ultimately, whether they were able to complete their treatment.

As you will see in a few slides, that's a big issue in this cohort. In terms of the design of the study, the goal was to recruit and follow about 1000 women who'd been newly diagnosed with ovarian cancer, we almost achieved that, that goal, we recruited the women as soon as possible after diagnosis and these were women diagnosed from all across Australia, from every state and territory, recruited by a team of nurses spread around the country. When we recruited them into the study, we asked them to complete a baseline questionnaire, to tell us about what they'd done before they were diagnosed. We also asked if they'd provide a blood sample, so we could look at genetic aspects of health. We then asked them to fill out a follow up questionnaire, every three months for the first year, and then every year after that up to four years. And we also collected a lot of clinical data from their medical records, about their treatments and how they responded to treatments and their outcomes.

So just generally, as I said, the data we collected the aspects of lifestyle, were things like diet, supplement use, smoking, alcohol, we also asked them a lot about their quality of life, how they were feeling at that time, their well-being, anxiety, depression, fatigue, coping, insomnia, and Vanessa is going to talk about some of the results for these aspects. And then as I mentioned a lot of information about their treatment, their side effects, their response to treatment, et cetera. So just to summarise, we ended up with a cohort of about 960 women, we actually recruited slightly more than that, but a number of had to be excluded, because it turned out that the cancer they had wasn't actually, didn't actually start in the ovary. Their mean age was about 60 years, they were diagnosed between 2012 and 2015. About 70% of

them had high grade serous cancers, so that's the most common type of ovarian cancer, it's also of the most aggressive type but interestingly, the type that responds best to treatments. And about 70% of them had advanced cancer, so stage three or four diagnosis. And this is typical of women with ovarian cancer, and really explains why, on average, the survival rates are not very good.

In terms of our progress, we've just finished the four year of follow up for the women who were recruited last into the study, about 900 of the women had completed at least one of the follow-up questionnaires with an average of five questionnaires per woman, which I think is a remarkable achievement. About 400 of the women completed at least six of the maximum seven questionnaires. So, we have a huge amount of data for these women covering a period now for about four years. The less good news is that almost two thirds of the women have already experienced a progression from their disease, and almost half of them have died. And I think this has been quite difficult for the nurses working on the study to deal with, they've established quite strong relationships through talking to these women regularly and the high mortality rates among the group make it a difficult area to work in. So on average, the women that survival at three years is about 73%, and five years is just over 50%. Again, emphasising why we try to, need to try to do something to improve this.

So, that's just an outline of the study itself and the sort of data we've collected. And now we'll just, we'll get into some of the first results from the study and just to say now that, it seems like it's studies been going for a long time, we started in 2012 but this sort of work takes a long time to do, it took us three years to recruit the women and then we needed to follow them for at least four years, before we really had enough data to be able to analyse. So, I said it's a long term project. But first I'll just talk a little bit about getting through treatments because if you're not familiar with the treatment for ovarian cancer, most women will have quite aggressive surgery and then the majority will also have chemotherapy, combination chemotherapy with

carboplatin and paclitaxel. Both drugs that are known to cause a range of side effects and this then has an impact on how well they are, able to complete their treatments. And this work is still preliminary, the papers will hopefully be submitted shortly looking at some of this.

But just very briefly, this was some work done by Medical Oncologist down in Melbourne. Among 634 of the women who were treated with, what we would call standard chemotherapy, six cycles of carboplatin and paclitaxel, we looked at the numbers that had side effects at a moderate or severe levels. So, this is ignoring mild side effects, but looking at side effects that might be serious enough, that they would actually influence treatments. And you can see from the numbers here that they're very common, about 40% of the women had haematological side effects. So, that's things like anaemia or neutropenia at a moderate or severe level, 28% had neurological side effects, so this is neuropathy, often due to the paclitaxel. 40% reported moderate or severe levels of a range of other side effects and altogether 70% of the women, almost three quarters had at least one side effect, that was at a moderate or severe level. And the impact of that then is seen in terms of how well they're able to complete their treatment. So, from the carboplatin which is the main drug, 40%, so two out of five women receive less than 85% of what's called the RDI, which is the relative dose intensity. If you're not from familiar with that term, it's a measure that covers both the dose of treatments, and also the duration as to whether it's given at the appropriate times. So, if a woman has to do half dose of her drugs, or if she has to have a delay in any of the cycles, that will reduce the relative dose intensity. And 85% is generally considered a level where you want women to be over that level for successful treatment. And we can see here that among this cohort, who because they took part in the study are already probably a bit more healthy than women with ovarian cancer in general, even among this group 40% receive less than 0.85 of the relative dose of carboplatin, more than half receive less than 85% of their paclitaxel dose. And overall, this means that around 40% had to have dose reductions,

of at least 15% or a delay of at least a week in their treatment. And we know from previous work that, if women can't complete their treatment, then this potentially will have an adverse effect on their outcome.

So, one of the things we're really interested in doing now, is trying to look at what women are doing during their treatment to see if there is anything that might help them get through the treatment without experiencing these severe levels of side effects. And we're also interested to try and identify whether we can predict the women who will have severe side effects, so that these can potentially be managed a bit more prospectively to try and control them ahead of time. We don't have any definitive results yet, the thing that is looking most optimistic is physical activity, and that women who are active seem to potentially do a bit better and get through treatment a bit better than those who don't. This is something that's also been seen in other cancer types and we'll come back to physical activity again later. And just of note, there is actually a clinical trial going on at the moment that is looking at prescribing physical activity, if you like to women having treatment for ovarian cancer to see if this, this might help. But the results from that are still a while off. But I'll hand over to Vanessa now, who will talk a bit more about the next stage of the women's journey, once they've finished treatment and the recovery stage.

VANESSA BEESLEY:
Hello, everyone. It's a pleasure to share with you some of the results today that I've been working on from the OPAL study. So, the first piece of work that I'll be focusing on is this question that Penny mentioned, when will I feel normal again after primary treatment for ovarian cancer? So, this is work currently under review with Gynaecological Oncology, so it is hot off the press. And the main aims of this work were to determine the proportions of women who had high physical symptoms or emotional symptoms at the end of treatment and to determine even when they return to normal. Secondly, to identify the groups of women with distinct trajectories

of symptoms after chemotherapy. And thirdly, to identify the groups of women who were at risk of persistent symptoms or delayed recovery.

As Penny mentioned, we measured a number of patient-reported outcomes in this study, and you can see those listed there on the slide. So, we looked at the end of treatment and each of those different outcomes had an abnormal range that comes as a standard score with these instruments. So, I particularly wanted to focus on the third column in this slide, and we can see that about one in five women at the end of treatment are experiencing subclinical or clinical anxiety, or depression, about 13% have clinical insomnia, just over half of the women had clinical levels of fatigue at the end of treatment. And just under had quality of life that we would consider is lower than what we expect to see in the general population. And that's mainly driven by physical well-being where 74% had physical well-being scores lower than the general population.

The other thing that we look at here in this slide is the time it took women to return to normal for each of these symptoms. And you can see, depending on which symptom we look at, it's between two and five months after the end of treatment. With the exception there of emotional well-being where we can see that less than 50%, or more than 50% of women had not returned to normal by the 18 months of follow up that we looked at here.

So next, we looked at group-based trajectory models, to see what groups of women were following similar trajectories over time after the end of their chemotherapy. And before I introduce these results, I just wanted to orientate you to this figure. So, we've got a grey area up the top, which is our abnormal scores or our abnormal area, and a white area down the bottom, which is our normal range. So, if women started off in the grey area, and they persisted in the grey area, we call them persistently poor. If they move from the grey to the white, they start off poor and then improve. And if they're always in the white area, then we call them persistently good.

So for anxiety, we have two groups in the grey area, the teal and the purple group, which make up 14% of, of the full sample who have persistently poor symptoms. And we also have a group there in orange, who move from the poor zone to the good zone, making up 2% of the sample. For depression, we have one group in yellow, making up 3%, who have persistently poor symptoms of depression over time. And we have one group in purple who moves from the poor to the improved scores and that made up 12% of our sample. Now, we also have another two groups there that follow a different trajectory, the orange and the green group, who worsen over time, so that's 3% of our sample, having worsening trajectories. For insomnia, we have one group with persistently poor symptoms, 15% of the sample. And for fatigue, this scale switches in the opposite direction, so, we have the grey zone down the bottom or the abnormal zone down the bottom and we had five groups who started out in the abnormal zone, three of those had persistent trajectories, making up 29% of the sample and two of those return to normal quite quickly and making up 51% of the sample.

The next thing we looked at were the predictors in advance of women who had persistent symptoms over that 18 months. And what we can see here is that it was the younger women, aged less than 50, those who had multiple comorbidities, and those who had a previous history of depression or anxiety, who had higher odds of at least one persistent symptom. Additionally, we looked at the predictors at the end of treatment of delayed returned to normal and this was among only the women who had poor scores at the end of treatment. And what we can see here is that consistently across the board, if they had a worst score at the end of treatment, they were more likely to have a delayed return to normal for all of those outcomes. In addition, it was the women who had a history of anxiety, depression and multiple comorbidities that had delayed returned to normal for some of those symptoms. It was also women who had no partner, who had a delayed return to normal for insomnia and I'm not sure how to explain that result. And the other thing we saw was

that women who had neoadjuvant chemotherapy as opposed to adjuvant chemotherapy, had a delay in return to normal for anxiety and fatigue. And that's probably because women who are having neoadjuvant chemotherapy are sicker than those who are having adjuvant chemotherapy.

Next, we're gonna move on to the talking about what happened after treatment and we've defined this as the New Normal. So, which is a particularly apt name that we've just seen, as many women do have persistent symptoms over time. So, this really is a New Normal for them. And the first piece of work I'll be talking about in this part of the talk is looking at coping strategies and whether they can approve outcomes down the track. So, this work has been published in Supportive Care in cancer, you can see the citation there and look it up if you wish, or send me an email. And the two main aims of this work were to determine if or to identify the coping strategies that women are using, and look at their trajectories of use after diagnosis. And secondly, to identify if these coping trajectories were associated with anxiety, depression and quality of life down the track. We used the measure called the Brief COPE and this measure had 12 different coping strategies that you can see there and firstly, we wanted to determine rather than looking at each of them individually, whether some of these coping strategies clustered together in their use.

So, we did a factor analysis and identified three different factors, in green, there is the, what we've termed the active coping positive reframing coping strategies, which also include planning and humour in that one. Secondly, in purple, we can see there was an emotional and social support coping strategy. And thirdly, in red, we have a coping strategy that we've called acceptance or denial. Now, these two things are a mirror image of each other, so acceptance at one end of the scale and denial at the other end of the scale. So firstly, looking at the trajectories of taking action and positive framing, again, we've used these group-based trajectory models and what we can see here is that we've identified four different groups of trajectories over time, we've got a high stable group with 12% of the sample there, a medium stable group, a medium

decreasing group, and a low stable group. And you can see there's a little bit of variation as to where women start off in their coping trajectory over that three to nine month period after diagnosis. But in general, women have a stable use of taking action and positive framing over this time period. For use of social and emotional support, again, we've identified four groups, a high stable group with 8%, medium decreasing, low decreasing, and low increasing group. And what we can see here again, is there is variation in where women start out in their use on this, on the scale. But for this particular cluster of coping strategies, we have 84% of our sample with decreasing use over that three to nine month period. And finally, we looked at the acceptance denial, coping cluster and there were two groups here, where about one in four women who accepted their reality, and then the remainder of women use some level of denial, most of them not too much but you can see a couple of outliers there down at the bottom of the scale in those dots who are using quite a bit of denial.

Now, importantly, we looked at whether those coping trajectories were associated with patient-reported outcomes over the 12 months. So, over those three to nine months, were associated with patient-reported outcomes at 12 months after diagnosis. And I've highlighted here in green, the groups of women to do better. So, it was the profile of women who had high stable use of taking act in positive framing, high stable use of social and emotional support and those women who accepted denial, who did better down the track in terms of their quality of life, and also in terms of anxiety and depression in some instances. So, this really tells us and shows us the importance of coping skills training, and also therapies that promote acceptance in terms of improving outcomes down the track. And finally, the third piece of work I'll be talking about from the OPAL study, is looking at the hidden burden of anxiety and depression. This work is currently in preparation.

So, we have seen a number of studies done looking at anxiety and depression in women with ovarian cancer. However, most of those have been cross-sectional at one point in time, or they have not measured whether women are using medications for

anxiety and depression in addition to symptoms, or they've not considered whether women have a previous history of anxiety and depression. So, our aim was to prospectively quantify the total burden of anxiety and depression. And to determine the proportion of women who experience it for the first time after their cancer diagnosis, the proportion with persistent symptoms, and look at whether the women with symptoms are using appropriate medication or services for their symptoms. And then in addition, we looked at the predictors of first time and persistent anxiety and depression.

So, to classify the total burden, we've classified women to four groups at each time point that we measured post-diagnosis. So, the group at the bottom in the dark, the darkest teal, we can see about 10% of women had clinical symptoms of anxiety and depression at each time point. The next darkest teal group, we can say that about 15% of women were on anxiety and depression medications at each time point. And these two groups make up our clinical cases of anxiety and depression. Now in addition to this, we had another group, the next darkest teal group with about 15% of women each at each time point experiencing subclinical symptoms. So, that's fairly consistent across all the time points in terms of the proportion in each of those groups. But now if we turn our attention to the final column in this slide, we can see that over that four year time point, about or 63% of women had their mental health affected at some point in time, with 43% of women experiencing anxiety and depression at clinical levels. So, this is a really high proportion over this four month... four year time point.

Now, in addition, we looked at among those women who had symptoms, who was using appropriate care, and we found that only 45% of women were using appropriate care. And that's based on the guidelines to finding appropriate care as a psychologist, psychiatrist, or use of medication. And then also, we wanted to look at the proportion with first time and persistent anxiety and depression. And you can see here that about one in three women had anxiety and depression for the first time after their cancer diagnosis. And about one in five women, 22%, experienced persistent anxiety and

depression after their diagnosis. Now, the predictors of first-time anxiety and depression included women who were younger, in particular, those less than 50, and women who had lower optimism prior to their diagnosis of cancer. And in terms of the predictors of anxiety and depression, that persisted after their cancer diagnosis. Again, it was the younger women but also, we saw that it was the women who were using more denial to cope with their illness, who had a high symptom burden, and who had poor sleep quality. And these women were likely to have persistent anxiety and depression. And this is in addition to the women who had a prior illness of mental, had a prior mental illness before the cancer. So, this really shows us that we have significant levels of anxiety and depression in this group, much higher than it has previously been reported. And some of these factors that we've identified here could be really useful in terms of closely monitoring these women with these high risk factors, and getting them into appropriate care earlier. So, I'm now gonna hand you over to Penny, who's gonna talk about lifestyle.

PENNY WEBB:
OK, thank you, Vanessa. So, this is really coming back to the main reason we set up the study, the OPAL study in the first place and that was to look at, is there anything women can do to influence their outcomes after they finished treatment? And as I said earlier, this is not quick work, we've had to recruit the cohort and follow them for four years before we've really been able to start looking at these data. And I'm gonna just give you a few hints of what we're seeing at the moment. The results are still only preliminary because as I said, we've already only just finalising the data, now we've done some early analysis, but I wanted to wait until we had enough follow up to really look at things properly before we started publishing the results.

So, the first thing I'm gonna talk a bit about is diet and dietary supplements, because I think this is one thing that women in particular often want to know about. and probably because there is now so much information or misinformation perhaps available on the Internet for people who go looking, trying to find reliable, reliable

information, they may end up finding a lot of stuff that is not that reliable at all, and certainly not evidence-based. So, the reason we think diet might be important, obviously, what we eat affects our health to a large extent, most of the work really so far has been done in breast cancer and there are definitely data they're suggesting that women who have a more healthy diet that's associated with lower levels of markers of inflammation, and therefore the theory is that it would also be associated with improveed survival. Unfortunately, the data so far are not that clear cut, there have been a couple of notable trials run in the United States. First, the WINS trial in breast cancer, randomised women to a low fat diet or their normal diet and they did see a lower recurrence rates, or lower recurrence of breast cancer among the women who were randomised to the low fat diet, which was very encouraging.

However, a second study, the WHEL study randomised women to what they call the healthy diet, which had many similarities with the low fat diet. And they didn't see any difference in terms of the recurrence rates, or outcomes of the women in the, those two groups. It's unclear why the trials have given different results but the one real difference between them is that the women in the WINS study who were on the low-fat diet actually lost a bit of weight, whereas the women in the other study did not and the suggestion is possibly it was actually the weight loss in that group that may be led to their lower recurrence rates. So, there are some suggestions that diet and the impact that has might influence cancer survival. But certainly, when we started this study, there was very little for ovarian cancer.

And I think it's important to remember that breast cancer and ovarian cancer, they're both hormonally related cancers, but they're very different diseases. Most women who have breast cancer won't die from their cancer, they will die from something else but most women from ovarian cancer, unfortunately, will die from their cancer. So, we've been interested in the relationship between diet and survival from ovarian cancer for a while. This slide shows results from two studies we've done previously and in these studies and in most other studies to date, we've only had information

about what women have done before they were diagnosed with cancer. So, most studies recruit women with cancer into the study, they asked them what they did before they were diagnosed and then they might follow up over time to see how long women live for and to look at survival. But as far as I'm aware, our studies, the first study to systematically go back to the women after they were diagnosed, to ask them about their lifestyle after diagnosis.

So, these data are based entirely on what women did before they were diagnosed and we're making the assumption which is probably not too unreasonable, that in most cases, women will have a similar diet after diagnosis to what they did before diagnosis, but it is an assumption. So, this graph on the left show some work done by a PhD students way back in 2003. This was from a group of women diagnosed in the early 1990s and if you're not familiar with survival curves, what this shows is the survival experience of these women over time from diagnosis. So, starting at diagnosis time zero on the left, 100% or all of the women were obviously alive. And then as we move forward in time, over 10 years, women, unfortunately, died and so these curves dropped down. But what you can see is that consistently, the red curve, which is the group of women who ate the highest levels of vegetables, had consistently better survival than the women who ate fewer vegetables. So, this suggested back then that there might be something about a healthy diet that might influence survival, even from a cancer like ovarian cancer.

We then did some similar analysis, again, done by a PhD student, published a couple of years ago, this was in a cohort of women diagnosed about 10 years later than the previous study. The Australian ovarian cancer study was, in some ways, the forerunner to the OPAL study, again, it recruited women from across the whole of Australia. And what Mary found was that a number of aspects of diet, things that we might consider as markers of a more healthy diet, things like higher fibre intake, higher intake of green leafy vegetables, more fish, polyunsaturates, a lower glycaemic index. So, eating more complex carbohydrates, and fewer of the white sugar, white bread type

carbohydrates, all of these things seem to be associated with better survival. So, that suggests that possibly there might be some benefits to a healthy diet and this was confirmed really, in a study published from the United States a few years back, this was an analysis done in the Women's Health Initiative study, you may have heard of that study, it was partly at least a very large randomised trial of the use of menopausal hormone therapy that ended up having massive effects on a hormone high being used because of the results they found. But they also asked the women about their diet, again, they only had information about what women had eaten before they were diagnosed with ovarian cancer.

But they showed very impressive differences in terms of women who reported higher overall diet quality before they were diagnosed, had lower mortality than women with a lower diet quality. And they actually saw 25% reduction in the risk of death for the women in the top third versus the bottom third so quite remarkable, have strong effects. In terms of what we've seen, we've looked at this very carefully, I had a student working on this last year, because we obviously wanted to try and confirm their results. And importantly, we wanted to look at this using information about women's diet after they were diagnosed. But unfortunately, as you can see from the note here, preliminary results do not suggest a particular benefit for diet either before or after diagnosis. But I should say that, one reason I put this up as preliminary, is we're hoping that now we have a bit more survival data for the women, that possibly we will be able to see something. We're going to redo the analysis in a few months and then if we still don't see any benefit, well, I guess that's what we're seeing in our data, which, arguably are based on better data than the previous study because we do know what women actually ate after they were diagnosed. It's disappointing but a fact of life.

The next thing I'll talk briefly about is smoking. So, smoking is an interesting thing in the context of ovarian cancer, we obviously know that smoking is bad for health in general, we know that it increases a woman's risk of developing one of the most rare

types of ovarian cancer, it doesn't seem to increase risk of the more common types, but it does seem that smoking might influence survival from ovarian cancer, so this is the disease, where most of the women are dying from their cancer. These are data from an international consortium where they pull data from about 18 studies worldwide. If you're not familiar with forest plots, the line down the middle here shows where we would expect the estimates to be if there was no association between smoking and survival. Any points to the left of the line suggests that smokers have better survival, any points to the right of the line have suggest that smokers have worse survival. And the lines, horizontal lines show the uncertainty around those estimates. And we can see here that of these 18 studies, most of them didn't give conclusive results. The lines all cross the central line, but the points themselves are mostly to the right of the line. I think by the data from all of these studies, we get an estimate of about 17% higher mortality among smokers. In red, I've highlighted the data from our Australian study down towards the bottom, which actually found one of the stronger associations. So, this shows fairly convincingly that smokers and again, we're talking before diagnosis have worse survival than non-smokers.

So, we were really interested in looking at this in our study and particularly looking at what happens if women stop smoking. So, smoking in Australia, we're lucky now is relatively uncommon compared to other countries. So, we had about, only about 12% of the women said they were smokers one year before they were diagnosed with their cancer. And about half of those women said they stopped smoking around the time of their diagnosis. And what's really positive to see is that about 80% of them remained non-smokers throughout the time we followed them. Among the other 50%, who were still smoking around diagnosis and just after that, about a fifth of those women stopped smoking later, and another 10% obviously tried to stop smoking but started again.

So, in terms of looking at quitting smoking, we don't have very large numbers to be able to do this. Only about 5% of our women were smoking at 12 months after

diagnosis, but what I can tell you is that we, like others, see that both current and former smokers do have significantly worse survival than never smokers. What we're still trying to tease out is whether stopping smoking at diagnosis will have a significant impact on a woman's outcomes. Obviously, once a woman is diagnosed, if she smoked in the past, she can't change that, we need to know whether stopping smoking at diagnosis will make, make a difference. And I can tell you that work from other groups, looking at the interaction between smoking and chemotherapy suggests that it might.

So, just finally, I'll say a little bit about physical activity, but earlier I alluded to that being potentially the most promising behaviour that might influence side effects and how women to get through chemotherapy. And there's certainly data from other cancers suggesting that, being active might help patients get through treatments, and physical activity or higher levels of activity have been associated with better survival, both for women with breast and bowel cancer. But as I said previously, it's important to remember that these cancers are quite different from ovarian cancer, both breast and bowel cancer, most women won't die from those cancers, they'll die from heart disease and other things, whereas when we talk about ovarian cancer, ultimately will be the cancer that will claim most of those lives.

So, we may not expect things that work for breast and bowel cancer to have the same effect for the other cancers. We've done some previous work looking at ovarian cancer, Vanessa has shown that women who are less active have lower quality of life and increased levels of depression among women with ovarian cancer, and the consortium I mentioned has also suggested that women who are inactive before their diagnosis have worse survival. Again, this is something we just started looking at in the OPAL study and I can tell you that our preliminary results do suggest a benefit for exercise and for exercise after diagnosis, the women who exercise more tended to have better survival. But this is a cautious result at the moment because we do need to be sure that it is the exercise that we think is affecting survival. Obviously, if women are very sick, then they are gonna be less likely to do high levels of exercise. So as I

said, it's a promising result but still a slight caveat there at the moment, but we're excited about this one.

So, just to summarise very quickly, the things we talked about today firstly, that in this cohort, women with ovarian cancer, moderate and severe side effects are very common, and a high proportion of women can't complete their plan treatment, so we need to find ways to improve this. As Vanessa said, the side effects that women experience, do usually resolve within about six months after treatment. But there's quite a sizable proportion of women who do experience long term problems and we need to find better ways to identify those women and to manage this. Vanessa also showed you that coping strategies, might help women manage quality or improve their quality of life, manage distress, and we need to consider whether there might be interventions to help women improve their coping skills. Vanessa also told you that... I showed you the high proportion of women who do experience ongoing distress and we need to get better at monitoring these women, identifying those at risk, and also making sure that women get appropriate treatment to manage this. And finally, is lifestyle important? I think the best evidence so far is that exercise is important and not smoking. It's not so clear whether a woman stopping at diagnosis will make a difference, it seems logical that it would. The data for diet, I think shows but we still need to do a lot more work to see whether there really are benefits of improving diet after diagnosis, so we need better data here.

Hopefully, we will generate that over the next year or two, so watch this space. Then I'll just finalise.... finish with some quick acknowledgments, the rest of the OPAL team, particularly the consumers, it's a strange term but commonly used, Merran, Helene, and Karen, who provided a much more patient-oriented view on the study, all the doctors and hospitals that took part, the people who funded us and most importantly, the amazing women who took part and completed the questionnaires, even when many of them were very sick, we are totally indebted to them. So, thank you very much and if you have any questions for either Vanessa or myself, please ask them.

And please don't be shy about asking questions. (LAUGHS) You've got a captive audience here, we're very happy to answer them for you.

So, we just had one question from Louise, or one comment from Louise, thank you very much. We're glad you enjoyed the presentation.

OK. OK, so we've had one question coming from Leah McIntyre, asking about whether we stratify the levels of exercise in our questionnaire. So, measuring physical activity and exercise is very tricky, we asked women to report how often they did a number of different types of exercise. So, we asked them how many times a week they would walk for more than 10 minutes, how often they did moderate exercise. And we gave them some examples of that, how often they did strenuous exercise. And we also ask them, on average, how long they spend doing it at each time to get an estimate of the total amounts of exercise they did at different levels during the week. One thing we know is that women tend to overestimate how much exercise they've done. If we believe the data at face value, then all of the women were doing a lot of exercise, which I suspect was not true. But yes, we did try to measure the amounts of exercise, and when we get more into the analysis we'll be separating out. Those who've done a lot of exercise, those who've done less, and we'll also look at the types of exercise, whether walking is enough or whether exercise needs to be more, more vigorous.

We've had another question from Sherryn Davies, I might answer this first, then I'll see if Vanessa wants to add anything. So the question, was there any particular result that surprised you most? I don't know if surprised is the right word, but the one I'm most disappointed by at the moment is our work looking at diet and diet quality, the previous study from America had shown such a strong effect, we really hoped we might see something similar in our data. And as I said at the moment, we're not, although we do need to do a bit more work. So, that was a disappointment, I guess, perhaps not unexpected, often, the first study that publishes the result finds the

strongest association and other studies then don't find such strong results but I might ask Vanessa, whether she has anything she'd like to add there.

VANESSA BEESLEY:
Yeah, guess in terms of surprising results, because I had read a lot of the literature in anxiety and depression and we had been seeing quite low levels. For me, it was quite surprising to see 43% of women experiencing clinical levels of anxiety and depression at some point in time, because the previous studies had really reported it much lower around 15 to 30%, in some studies if you include subclinical in that category, but we're not including subclinical symptoms in that category. So, I guess this was the most surprising to me and really shows how much more work we need to be doing both in terms of screening for distress across the board. And then really quickly getting people into appropriate care, which doesn't seem to be happening either, 55% of women not getting into appropriate care seems like a very high number to me.

PENNY WEBB:
Thanks, Vanessa. I mean, hopefully, hopefully, you will realise if you want to ask questions, you just type them in the chat box. But I will also say that this final slide has our institution there, it doesn't have our email addresses, but if you go to the institution website, if you have questions you want to ask, in private afterwards, you don't want to ask them in a public forum. You can either contact the Cancer Council, or contact us at the Institute and we'll do our best to answer them for you. Are you gonna say something?

VANESSA BEESLEY:
There is one more.

PENNY WEBB:
So Vanessa may want to comment on this, I'll have a first go, I think it's a good question. I think there's a very close relationship between fatigue, physical fatigue, and also emotional fatigue, we often see that women who report physical fatigue will

also report higher levels of something like depression. We haven't tried to separate the two yet, but that's definitely something we will look at. And in terms of looking at things that impact or effect chemotherapy completion, fatigue is one of the things on the list to look at there.

VANESSA BEESLEY:
Yes, I just echo that, I did have a very preliminary look to try and stratify emotional and physical fatigue but as Penny said it's early days, I think we need to do a lot more work there. And we do know that fatigue is one of the highest unmet needs, I think it's second on the list for ovarian cancer, so it is something that we really do need to focus on.

ANNA GORDON:
I think we'll end our webinar on this note, thank you so much to Penny and Vanessa for being our presenters this morning. It was certainly very interesting and a lot of valuable data and I look forward to hearing further results as you get more information. Shortly after this webinar, you will receive an evaluation form and we would really appreciate if you could complete this as your answers will help us plan and improve future sessions. Please check our website on cancerqld.org.au, to find out about our other upcoming health professional events. And if you haven't registered with our Health Professional Cancer Network, I'd like to encourage you to do so, it's free and really easy to do on our website and you'll be able to receive updates and services, upcoming events, networking opportunities and such. And that brings us to the end of our webinar. Thank you so much again to our presenters and participants and have a great day.