Community Review Criteria for Cancer Council WA Research Grants: Guide for Applicants

Introduction

There is increasing recognition of the benefits of involving community members (sometimes referred to as consumers) in all parts of the research process, including the allocation of research funding. Effective community involvement in our research funding decisions can help to provide a broader perspective to our decisions, improve accountability to our donors, ensure the research we fund is relevant to the WA community and improve how the results of the research are communicated to the wider community.

Cancer Council WA has for many years recognised the importance of involving community members in our research funding decisions; however, we have recognised that our process for involvement needs improvement to be fully effective. In 2015 we looked at evidence-based best practice from other organisations (in particular Cancer Council NSW, Cancer Australia and the National Breast Cancer Foundation) and the growing body of guidance / published literature on consumer involvement, as well as consulted with our existing community representatives to identify ways we could improve. This encompasses the recruitment, training and support of consumers as well as the process for consumer review of grant applications.

The key difference for researchers applying to our grant schemes is that we have introduced a set of new community review criteria, in addition to our existing criteria. The community criteria have been developed using the results of peer-reviewed qualitative research conducted by Cancer Council NSW to identify the values the community deem to be important in judging research.[1] They are also closely aligned to the criteria used by Cancer Australia to assess the Priority-driven Collaborative Cancer Research Scheme (PdCCRS). These criteria do not apply to our student vacation scholarships; see the separate 'guidance for applicants' document for this scheme.

The community review criteria is assessed by a panel of trained community members using a standard scoring system. Further guidance on answering the criteria is provided below. Remember that community reviewers have been trained in assessing research grants but are not research experts and so it is essential that responses are completed using plain language. **It is also important to remember that the community reviewers DO NOT see your scientific application**, the community criteria is the only representation of your research they will see.

For more guidance on writing in plain language, see the Cancer Council WA publication 'Writing 'Plain Language' Summaries: Guidance for Researchers'.

[1] Carla Saunders and others, 'Beyond Scientific Rigour: Funding Cancer Research of Public Value', *Health Policy*, 84 (2007), 234–42 <http://dx.doi.org/10.1016/j.healthpol.2007.05.002>.

Cancer Council WA Community Review Criteria

1. Research outcomes and the extent of potential benefit (impact)

Identify the anticipated direct outcomes of your proposed research. Describe how these outcomes have the potential to have a direct, beneficial impact on either the incidence or impact of cancer on our community. This includes short, medium and long term outcomes. If applicable, describe any particular relevance of the research to Western Australia and / or any specific benefits to the people of Western Australia from the research taking place here rather than elsewhere.

Description

This criterion gives you an opportunity to explain your research outcomes (short, medium and long term) and the potential for the proposed research to have a direct, beneficial effect on the incidence or impact of cancer. Be clear about whether this impact will be local, national and / or international.

Give details of any specific relevance of your research to Western Australia, e.g. the cancer you are studying is particularly prevalent here or your research takes advantage of infrastructure, skills or expertise that are unique to WA. Outline any benefits to the people of Western Australia from the research being conducted here rather than elsewhere, e.g. faster implementation of improvements in patient care or access to new treatments. Note: while local relevance will be taken into consideration, it is not necessary for proposals to have specific local relevance to score well on this criteria, it is the overall benefit to the community that is of primary importance.

It is important to consider benefits from the perspective of the general public as well as those more directly affected by cancer. Some examples are:

- Identifying the mechanisms by which cancers arise.
- Developing ways to personalise cancer treatments.
- Identifying and/or testing effective ways of preventing disease. This might include improvements in the environment or individual behaviours.
- Identifying those at high risk of developing cancer.
- Improving existing or identifying new cancer care delivery approaches, treatments and / or diagnostic methods.
- Improving access to information, and the quality of information available.
- Easing physical and/or mental suffering of those affected by cancer.
- Maintaining or rebuilding dignity and quality of life.

Be specific and descriptive, and remember the 'how' is important. It is also important to set the scene, is there any epidemiological information you can use to help contextualise the potential benefit?

When assessing this criterion, the community reviewers may consider the following:

- Has the researcher provided some epidemiological background (for example, how common the cancer is, what the outcomes tend to be, particular population groups who might be affected), to help contextualise the potential benefit?
- Has the researcher explained the extent of the problem and its importance?
- Has the researcher clearly explained the outcomes of their research?
- Has the researcher explained how the research will generate tangible benefit(s) to human life?
- What is the extent of the benefit(s) / how important are they?
- Does the research have any specific relevance to Western Australia?
- Are there any specific benefits to the people of Western Australia from the research being conducted here rather than elsewhere?
- Has the researcher indicated the probability, magnitude, and/or duration of these potential benefits?
- Has the researcher indicated when in the future the potential benefits might be achieved?

2. Pathway for realising the benefit (translation)

Provide a clear description of the steps required to reach the stated benefits of the research, ie the steps that need to take place for the research to have a direct, beneficial impact on either the incidence or impact of cancer on our community. This may include further steps beyond the scope / timeframe of the proposed research.

Description

In many cases, further steps are required before the proposed research will have a direct beneficial impact on the incidence or impact of cancer in our community. These steps might include additional laboratory based research, testing on humans, changes in clinical practice, product development, regulation and / or policy changes.

In this criterion, we are asking you to outline in broad terms what these steps are. We don't expect you to be an expert in all these steps, but do expect you to know what they might be and be able to describe them in broad terms and with rough timeframes. The pathway should describe the steps required to realise the **benefits** of the research, not the results of your research project. We are **not** asking you to restate the aims and objectives of your project or to provide a detailed description of your research methodology. We **strongly encourage** you to use **numbered steps** with **broad timeframes** and to indicate which steps are in the scope of the proposed research and which are beyond it. Be clear, direct and to the point, and **avoid** generalized discussion.

Identifying the pathway required to reach an applicable benefit, and highlighting which steps the proposed research will be addressing, allows the reviewers to judge when and how the benefits of the proposed research project will be realised.

When assessing this criterion, the community reviewers may consider the following:

- Has the researcher provided a description of the broad steps or stages required to reach the stated benefits of the research?
- Do the steps or stages appear reasonable?
- Are the steps or stages achievable?
- Are there any significant gaps in the steps or stages required to reach the stated benefits?
- Do the steps or stages represent significant constraints to achieving the actual benefits of the research?
- Has the researcher provided an estimate of broad timeframes for the achievement of each step or stage so it is clear when in the future the benefits might be achieved?

3. Equity

Explain which patient group(s) will benefit the most from your research (e.g. type or stage of cancer) and any equity implications. For research involving people, justify the selection of the study sample and explain why you have included and excluded particular groups who could potentially benefit from the outcomes of this research. If relevant, outline how the proposal addresses an under-studied or under-served population and / or a population with a high burden of disease or poorer outcomes.

Description

Equity in research asks the question 'who benefits?' Equity in research is commonly thought of as striving for equal benefit from research. There is no universally accepted best or right answer for how research benefits should be distributed in society, although ideally everyone who could have an opportunity to benefit from research should, particularly populations with poorer outcomes (which may include patients with specific tumour types or specific age groups, Aboriginal and/or Torres Strait Islander people, people of culturally and linguistically diverse backgrounds, or patients in regional / rural locations).

For example, a research project that focuses on a particular cancer or group of people, should explain the rationale behind this focus, and address how the benefits of the research may be expanded to other groups in the future. It is **not** the case that a study of, for example, ovarian cancer is inequitable because the benefits do not apply to men, or prostate cancer is inequitable because the benefits do not apply to women. However, a study of ovarian cancer may be inequitable if the results could **only** benefit women with the resources to access costly treatment delivered in an inner-Perth facility, and the service delivery model was unlikely to be extended to women from rural / regional and / or less privileged backgrounds. In this example, equity of treatment access may be deemed to be of concern. In addition, along with equity of opportunity, **equity of outcome** is an important component of the concept of equity. For this reason, community representatives highly regard evidence that research results may benefit populations with poorer outcomes.

Reviewers tend to assign most responses to this criterion a mid-range score, with lower scores assigned to responses in which the research is perceived to exclude

some groups, and higher scores assigned to responses in which the research is seen to particularly benefit groups with poorer outcomes.

When assessing this criterion, the community reviewers may consider some of the following (the research is not required to meet all these expectations)**:**

- Has the researcher explained how the findings could be generalised or applied to other population groups who are not part of the research?
- Does the research have the potential to provide benefit across all relevant persons, groups and/or places?
- Does the research address an under-studied or under-served population
- Does the research address a population with a high burden of disease or poorer outcomes?

4. Community involvement

Outline how community representatives (consumers) have been involved during the development of the research proposal and the plan for ongoing community involvement in the research. Explain how this / these community representative(s) are 'qualified' to be involved.

Description

In answering this question, you should describe community involvement (also referred to as consumer involvement) in the research design and plans for ongoing community involvement throughout the research.

Different groups use different terms for consumer / community involvement and define consumer differently. The NHMRC defines consumers as: 'patients and potential patients, carers, organisations representing consumers' interests, members of the public who are targets of health promotion programs and groups asking for research because they believe that they have been exposed to potentially harmful circumstances, products or services'.[2] In selecting the community representatives to sit on our grants committees, we are using the definition 'people with a connection to cancer e.g. through personal experience of having cancer, caring for someone with cancer, volunteering for a cancer related organisation etc'. We do not stipulate which definition you should use, but there are a few things a community representative **cannot** be, namely:

- other researchers (especially if connected to your research / working in your lab)
- clinicians / practitioners representing their professional role
- the subjects (participants) in your research

There are many opportunities for community involvement in *all* stages and *all* types of research. A reasonable and appropriate level of community involvement may vary, depending on the nature of the research being undertaken, and could include almost any kind of **two-way** interaction between community members and researchers.

[2] Cancer Australia, 'Consumer Reviewers for Cancer Australia's Priority-Driven Collaborative Cancer Research Scheme: Expression-of-Interest Background Information' (Cancer Australia, 2012), p. 1.

Community involvement must be **specific to the research** which is the subject of the funding application, and must allow for a **two-way conversation** between the researcher and informed community member(s) both during the development of the proposal and throughout the conduct of the research.

Community involvement in a specific research project is **not**:

- Researchers disseminating their results to community members
- Community members sitting on institution advisory groups (but they may be worth consulting on how you could involve community members directly in your research).

There is no single best method of community involvement. Even basic science / laboratory-based research can and should legitimately incorporate community involvement, and proposals with no involvement will score zero. Some examples of community involvement are:

- Provide informed input on strategic priority setting and direction.
- Work with researchers to define or refine the research topic.
- Provide informed input on research design and proposed methods.
- Participate in project advisory committees.
- Conduct lay reviews of research proposals.
- Participate in recruiting participants to research.
- Assist researchers to develop links to hard-to-reach populations.
- Conduct reviews of participant information sheets and consent forms.
- Assist researchers to pilot a research questionnaire.
- Produce newsletters for members of their organisation that chart the progress of research.
- Support the development of plain language summaries.
- Assist in disseminating information to the wider community.
- Participate in discussions and decisions around human tissue ownership and access issues.

We **strongly** advise you to refer to guideline documents outlining frameworks for consumer participation in research, including those produced by the National Health and Medical Research Council (2004; see www.nhmrc.gov.au/guidelines-publications/s01) and Cancer Voices Australia & Cancer Australia (2011; see canceraustralia.gov.au/sites/default/files/publications/national_consumer_framework_web_504af020f2184.pdf) to ensure that you genuinely appreciate who constitutes a consumer and what constitutes legitimate consumer involvement.

You can find useful resources at:

www.involvingpeopleinresearch.org.au/

https://www.nhmrc.gov.au/about-us/consumer-and-community-engagement

https://consumerinvolvement.canceraustralia.gov.au/consumers

Reviewers highly regard consumers / community members who are: (i) named; (ii) trained; and (iii) networked. That is, you should name the consumer(s) / community member(s) who are involved in this **specific** research, should identify how they have been trained to ensure that they are 'qualified' to act as consumer / community representatives on this project, and specify with which organisation(s) they are networked (for example, the Consumer and Community Participation Program).

Specifying these details assures reviewers that you have indeed consulted specific consumers / community members; that these consumers / community members have sufficient research knowledge to enable them to provide informed input into the project; and that these consumers / community members have a supportive network around them to facilitate their awareness of the broader issues of concern to cancer consumers / community members.

If you are having trouble identifying appropriate community members to help with your research, you can contact The Consumer and Community Health Research Network (CCHRN) .. Note that it may take some time to identify a suitable community member so allow plenty of time.

We **strongly advise** you to have a community member review your Community Criteria Review form to ensure its comprehensibility in terms of both the language used and as a stand-alone document able to be read without reference to the Scientific Criteria Form.

When assessing this criterion, the community reviewers may consider the following:

- Has community consultation into the development of this **specific** project already been undertaken?
- Have the researchers clearly identified the nature of community consultation to date?
- Has an individual community member, or a consumer organisation, agreed to act as the consumer / community representative on this project?
- Are the community member(s) named?
- Have the researchers explained what training and/or experience the community member(s) have undertaken which renders them 'qualified' to act as community representative(s)?
- Are the community member(s) networked as a member of a broader consumer / community organisation?
- Are there formal processes / structures in place that link the researchers with consumers / community members? For example, is a community member named as an Associate Investigator on the proposal, or is a community member nominated as a member of the project Advisory Group?
- Given the nature of the research, is the extent and type(s) of community involvement appropriate? For example, it would be expected that community involvement in a clinical trial would be more extensive than consumer / community involvement in a basic science study.
- Is the nature of ongoing community involvement clearly described, including the matters on which community members will be consulted and the mechanisms by which this consultation will occur?
- Have researchers identified the preferred approach of community members for ongoing involvement in the research?

Consumer and Community Health Research Network

Do you need help with involving consumers in your research? Want to find great community members to assist with your work? The Consumer and Community Health Research Network offers support, training and advice to help researchers involve consumers and the community in their work. Find out more at www.involvingpeopleinresearch.org.au or contact them at ipir@telethonkids.org.au.

Examples of highly rated responses from previous rounds

Plain language summary

Example 1:

Brain tumours cause the most deaths of children due to cancer. The team have found a new class of drugs, called CHK inhibitors (iCHKs) that block the ability of cancer cells to fix the DNA damage that is caused by chemotherapy. iCHKs have never been tested in children with cancer, but they have been used in adults and shown to be safe and effective so far.

Prior to giving it to children, it needs to be demonstrated that it makes mice with brain cancer live longer without adverse side effects. To do this, childhood brain cancers will be mimicked in the lab by growing cancer cells from children in mouse brains. These mice will be given the iCHKs in combination with conventional chemotherapies used to treat childhood brain cancer, to determine if the new combination enables them to live longer. These results will show if iCHKs are good drugs for children with brain cancer and, if so, how they should be given to patients. With this information it will be possible to design new clinical trials and work towards the aim of achieving higher cure rates and better quality of life for patients.

Example 2

Death from cancer usually occurs when it spreads to other parts of the body. To spread, cancer cells must be able to move and an immune cell called the macrophage helps them to do this. Macrophages also dig paths for tumour cells to reach the bloodstream and hitch a ride to other organs. To attract macrophages, tumours make a protein called CSF-1, which stimulates macrophages to move through tissue.

The purpose of this project is to identify drugs that can switch off the movement in macrophages. The team will then see if loss of macrophage movement can reduce

invasion of breast cancer. This will first be tested in laboratory-based tests and then in mice.

The chosen focus is on breast cancer because it is very common in women and has a grim outlook once it has spread to other organs. However, macrophages help a number of other cancers like prostate, lung, brain and stomach cancer to spread beyond their boundaries, potentially extending the findings from this research to develop better drug treatment for other cancers.

Example 3

Chemotherapy is used to treat many types of cancers. Unfortunately, chemotherapy often fails because cancer cells adapt and eventually no longer respond to the drug. This is known as chemotherapy resistance and affects the treatment of thousands of cancer patients every year.

This study investigates a molecule called gomesin, which has been isolated from a Brazilian spider. Gomesin has been shown to kill cancer cells but little is known about how the peptide works. This research combines computer-based methods and experiments to investigate, in detail, the anti-cancer activity of gomesin. The results of this study will help the future development of new anti-cancer drugs that are less likely to cause chemotherapy resistance.

Research outcomes and the extent of potential benefit (impact)

Example 1

In the advanced stages of disease, prostate cancer spreads to bone in over ~80% of cases. Presently, it is incurable and also produces many other health problems for patients. Therefore, the ability to delay and reduce tumour growth and progression while alleviating bone pain and preserving muscle and bone mass is of **major clinical interest** and **direct relevance** to advanced prostate cancer patients.

Exercise has been shown to positively change tumour biology. Participating in physical activity and exercise produces biochemical changes in the body which has the ability to interfere with tumour formation and slow tumour growth through different mechanisms. This is an exciting new frontier for cancer treatment which requires rigorous exploration. If the mechanisms from which exercise exerts its anti-cancer effects can be clearly identified, it will allow other disciplines to try and formulate drug therapies which can replicate these anti-cancer effects which will increase treatment potency and advance towards curative outcomes.

Currently, the influence of exercise to change tumour activity and preserve bone integrity has only been demonstrated using animals in research in the past two to three years. This new frontier has yet to be examined in humans. Our proposed research project will be **the first of its kind in the world** with the potential of large benefits and high impact direct to the community of cancer patients. Not only will this provide a benefit to advanced prostate cancer patients; **it will also have benefits to all cancer patients at the advanced stage of disease when their cancer has spread to bone**.

Previously our team designed and successfully delivered an exercise program to advanced prostate cancer patients with tumour spread to the skeleton in a safe and effective manner. It was the first time this high-risk and fragile patient group was included in exercise interventions. Cautiously, we only included exercise that avoided bones with tumours. However, for exercise to effectively slow tumour growth and interfere with tumour activity, **it needs to directly engage the bones with tumours** as shown in animal studies. **This proposed study will be the first worldwide to directly exercise bones with tumours in humans**. Our research team has strong experience delivering safe exercise programs to advanced prostate cancer patients.

Importantly, the feasibility, safety and effectiveness of providing exercise to advanced prostate cancer patients under highly controlled and supervised conditions using accredited exercise physiologists who specialise in cancer management will be the central focus of our research. Not only is it important to identify the anti-cancer effects of exercise; we need to be-able to demonstrate that it can be safely delivered and well tolerated by patients. **Through this project, if successful, we will be able to translate this directly to the community** through exercise clinics across Perth and regional Western Australia, as well as nationally and internationally, under the supervision of accredited exercise professionals.

Lastly, the eventual outcome of this project will ensure that advanced prostate cancer patients, with tumours located in bone, will be-able to also receive the broader health benefits of exercise that were otherwise available to localised prostate cancer patients, including preserving muscle and bone strength; improving heart and lung health; improving patient tolerance to other therapies; increasing the effectiveness of chemotherapy; increasing physical function; improving psychological well-being; and enhancing quality of life. Ultimately, **the biggest benefit and largest impact of all will be increased survival.**

The potential impact of this research is substantial. Given that advanced prostate cancer patients have **no curative treatments**; **developing strategies with anti-tumour effects coupled with broader health-benefits to consumers is of significant interest, worthy of rigorous pursuit.**

Example 2

Whether you smoke cigarettes or not you can develop oral cancer. Unfortunately, despite aggressive treatment 50% of people will not be cured. The rate of diagnosed oral cancers is increasing, mainly in young people under 45 years of age who have no known risk factors. Oral cancers and the treatment cause significant suffering by causing pain and affecting appearance, speech, and nutrition. Oral cancers can be hard to identify and monitor due to the anatomical location, and current methods of diagnosis are unable to reliably identify high risk cancers that have already spread to the lymph glands or will not respond to treatment.

As there are no molecular markers in routine use for head and neck cancer care, this research looking at new blood based cancer markers has the following potential benefits for cancer care;

1) Having a molecular marker can improve the identification of high risk versus low risk cancers, allowing doctors to appropriately allocate treatments. This will then improve the likelihood of cures.

2) Developing a molecular test will help disease monitoring – it could help predict when precancerous lesions are at risk of turning into cancer to aid primary prevention, and will improve surveillance after treatment. This will lead to better health outcomes.

3) Developing blood based tumour assessments and blood based mutation testing, or “liquid biopsies”, will revolutionise patient care and may save the need for invasive procedures.

4) The blood based mutation testing will focus only on mutations that already have treatments available to combat them, thus simultaneously, permitting the identification of novel treatments for patients.

5) As there are similarities between head and neck cancers and other cancers like lung cancer, due to similar risk factors such as smoking, findings of this research is readily applied to other cancer types.

This research will also benefit WA health and infrastructure via the following;

1) The research proposal will help formalise an effective translational research collaborative network at one geographical location, encompassing all aspects of patient care from the precancerous stage to the advanced stage. This is achieved through the collaborative work of oral dental health specialists (Dental School, UWA; Oral Health Centre of WA; SCGH), ear nose and throat surgeons, radiation doctors, chemotherapy doctors, pathologist and scientists. This collaborative network will allow the coordinated and efficient service delivery, with rapid achievement of research goals across multiple health sectors.

2) This research will help establish the framework of a comprehensively annotated head and neck cancer database and tissue bank available for future, which again enhances a coordinated, more cost-effective research strategy. SCGH is currently the only hospital in WA with an active head and neck cancer registry.

3) This research also helps to continue successful interstate collaborative research efforts in head and neck cancer to fast-track research discoveries. Already established collaborations include those with the Peter MacCallum Cancer Centre, Victoria, one of the world leading institutions for head and neck cancer care and research.

Pathway for realising the benefit (translation)

Example 1

My research is the development of a novel biomarker to predict successful responses to cancer immunotherapy.

The first steps of translation are presented in our project proposal, where I will assess the precision of our biomarker in an investigator-initiated national phase 2 trial in mesothelioma patients (the ‘DREAM’ trial), where combination chemotherapy and immunotherapy is being assessed. Patients’ samples, treatment outcomes are

all available to us.

To strengthen the push for translation into other cancer types, I will retrospectively examine publically available sequencing data from cancer immunotherapy clinical trials worldwide and correlate our biomarker with patient outcomes.

Our team will disseminate our findings through publications in peer-reviewed journals and conference presentations, as this are essential steps in translation to practice and policy. Key meetings include: International Mesothelioma Interest Group meeting, the Australian Lung Cancer Conference, World Lung Cancer Conference, Lorne Cancer, Keystone Symposia – Cancer Immunotherapy, and the Australasian Society of Immunology Annual Scientific Meeting.

If we identify an accurate, novel biomarker, a possible way to translate this into the clinical setting would be through the Australian Lung Cancer Trials Group (ALTG).

Step	Description	Status
1	Establishing protocol to analyse T cell receptors *We have developed the necessary sequencing protocols and analysis software for analysis of T cell receptors*	Completed
2	Testing if changes in T cell receptor diversity can predict responses to therapy *This project will directly investigate how T cell receptor diversity changes after therapy in preclinical models. It will also inform if these changes are associated with benefit to therapy*	This project (2019-2021)
3.	Collection of samples from lung cancer patients undergoing chemotherapy and immunotherapy *We have access to ongoing clinical trials where samples are being routinely taken, stored and analysed for other immune-related parameters.*	Completed
4.	Testing T cell receptor diversity in patient samples *We will examine changes in T cell receptor diversity after therapy in clinical trial samples obtained in WA.*	This project (2019-2021)

5.	Disseminating of data to scientific communities and consumers	Future (2020 - 2022)	
6.	Improving biomarker accuracy via mathematical and bioinformatics approaches, and from publically available clinical trial data sets.	Future (2020-2022)	
7.	Validating T cell receptor diversity as a biomarker in a mesothelioma trial cancer clinical trial.	Future (2022-2027)	
8.	Implementation of T cell receptor diversity as a biomarker	Future (2027 and beyond	

Example 2:

Step	Description	Status
1	Examine the digging machinery of macrophages in real time as they dig through proteins surrounding cells. *Macrophages form special structures called podosomes that digest extracellular proteins but precisely how they do it is not known. Since cancer cells use the tunnels dug by macrophages to invade through tissues and we aim to identify drugs that halt this process, it is important to understand precisely how macrophages dig the tunnels.*	This project (2017)
2	Test whether drugs known to block macrophage movement blocks breast cancer cell invasion in cells grown in the lab. *We have already shown that fast moving macrophages enhance breast cancer cell invasion in cells examined in the lab. This step will confirm that the opposite effect, i.e. blocking macrophage movement, can prevent cancer cell invasion in a simple system in the lab.*	This project (2017)
3	Identify new controllers of macrophage movement that can be targeted to block breast cancer cell invasion. *Although drugs have already been identified that stop macrophage movement, we would like to find newer drugs that are specific for just macrophages and that only target movement to reduce the incidence of side effects.*	This project (2017 - 2018)
4	Determine whether fast moving macrophages enhance breast cancer cell invasion in the mouse. *We have shown that faster macrophages cause more cancer invasion in the lab and we want to extend these studies to*	This project (2017 – 2019)

	animals. If animals with fast moving macrophages have more breast cancer invasion and spread, it will provide strong support for further pre-clinical studies using macrophage movement inhibitors.	
5	Test whether drugs known to block macrophage movement also block breast cancer cell invasion in the mouse. *It is critical to evaluate whether inhibition of macrophage movement can prevent or reduce breast cancer cell invasion in an animal model.*	This project (2017-2019)
6	Analysis of breast cancer samples to develop a test that detects actively migrating macrophages. This test will be used as a signpost for active cancer invasion. *Macrophages have been shown to collect in areas of active breast cancer invasion. However, it is not known whether these macrophages can be differentiated from harmless macrophages in tumours. Should our marker for actively moving macrophages pinpoint those macrophages invading with tumour cells, it will not only provide a new diagnostic test for invasive breast cancer but it will indicate which women should be treated with drugs to block macrophage movement.*	This project (2017-2019)
7	Commence clinical trials to test if macrophage movement inhibiting drugs shown to block breast cancer invasion in mice are beneficial in treating invasive breast cancer in women. *If our pre-clinical studies of macrophage movement blocking drugs show reduced breast cancer invasion in mice, the next step will be to determine whether these drugs can reduce breast cancer invasion in women. One of the drugs (GS1101, called Idelalisib in the clinic) is already in clinical use for an adult leukaemia and its use in the treatment of invasive breast cancer could be quite rapid and cost effective. The remaining drugs will have to undergo rigorous clinical trial testing before they can be used to treat breast cancer.*	Future (next step after this project (2020+)
8	Clinical trials to test whether drug(s) shown to block invasive breast cancer in women can similarly block invasion of other solid tumours such as prostate cancer. *High numbers of tumour associated macrophages indicate low survival rates in a number of cancers as well as breast cancer. Thus, should one or more macrophage movement blocking drugs effectively improve breast cancer survival, we should examine how well they work in the treatment of other solid cancers like prostate cancer and melanomas.*	Future (final step (2025+)

Example 3

There are a series of steps to be taken before final approval of new medicine and clinical translation is achieved. These include:

- Preclinical studies,
- Phase I clinical trials – to assess safety and determine maximum doses that can be tolerated by patients,
- Phase II – to assess if the drug works as expected and further assess safety,
- Phase III – to compare the new treatment (risks and benefits) with the current best treatment available.

Our research is examining a potential new class of medicines that may be effective in the treatment of childhood brain cancers. They are called CHK inhibitors (iCHKs) because they block the actions of specific proteins in the cell called CHK1 and CHK2. Even though these drugs are in phase I and II clinical development for adult cancer, since we aim to use them in children, a phase I trial needs to be repeated in this younger population. This project will provide evidence to justify a phase I clinical trial in children with cancer.

The research being undertaken in this project is in the "advanced preclinical" phase. This means that we have performed a large amount of laboratory research leading to this point. For our project this has included:

1) Develop procedures that inform patients about our research and that request donation of their cancer tissue to the laboratory for research purposes (informed consent).
2) Determine the correct conditions to keep human brain cancer cells alive in the laboratory.
3) Perform an experiment that examined more than 3000 existing drugs to find medicines that can kill brain tumour cells in a test tube. For this, we used brain cancer cells isolated from six patients.
4) Evaluate several new drugs from step 3 for their ability to improve the cancer--killing effects of chemotherapy using human brain cancer cells in the lab.
5) Validate the results of step 4 using mouse models to determine if new combination treatments can extend the survival of mice with brain cancer.

In step 5, we evaluated three iCHKs in combination with one of the drugs used for medulloblastoma treatment (cyclophosphamide). They were tested in three different mouse models and all had the same outcome. This was significantly longer survival. The next phase is to determine if these new drugs should be combined with cyclophosphamide, or if they work better with another chemotherapy.

The next steps are:

6) Test iCHKs on brain cancer cells growing in a test tube in combination with other chemotherapies already being used in clinical treatment (cisplatin and gemcitabine) – *Completed.*
7) Confirm results of step 6 using mouse models of childhood brain cancers – ***THIS PROJECT****.*
8) Engage with pharmaceutical companies to gain support for a clinical trial in children with cancer -- a*lready initiated via US collaborators.*

9) Toxicity assessments of the best new drug combination in several mouse models, including mice with a functioning immune system – *Next step*
10) Perform studies to understand how quickly the drugs are excreted from the body – *Next step.*
11) Test the new treatment in multiple different types of medulloblastoma (in mice) to identify the patient population most likely to benefit – *Next step*
12) Identify ways to measure treatment response that will be incorporated into the clinical trial design – *ongoing*.
13) Present preclinical data to clinical trials groups. *Data for medulloblastoma will be ready to present towards end of 2018. Data for ependymoma will be ready towards end of 2019.*
14) Design a phase I clinical trial to assess safety of the new combination treatment in children with brain cancer. Obtain broad input from clinicians, scientists and statisticians to refine design – *Future (2018--2021).*
15) Apply for funding to run an international phase I clinical trial – *Future work.*
16) Implement the phase I trial in paediatric hospitals across Australia.

If the new treatment passes phase I, the next stages of clinical development will be phase II and phase III clinical trials

Equity

Example 1

This project will enhance patient support, health and wellbeing in a population that is in **considerable need of attention**. Patients with advanced-stage prostate cancer are **often excluded from exercise interventions** due to numerous barriers. We are excited to offer this population with an opportunity to participate, with the goal to significantly reduce disease burden and **improve survival**.

This project crucially focuses on prostate cancer patients with **a high disease burden**, specifically prostate cancer with has spread to bone. This is an understudied population in exercise oncology due to the fear of patients and clinicians alike that adverse skeletal events may arise from bone lesions. However, preliminary evidence from our team in advanced prostate cancer patients has shown that carefully considered and well-supervised exercise programs in **these high-disease burden populations <u>can be</u> tolerated, safe and feasible.**

We will compare outcomes between usual care (standard, current prostate cancer therapies and treatments) with an innovative and evidence-based modular multi-modal exercise program with spinal isometric training to **suppress tumour formation and progression**. It is our intention and expectation that this intervention will **effectively interfere with tumour growth**. We also intend on delivering many of the associated health benefits that are derived from exercise in cancer patients more broadly, thereby reducing the burden of disease and associated co-morbidities.

Importantly, we are **proposing and evaluating the role of a non-invasive, low-cost therapy in the management of advanced prostate cancer which also has the ability to promote effectiveness and tolerance of other accompanying therapies** (such as chemotherapy from an increase in blood supply to tumour sites, for example). Further, the intervention has been deliberately developed so that it can

be **immediately translated into practice in community-based exercise clinics under the supervision of appropriately trained exercise physiologists.**

This project has the potential to provide a relatively low-cost, effective service to **this unique and high risk population** nationally and worldwide. It can be delivered regardless of age, ethnicity, education level, socioeconomic status or geographic location. **It also has the potential to translate to other patients with advanced-stage disease for other cancers.**

Example 2

Patients with oral cancer of any disease stage will benefit most readily from this research. The research focuses on one head and neck cancer site as this will permit research in a uniform group of participants aiming to minimise the presence of other confounding variables. However it is likely that these results will be applicable to other head and neck cancers, and cancers of other sites, as the principle of this research is to look at parts of cancer that are secreted into the bloodstream which occurs in all cancer types.

Head and neck cancer is a poorly researched type of cancer, with no molecular markers available in routine clinical use. Over the last 20-30years no treatments have improved the chance of patient survival. The rate of oral cancers, specifically tongue cancer, is still increasing in young people without known reasons. Patients with tongue cancer have the worst chance of surviving compared to any other head and neck cancer type. In addition, head and neck cancers and its treatment causes significant suffering for all patients due to the sensitive anatomical location of the disease, which affects speech, nutrition, and appearance. As a result, head and neck cancer sufferers are often unable to advocate for themselves as the cancer has affected their very ability to speak. Therefore, it is crucial we identify means to improve the diagnosis and treatment of oral cancers.

This research also looks at molecular differences between precancerous lesions and cancers, and can also assist in primary prevention in cancer. So, the research may simultaneously help to prevent cancer development.

Community involvement

(Note: names of specific community members and their organisations have been removed for privacy)

Example 1

At an early stage of the development of this proposal, Dr WW has met with XX, the Consumer Advocate from Consumer and Community Health Research Network, to discuss how consumers could be involved. With her help, two community representatives have participated in the development of this proposal, YY and ZZ. YY was the primary carer for her husband, who had brain cancer. ZZ's husband currently has brain cancer and she is his primary carer. Both YY and ZZ have reviewed the application and provided valuable feedback. They have also edited the Plain English Summary and Community Review Criteria sections of the application, which has made them more accessible to the general public without a science background.

To ensure the research will lead to practical benefits for the cancer community. YY and ZZ will also be 'research buddies' during this project. If the project is funded, we will meet three times: at the beginning of the project to finalize the aims and plans of the project; at the halfway point to discuss the progress of the project; and 1 month before the end of the project to discuss the findings and also how to communicate them to the cancer community. We also hope to develop the relationships and consumer involvement capability to involve both YY and ZZ as research buddies for potential future developments of this project, or others.

Dr WW attended the 1-day training workshop for researchers, Consumer and Community Involvement in Research, on 2 July 2018. The workshop provides useful and practical guidance to help scientists involve community representatives in their research, with the goal of improving the design of research projects and the communication of scientific discoveries to the general public.

Example 2

Two community representatives were involved in the preparation of this research proposal. XX is a breast cancer survivor who knows first-hand the impact of chemotherapy and the potential impact of drug resistance. YY is a melanoma survivor who works in the field of integrative oncology and helps cancer patients to deal with the side effects of cancer treatment using scientifically validated methods (including Nutrition and Yoga therapy). XX and YY have reviewed the application and their feedback has helped improve the overall application as well as the lay summary, by identifying words and concepts whose meaning might be less obvious and requiring explanation to readers without a scientific background. Their advice has also helped to better communicate the long-term benefits of basic research for the cancer community.

Involvement of consumers in the research project

XX and YY have also agreed to be consumer representatives ('research buddies') for this project. As noted in the NHMRC framework for consumer participation [10], the aim of consumer involvement in basic research is to help consider implications of the research and how it will lead to practical benefits for the cancer community in the future.

To achieve this, input from XX and YY will be sought at three stages of the project:

i) At the start of the project (April 2017), to present the aims of the study and discuss the anticipated outcomes;

ii) Halfway through the project (October 2017), to discuss the progress of the project;

iii) At the end of the project, to present the findings of this project and how it will be ensured that the findings will be translated into further studies involving cancer researchers in WA.

To ensure that I am adequately prepared for this, I will attend a one-day training workshop for laboratory-based researchers run by the 'Involving people in Research' team at UWA (scheduled for November 2016).

Raising awareness of venom-based drug design and the importance of basic research in WA cancer community

In my experience people are intrigued by the idea that the venom of animals such as spiders, snakes and centipedes, can be used to develop drugs. The idea that something that can kill us can be used to treat cancer, stroke or chronic pain is indeed fascinating. Venom-based drug design is also an ideal topic to raise awareness of the importance of basic research and the use of computer-based approaches to accelerate and enhance drug development.

This can be communicated in the form of a public lecture or a presentation at a community forum.