Breast Cancer Aotearoa Coalition Submission to the Health and Disability System Review May 2019

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1. **What are the key values that you would want to underpin our future public health and disability system?**

BCAC would like to see the following values driving our health and disability system at all levels:

a. Fairness – access for all, deal with current inequities – not only ethnic but also socio-economic, regional, people with/without disabilities, with/without co-morbidities, with/without cancer, with/without a terminal diagnosis.

b. Quality – care that produces health outcomes as good as or better than those in other OECD countries, is timely, responsive, uses the best medicines and technologies, equipment, facilities, administrative and data systems, communication models, and trained staff. Vigilance, interventions and care tailored to individual risk profiles and disease characteristics. People-centred and co-design etc. come in here (if these people-centred approaches don't actually produce better health outcomes then don't do them even if they sound nice!); constant monitoring and evaluation, with prompt, evidence-based changes if systems are not contributing to better quality and more equitable health outcomes.

c. Compassion – not just 'people-centred' but caring and kind, for example, patients are not forced to publicly fundraise for their treatments; quality of life (as reported by patients) is prioritised at all times. (Intersects with quality and fairness.)

d. Future-focused (preparedness) – innovative and constantly evolving, aspirational, always seeking improvement. Global focus - looking to the rest of the world for ideas, systems that can be used here, while recognising innovations of our own. Benchmarking against other countries.

In 2016, the Ministry of Health set the following values for the following ten years:

1. Acknowledging the special relationship between Māori and the Crown under the Treaty of Waitangi;
2. The best health and wellbeing possible for all New Zealanders throughout their lives;
3. An improvement in health status of those currently disadvantaged;
4. Collaborative health promotion, rehabilitation and disease and injury prevention by all sectors;
5. Timely and equitable access for all New Zealanders to a comprehensive range of health and disability services, regardless of ability to pay;
6. A high-performing system in which people have confidence;
7. Active partnership with people and communities at all levels; and
8. Thinking beyond narrow definitions of health and collaborating with others to achieve wellbeing.

While BCAC agrees that these eight dimensions should continue to underpin the New Zealand health system, the makeup of these current dimensions must be continually reviewed and adapted to ensure they fit the needs of New Zealanders today and in the future. For example, equity must be achieved by having all groups diagnosed and treated to a standard that is suited

to a developed country[1] (i.e. not equity at the lowest common denominator), and efficiency should not compromise quality or equity.

In addition, the following principles should be incorporated to achieve a successful public health system:

1. Responsiveness: A system that is not only responsive and receptive to a person's needs and values, but a system that provides responsive screening, diagnosis and treatment. In breast cancer, people need to enter the system and be seen forthwith so that they are in a stage that they can still be treated effectively.

2. Proactive: The system should be proactive enough to move quickly in the face of developments. There should not be a delay in New Zealand receiving the world class screening, diagnosis and treatment that our OECD compatriots receive.

3. Quality: Efficiency should not outweigh the drive for a quality healthcare system being provided to New Zealand.

4. Innovative: A health system that innovates and future proofs itself for a continually changing health landscape and population. For example, a health system which can adapt by utilising new technologies to improve early detection and likewise the development in personalised medicines and treatment for cancer and other diseases. A system that does not continue to take a "one size fits all approach" to health, but is flexible enough to harness the benefits of increasing precision, not only in health outcomes but also in cost savings (i.e. earlier screening with the correct modality and people receiving treatments that we know will work and not those that will not) to the ever developing individualistic approach. This is particularly relevant in cancer care where major advances in treatment have been made by identifying an increasing number of sub-types of each cancer and developing targeted treatments for each. Continuing with the old strategies of 'cut, burn and poison' is not the future (or even the current reality for some cancers) of cancer care.

2. **If you imagined the ideal health and disability system for New Zealand in 2030, how would people's experiences differ from today?**

The ideal health system would ensure:

a. We improve population outcomes and eliminate ethnic inequalities in breast cancer stage at diagnosis and mortality through initiatives across the breast cancer pathway— prevention, risk assessment, detection, diagnosis, treatment, care and support along with additional funding for much needed resources, smart technology and improved infrastructure.

b. That investing at the front end of the pathway will eventually reduce the need to invest to the same degree at the end of the pathway.

c. That women diagnosed with advanced breast cancer live longer, fuller, healthier lives. That through swift access to new medicines, advanced breast cancer would become a chronic illness, rather than a death sentence. That access to new and developing treatments and medicines is facilitated by a forward-looking system.

d. That women would be diagnosed earlier. This can be achieved through targeted access programmes for screening for particular groups, for instance Pasifika women get breast cancer younger and have worse outcomes generally[2]. We know however that Pasifika women do just as well as women in other cohorts when part of a screening programme. Screening programmes targeting this group would allow women in this cohort to be diagnosed earlier, and this would lead to increased survival. Identification of risk factors for specific groups would allow closer monitoring, and earlier diagnosis. That decisions about access to screening and treatments are informed by evidence and/modified as new evidence emerges from research.

e. That your access to treatment would not be determined by where you live (the post code lottery) or your ability to afford private healthcare. For example, access to clinical trials is restricted to the centre or DHB that is hosting the trial. In order to be treated in a DHB, a person must have a residential address within that DHB's zone. What little access New Zealand patients have to clinical trials is, for some, completely removed as a result of living in the wrong place. Some of these patients would be willing to travel, but the hospital staff are reluctant to accept them into their trials as a result of the stringent rules set by DHBs.

f. That women in South Auckland (which is home to a large portion of low socio-economic and ethnic minorities) cannot currently receive chemotherapy or other drug therapies at Middlemore hospital[3], leaving women to travel unreasonable distances across the city to have treatment. This leaves many unable to work, or attend work for any part of a treatment day, as the journey and treatment itself takes up the majority of the day, when this would not always be necessary if treatment was available locally.

g. That there would be clear guidelines established and implemented for breast cancer care, and more generally in cancer care. These would be benchmarked against international standard, for example the ESMO Clinical Practice Guidelines[62] which are updated biennially based on the latest evidence and developments in breast cancer treatment.

h. That oncologists would have available to them all the treatment options necessary to tailor effectively (and efficiently) treatment plans, which could cure more at the early stages, and provide more wholesome lives for patients whose disease has advanced, allowing all patients to remain contributing members of society.

i. Primary health practitioners would receive additional training in cancer diagnosis and care.

j. That people would be seen without delay, and would be moved quickly through the relevant system/s. Patients would be involved in their care, with seamless referrals to the next stage and follow-up appropriate to their condition, without delay. Information between specialities

or linked to a patient's NHI number, so that co-morbidities can be dealt with by a multi-disciplinary team.

3. **What system level changes would you recommend to improve equity of health outcomes and wellbeing? What impact would you expect these changes to make?**

Increased provision of services in the community: For example, the funding of medicines of sub-cutaneous Herceptin would allow primary health carers to deliver life-saving medicine within a primary care setting, providing further access to many women who are inhibited to attend long treatments at a hospital, because of financial pressures, such as needing to work, being rural, or living in parts of big cities (e.g. South Auckland) without means to get to appointments. BCAC recognises that some DHBs are working towards Local Delivery of Oncology services; this needs to be resourced adequately and accelerated.

Establishment of an independent national cancer agency: Establish a stand-alone agency to implement a cancer control strategy that is free from political persuasion and direction.

The Canadian Partnership against Cancer is a publically funded independent body which is "focused on the long-term objectives of reducing the incidence of cancer, reducing the likelihood of dying from cancer and improving the quality of life of those affected by cancer. [Its] work spans the continuum of cancer control – from prevention and screening through diagnosis and clinical care to palliative care and survivorship – and cuts across that continuum with initiatives to monitor and improve cancer system performance and mobilize evidence to drive policy and practice improvements".[4]

Increased engagement at the consumer and community level: Co-design in health is a compulsory tool that is used across New Zealand. That the value of the engagement approaches being used are constantly monitored, evaluated, and adjusted if they are not delivering expected benefits. Until people are involved in the planning process there will be system level changes but until a meaningful co-design process occurs, the changes cannot be realised by health system consumers.

That people with experience of a condition are involved in planning services. For example, involving Māori and Pasifika women in planning services to their communities, using their language and not just a direct translation, but with words that ensure the messages are communicated.

A system that encompasses a diverse population: A system that can provide the best quality of care, taking into account different cultural and socio-economic needs.

A more streamlined efficient health system: The reduction in the number of DHBs, and/or an overhaul of the DHB model, would result in more streamlined approaches across New Zealand. Currently, we understand there is deviation in treatment approaches among different DHBs, which compromises patient care, and the standard of treatment they receive.

Accountability of PHARMAC and other public entities: The introduction of consumer representatives at the decision-making level in cancer decisions, rather than at a consultation

level. For example, we know that consumers communities participate in the decision making of many other health technology assessment agencies, e.g. Australia, Scotland, England and Canada[5] (and many more), unlike PHARMAC whose Consumer Advisory Group is only able to comment on the way PHARMAC "consults" with the New Zealand public.

IT infrastructure: A streamlined IT infrastructure with appropriate systems and communication mechanisms to provide seamless care among health providers. This is particularly important for women in remote locations who may have treatment for various illnesses in different centres.

A system that is sufficiently funded so that New Zealanders gain access to screening on a timely basis with the appropriate modality and frequency. This system should be complemented with diagnostics to determine optimised treatment which patients would not have to personally pay for to gain access to cancer medicines that are evidence-based and recommended by their oncologists. This would allow equitable access for all New Zealanders so that families aren't forced to cash in retirement savings, sell properties, set up 'Give a Little' pages and fundraise to purchase the lives of their loved ones.[6]

4. **What system level changes would have the most impact on improving health outcomes for Māori?**

Timely and equitable access to screening and treatment facilities at a local level, regardless of ability to pay.

Both better engagement at community level and developing a system that caters to a more diverse population would have the most impact of improving health outcomes for Māori and reducing inequities. For example, we need to consult with Māori women regarding screening and provision of care to Māori women. Until Māori women are consulted effectively, it is impossible to know what will work.

Working with Māori to develop a system that is flexible enough to incorporate kaupapa Māori to ensure Māori solutions to Māori problems, realising the partnership principles of the Treaty of Waitangi, and acknowledging the different approaches and needs required by different iwi.

More Māori are needed in the Ministry of Health and throughout the health system generally.

5. **What system level changes would have the most impact on improving health outcomes for Pasifika people?**

Both better engagement at community level and developing a system that caters to a more diverse population would have the most impact of improving health outcomes for Māori and reducing inequities.

Working with Pasifika to develop a system that is flexible enough to incorporate Pasifika solutions for Pasifika problems. Targeted Pasifika programmes, like the targeted Breast Screen Aotearoa advertisement developed in consultation with Pasifika groups, which raised Pasifika screening rate by 12% to 71.9%. [7]

Providing programmes that cater for specific risk factors, such as early mammograms for Pasifika women as Pasifika women are likely to get cancer younger and the cancer is twice as likely to be aggressive than that of other groups.[8]

6. **What system level changes would have the most impact on ensuring that disabled people have equal opportunities to achieve their goals and aspirations?**

New Zealanders with disabilities have additional challenges accessing cancer prevention and care in New Zealand. An ideal system would consider, for example, how women in wheelchairs access mammography screening caravans. Or how blind or visually impaired women get information about treatment that often comes as a pamphlet or information sheet.

An ideal health system would see additional consultation with communities of those differently abled regarding changes required to ensure equity is achieved for this cohort in the cancer (and other health) sphere.

7. **What existing or previous initiatives have best delivered improved and equitable health outcomes and wellbeing in New Zealand or overseas? Why have these approaches worked, and what is their potential to deliver further improvement?**

BCAC will answer this question using breast cancer as a case study.

7.1 Overview

Breast cancer is the most commonly diagnosed cancer in NZ women.[9]

It disproportionately affects Māori and Pasifika women (Lawrenson, 2018). [10]

Although many women diagnosed with early breast cancer will survive at least five years, up to 30% of all cancers will eventually advance[11] depending on subtype.

Advanced breast cancer (ABC) is incurable but with good treatment, many women can survive and lead productive lives for years. Unfortunately, New Zealand's record in treating people with ABC is appalling. Our median survival time is just 16 months, compared to 2 to 3 years in European countries and the USA (*I'm Still Here*, BCFNZ report).[12]

An international report recently predicted mortality in New Zealand to 2020 would be less favourable than other countries in the Americas, Asia and Oceania, ranking us alongside Argentina, Cuba, Venezuela, Israel, and the Philippines (Caroli et al, 2018)[13]. This highlights how we need to improve how we both manage and treat breast cancer in New Zealand.

Improving population outcomes and eliminating ethnic inequalities in breast cancer stage at diagnosis and mortality can be achieved through initiatives across the breast cancer pathway—prevention, risk assessment, detection, diagnosis, treatment, care and support along with additional funding for much needed resources, smart technology and improved infrastructure.

These initiatives should be evidence-based and supported by ongoing research, both overseas and in New Zealand.

Below we give examples of initiatives and approaches at each stage of this pathway which could lead to better and more equitable health outcomes.

7.2 Prevention and risk assessment

Understanding breast cancer risk factors for individuals and population groups is vital for providers to effectively target public health initiatives such as screening programmes and health messages. This ensures consumers are well-informed, proactive, and ready to take personal responsibility for their health, and to engage constructively with providers.

Raising health literacy in culturally accessible ways, among consumers is a key step, as is improved and ongoing training in breast cancer risk assessment for primary health care providers, breast nurses, physicians and clinicians.

Breast cancer risk assessment is an active area of research and new practical tools that could help health professionals and consumers are now becoming available. New Zealand should be taking full advantage of these new more objective technologies to better target services and make savings by optimally directing resources to where they will have most impact.

7.2.1 Health literacy

Breast cancer is a life-changing event and there have been recent advances with improved neo-adjuvant, adjuvant, advanced and palliative treatment strategies for each characteristic molecular breast cancer subtype. However, there is little understanding of the evidence relating to risk factors and how these might be managed or reduced.

A recent Australian Government and Cancer Australia publication, *"Risk Factors for Breast cancer – A review of the evidence"* (ISBN)[14], is an excellent example of the detailed well researched and evidence-based information which is not readily available to New Zealanders on a timely basis. It debunks many of the myths that exist, while highlighting real risks which our population needs to understand. This document also highlights mitigation factors where relevant.

7.2.1 Recommendation 1: Provide information summaries to New Zealand senior students' health programmes at secondary schools.

7.2.1 Recommendation 2: Provide information summaries to primary healthcare teams so that they also may better appreciate these issues.

7.2.1 Recommendation 3: Provide information regarding lifestyle factors to consumers to help them to understand how they may play a role in reducing risk.

7.2.1 Recommendation 4: Develop, support and implement strategies to improve health literacy programmes to improve Māori and Pasifika health outcomes including the Māori and Pasifika mHealth's initiative to support healthy lifestyles developed through the Healthier Lives research initiative[15], supplemented with community engagement.

7.2.1 Recommendation 5: Integrate these initiatives where relevant into Standards of Care at all levels.

7.2.2 Risk assessment

Breast cancer risk assessment in New Zealand is limited and more generally occurs at the point of diagnosis unless there is a strong family history (FH) of breast cancer. A recently published survey shows that approximately half of New Zealanders were unable to name any risk factors for breast cancer (Richards, McNoe et al. 2017).[16]

A recent study (Brentnall et al, JAMA Oncology, 2018)[17] has shown that assessments of breast cancer risk made using the Tyrer Cuzick model combined with a breast density measurement were valid for many years after evaluation, and could therefore be used to guide long-term, systematic, risk-adapted screening and prevention strategies. An assessment of breast cancer risk factors by a team from the University Hospitals Leuven, Belgium indicated that the most effective breast cancer prevention strategies could be obtained by an objectification of the breast cancer risk assessment process (S. Woussen et al, ECR, Online, 2019).[18]

The US Preventative Services Task force found that although risk assessment models demonstrate good calibration for predicting risk in a population, their discriminatory accuracy to correctly classify individual women who will develop breast cancer over the next five years from those who will not were modest unless they included breast density, postmenopausal hormone use, and a more extensive family history [19]. In considering risk assessment it is important to also ask whether rationing services at the risk assessment end of the pathway is running the risk of lowering levels of surveillance and therefore detecting cancers too late (and at a more costly stage) and so this needs to be done with care as there is no guarantee that an assessment is fool-proof.

7.2.2 Recommendation 1: BCAC stresses the need to introduce an up to date objective risk assessment tool such as BODICEA which recognises a broader range of breast cancer risk factors to identify differing levels of risk.[20]

The Genetic Health Service of New Zealand (GHSNZ) expect to introduce the updated version of BODICEA to strengthen the risk assessment case later this year. It includes a comprehensive range of factors: family history and over 300 genetic indicators (SNP's), breast density, weight, age at menopause, alcohol consumption and use of hormone replacement therapy. Genetic sequences – called SNPs – are thought to account for as many as 50 per cent of hereditary breast cancers. Although individually some of these things have a small impact on the likelihood of developing the disease, researchers found that by considering all of them at once, plus breast density, family history and genetics, they can identify groups of women who have different risks of developing breast cancer. This makes calculating risk more precise than ever before.

7.2.2 Recommendation 2: BCAC recommends introducing a differentiated risk approach to:

- tailor breast cancer screening depending on an individual's risk including determining what age a person is first invited for breast screening or how regularly they are invited to receive it and the form of screening offered and
- make decisions regarding preventative therapy (such as prophylactic use of tamoxifen, raloxifene or aromatase inhibitors)[19] depending upon the patient's age and stage in life and

- encourage people to think about the ways they could reduce the risk themselves, for example lifestyle factors or preventative mastectomy.

Professor Antonis Antoniou, lead author at the University of Cambridge, said of the latest version of BODICEA: "This is the first time that anyone has combined so many elements into one breast cancer prediction tool. It could be a game changer for breast cancer because now we can identify large numbers of women with different levels of risk – not just women who are at high risk. "This should help doctors to tailor the care they provide depending on their patients' level of risk. "The team hope this means more people can be diagnosed early and survive their disease for longer."

Once again, we stress that rationing of services at the risk assessment end of the pathway should not lower levels of surveillance with the risk of detecting cancers too late (and at a more costly stage), for example in younger women or those who have an unidentified mutation. Any risk-adjusted screening tool should be introduced with care and results closely monitored as no assessment system is perfect.

From the BODICEA model, researchers have also created an online calculator Can Risk, for GPs to use in their surgeries. GPs, practice nurses and genetic counsellors in the UK are testing this tool before it is considered for wider use. In time this trial will enable more tailored screening to develop so that those indicated at risk may receive the focus required. Currently we are aware of many young women with symptomatic breast cancer who have been turned away from their GPs without further investigations because of their young age. Introduction of any risk tool will need to be undertaken with improved education of GPs on how to manage individual patients.

7.2.2 Recommendation 3: BCAC would like to see patients having access to an online tool in line with the UK trial or app which they could also update when necessary, whether this is triggered at GP or clinician level will be determined following the trial.[21]

The GHSNZ provides an excellent service for those with a clear family history within their limited resources. GHSNZ offer, alongside other key stakeholders such as GPs and identified clinicians, risk assessment, genetic counselling, psychosocial support and preventative surveillance including mitigation suggestions and treatment options.

7.2.2 Recommendation 4:

- GHSNZ receive additional funding
- an increased number of genetic counsellors
- improved/updated systems along with development of a register for medium to high risk patients who require surveillance similar to the Familial GI Cancer Service funded by the Ministry of Health (MOH) as those responsible for guiding this target population have no easy means of identifying and tracking them
- those at medium/high risk not yet diagnosed with breast cancer receive funding for psychosocial counselling as they have not yet entered the cancer pathway[22].

7.2.2 Recommendation 5: BCAC recommends refinement and adoption and subsequent implementation of breast cancer standards (Tumour Standards were developed in 2013 but not implemented[23]) and guidelines for people to navigate and enter the breast cancer pathway either through risk assessment, prevention, surveillance or treatment services particularly for those whose family history or risk is less clear.

Implementing a broad risk assessment approach complemented by a health literacy programme is important because it is more common today that people learn about this disease at the point of diagnosis which precludes any opportunity for risk mitigation, tailored surveillance or intervention. Statistics indicate that Māori women may need to be screened earlier as their cancer is being found too late. A risk assessment profile may differentiate which women are potentially at most risk. Such an initiative alongside research would help detect the key cause of Māori women's earlier onset of the disease.[24]

7.3 Detection and screening

Better health outcomes and optimal use of public health resources could be achieved by tailoring the timing and modalities of breast screening to the needs of individuals and population groups based on their risk profiles.

For example:

- Research shows that annual mammograms between ages 35 and 39 for women with a medium to high risk of breast cancer can significantly improve the chances of detecting tumours before they have spread to the lymph nodes[25].
- It also shows that women aged 69-74 would benefit from screening[26].
- Using MRI as well as mammography for young women with a high risk of breast cancer can be cost-effective and contribute to reducing mortality of these women[27].
- Using MRI in addition to mammography for women with highly dense breast tissue has been shown to significantly improve cancer detection rates[28].
- Greater community and whanau involvement are needed to ensure engagement; participation of the targeted screening community is critical for both first and repeat screening[29].

New Zealand's current system of one-size-fits-all, relies heavily on just mammography. It is under-resourced (as well as undersubscribed) and is not optimised to detect breast cancers as early and late as it should. The current New Zealand screening programme misses 50% of all breast cancers, and of those detected via screening, 30% will go on to develop advanced disease and yet again 2/3 of advanced breast cancers were not detected through screening (suggesting detection was later than it should be)[30].

As stated above, a differentiated risk approach could help to tailor breast cancer screening depending on an individual's risk. It could help determine what age a person is first invited for breast screening or how regularly they are invited to receive it and the form of screening offered.

7.3.1 Screening modality, timing and frequency

In reviewing how and when women should be screened it is important to reflect on four significant trials which have reported in the last two years (PROCAS 1 and 2[33]; MRISC[34], RIscFaM[35] and DENSE[36]).

They collectively show that:

- Breast cancer stratified screening is seen as ready for implementation if breast density and SNP's are included (The PROCAS team, SABCS, December 2018).
- Annual screening detects breast cancers earlier for women with medium to high risk[37].
- Those with a family history and aged 35 to 39 had cancers detected significantly smaller and were less likely to have spread to the lymph nodes.
- Screening with MRI improves survival for women with familial risk of breast cancer (age 35 to 50 years) by 25% at $134 932 (€102 164) per LYG compared with 17% mortality reduction at $54 665 (€41 390) per LYG with mammography only (MRISC Trial).[38]
- MRI detects significantly more cancers and at a relevant earlier stage, fewer large and node positive cancers occurred and fewer interval cancers resulted from MRI while clinical breast examination CBE was shown to be so poor it was better discarded, and contrast mammography was less reliable (RIsc FaM Trial).
- Supplemental breast MRI screening utilising Volpara technology (C. Feedon et al 2019)[39] to measure breast density resulted in an improved cancer detection rate of 16.5/1000 with a significantly reduced interval cancer rate of 0.85 compared to mammogram alone with detection of 5.06/1000 (DENSE, 2019[36]).
- Mortality reduction has been proven for mammography and these trials clearly show that MRI performs better and detects biologically significant cancers earlier.
- Cost effectiveness and feasibility issues are being investigated within the DENSE trial, including reduced need for treatment and improved quality of life through early detection which will be published by year end.
- Use of abbreviated MRI[40] (14 m. vs 42 m.) is demonstrating adequate sensitivity and specificity (85% and 89%) in the differentiation of benign and malignant breast lesions and decreased false positivity in combination with Dynamic Contrast MRI. The basic European breast MRI takes 42 minutes; an abbreviated protocol would take 14 minutes and an unenhanced protocol 6 minutes. 2D and 3D protocols performed similarly with just a 0.1% difference. The results demonstrated benefit across all levels of the breast density scale (A, B, C, D) with critical improvements in C and D.
- One of the trials PROCAS 2[41] now utilises the BODICEA model to get a broader and improved differentiation of risk.
- While the PROCAS model is linked into Manchester UK's screening services the BODICEA model itself is clearly linking itself to the primary health service in the first instance.
- A new factor in the BODICEA risk assessment tool, breast density, is neither routinely measured nor reported in New Zealand. In the US a new Federal law for Breast Density notification saw US Senator Dianne Feinstein (CA), 15 February 2019, state that as part of the funding bill Congress passed, the FDA must now ensure mammography reports include appropriate breast-density information in order to catch breast cancer early. According to

DenseBreast-Info.org, the law directs the FDA, through the regulatory process to ensure that mammography reports received by patients and their providers include appropriate information about breast density.

- In New Zealand, BreastScreen Aotearoa neither measures nor reports breast density. Automated systems that use software utilising AI to measure density from digital mammograms give reliable density measurements. In New Zealand, Volpara technology is being used by Mercy Radiology in Auckland, St Marks Radiology and BreastScreen Central in Lower Hut. Volpara is a leader in its field.
- Of note a 2013 study involving 3,000 women showed that Māori women may have greater volumetrically dense tissue in their breasts than Pasifika, Pakeha and Asian women[42]. Greater constructive discussion about breast density among health providers, researchers and consumers would lead to better breast cancer outcomes in New Zealand.

7.3.1 Recommendation: New Zealand's publicly funded national breast cancer screening programme (BreastScreen Aotearoa (BSA)) be funded to:

- Develop a more strategic approach to screening which utilises new technologies and tools for example BODICEA or IBIS including breast density (utilising Volpara) (with SNPs) so that those of moderate and high risk may be screened early and often enough using the correct modality
- BSA retrospectively or prospectively initiate a trial to better understand the potential cumulative risk factors Māori and Pasifika women experience at an earlier age so that potential ethnic differences may be identified, and screening timing and modality corrected.
- BSA measure and report breast density to New Zealand women when they go for mammographic screening and those with highly dense breasts be advised of their potentially increased risk of breast cancer and the limitations of mammography as a screening tool for them and that they be recommended for supplemental screening using ultrasound and or MRI (full or as it is introduced abbreviated).

7.3.2 New screening systems

There are two additional clinical trials we wish to highlight for two different forms of screening occurring in New Zealand at present. These are not in clinical practice but are currently being trialled. Their mention is for completeness. Tiro Medical's Imaging Elastography system[31] which has no radiation and uses magnetic resonance elastography (MRE), which measures tissue elasticity or stiffness and is based on tissue response to vibrations, is undergoing a clinical study in the Canterbury region. Current resistance by some to screening with radiation may reduce with MRE technology. Secondly, University of Waikato professor Yifan Chen from the School of Engineering has developed a system which uses microwaves like a mobile phone. It is proposed as cheaper, painless and less harmful than current screening systems used to detect cancer in women. It would improve access in rural areas, and they suggest that for those at high risk it should perform similarly to MRI. The scan takes four minutes, probes the breast and distinguishes tissue density and abnormalities. The resulting images are immediate. Chen indicates that if someone has cancer it has different bioelectric properties compared to healthy tissue[32].

7.3.3 Screening engagement and participation

High levels of participation and effective and timely follow-up of identified abnormalities are necessary for screening to lead to improvements in breast cancer outcomes and to reduce inequalities.

Reasons for non-participation in breast cancer screening include practical difficulties such as access to transport, travel time, and inconvenience. A 2009 study revealed twenty percent expressed concern or fear of the procedure, or were influenced by negative reports from other women[43]. In 2009 Ross Lawrenson et al. retrospectively reported on a highly successful initiative based out of Te Whanau a Apanui Community Health Service ('TWAACH') which provides primary health care to a rural, coastal, predominantly Māori community in the Eastern Bay of Plenty. Involvement of TWAACH and the local community was critical as they facilitated the provision of information about and promotion of breast screening, improved the identification of eligible women, and improved the registration and appointment making processes. As a result, breast screening participation improved from less than 45% to about 98% in both 2005 and 2007. The general principles underlying the strategies employed have been implemented in other General Practice and PHO settings to improve breast screening coverage, reduce ethnic inequalities in coverage and ultimately, improve breast cancer survival. This has been seen most recently in Whanganui with its One Stop Shop and the results are clear. Research shows that for screen detected cancers there is no inequity and so improving detection and methods of detection alongside improved communication, health literacy and treatment as non-screen detected patients negotiate the care pathway would result in substantial improvement[44].

Cooperation between BreastScreen Midland and TWAACH improved the responsiveness of the system to local needs and facilitated access to breast screening. The on-going active involvement of TWAACH improved coordination for local women.

Strategies used did not require new services or resources, requiring only local input, flexibility and collaboration between existing services. BSA appears to be resource poor with inadequate supporting systems for the future with targets not being met in some regions. Their reports (December 2018) show (excluding 45-49-year olds) and keeping in mind the target is 70%, there are coverage issues for Māori in Auckland (59%), Waikato (59.5%), Bay of Plenty (64.5%) and Taranaki (63.3%) whereas Nelson Marlborough (73.5%) and Whanganui (73.3%) are doing extremely well. For Pasifika women, Counties Manukau are performing very well with (83%) whereas the Westcoast is performing poorly at 44%. Total numbers screened for all ethnicities do not meet 70% in Waitematā, Auckland and Tairawhiti. For Asian women no region is performing well with South Canterbury performing the worst at 28.5%.

There is also a worrying reduction in the number of women being rescreened within 27 months of their first mammogram. Rescreening targets are not being met: Only 51.6% of Māori and 51.9% of Pasifika women showed up for rescreening while other was at 66.9%. These statistics tell us that more women than necessary will go on to develop advanced breast cancer because their cancer will be detected too late.

7.3.3 Recommendation - BCAC recommends that:

- BSA, like other countries, implements a population register from which those to be invited are enrolled and from there are invited back for a rescreening schedule based on their level of risk.
- BSA follow the TWAACH model to encourage participation at community level, which is committed to 100% participation rather than registration alone as an end point.
- BSA focus on improving the number of women attending repeat screening through better information regarding risk and stronger community involvement.
- BSA reports findings for high risk women of a younger age, 30-49 years
- BSA provides regular interval cancer reports (cancers detected outside of screening)
- BSA be appropriately funded, including new systems to support a greater population base
- BSA work with researchers to implement technological changes such as radiological deep learning strategies to reduce costs in the short and longer term and
- MOH recognise the status quo is unacceptable and that doing more of the same is not improving breast cancer outcomes.

We therefore need to enhance early diagnosis through more strategic, comprehensive tailored risk assessment programmes to improve outcomes from our population-based screening programme with the need to incorporate different screening modalities beginning with MRI at an earlier age and greater frequency for those at high risk. Alongside these tailored approaches we need strong engagement from a community which is increasingly health literate, engages and participates on a timely basis with a system that understands local delivery and is culturally competent to ensure early diagnosis.

7.4 Detection beyond screening - diagnosis for early and advanced breast cancer

A recent US study published in the Journal of the American Medical Association (9 January 2018) looked at which factor - screening or treatment - was behind the global reduction in breast cancer mortality over the past several decades. It found that the answer is simple: both, depending on subtype (Sylvia Plevritis, PhD et al 2018)[45]. We know however that our Māori and Pasifika women have shared too few of these benefits. This needs to change while concurrently we improve the pathway for all. Earlier detection and diagnosis will be cost effective relative to the cost of subsequent treatment for a more advanced condition requiring more complex and potentially ongoing treatments.

New Zealand should be prepared for new technologies, some of which are being developed in New Zealand and elsewhere, which will transform cancer care; for examples see below.

7.4.1 Liquid biopsies and genomics

Liquid biopsies (circulating tumour DNA or RNA) are proving transformative in cancer diagnosis and monitoring, along with genomic technologies (Turner, N et al, 2018)[46] they can more nimbly diagnose breast tumours, identify relapse and predict or quantify treatment response, including tracking clonal evolution and the resistance to therapy it can bring (Reinhardt, Franken et al. 2017)[47] along with describing the heterogeneity of pre-treated advanced breast cancer.

"Liquid biopsies" of blood will supplement, and may in time displace breast tumour tissue biopsies as the gold standard for guiding therapy. Such assays are currently available in New Zealand through Sequenca Genetics, e.g. *Guardant 360*, but only for those who can afford it.

7.4.1 Recommendation 1: BCAC recommends the Healthier Lives CtDNA initiative lead by Professor Parry Guilford et al., continue to be supported and is pleased to see he has recently won an award from HRC for an "in dwelling" device to pick up the tell-tale cancer biomarkers[48]. This technology will move diagnosis and monitoring from the hospital to the community through maintenance therapies and quick assessments[49].

Likewise work in the blood genomics field has culminated in a recent publication in the Journal Science of the CancerSEEK method, which combines detection of cancer mutations (highly specific but relatively insensitive) with protein markers of cancer (highly sensitive but relatively non-specific) (Cohen, Li et al. 2018)[50]. The Sweden Cancerome Analysis Network initiative aims to include all patients with breast cancer for tumour genomic analysis, and to deliver molecular subtype and mutational data back to the treating physician (Ryden, Loman et al. 2018)[51].

7.4.1 Recommendation 2: New Zealand researchers be supported to keep up with international progress in this area as they will require well-resourced population-scale approaches such as the use of novel genomic and molecular biomarker tests being introduced as more precise tools to guide therapy.

Moving diagnosis and monitoring from the hospital to the community through maintenance therapies and quick assessments will assist patients and an overly stretched hospital system. Increasingly these techniques will assist with early detection.

7.4.2 Predictive and prognostic analysis

Identifying biomarkers for breast cancer patients remains a critical challenge (Solinas, Gombos et al. 2017)[93] and should continue to be a focus of research teams in New Zealand. New Zealand research recently published in British Journal of Cancer (Dong Xu Liu, Feb 2019)[52] demonstrates that a cancer-related protein named SHON (secreted hominoid specific oncogene) can accurately predict if a patient will benefit from endocrine therapy, and a patient's response to chemotherapy before surgical removal of the tumour.

Clinical and pathological data

Breast cancer led the precision medicine charge several years ago with therapeutic stratification via oestrogen receptor immunohistochemistry and (Her2) *ERBB2* gene amplification testing. Professor Carlos Caldas and a team based in the UK and British Columbia have identified 11 subtypes of cancer by looking at faults in DNA and patient behaviour over a long period of time[53]. Differences define how breast cancers will behave and the likelihood of their return post-surgery. Laboratories worldwide have helped to develop and validate this universal classification of breast cancer. The value of this approach is being trialled through the Personalised Breast Cancer Programme – with the aim to tailor treatment to individuals based on their DNA. This programme is also seeking to develop

treatments for women within the 11 subtypes when it becomes clear they are not responding to existing therapies. They are also looking to develop a test to be more easily used in the NHS.

To further assist in treatment decisions, Predict v2[54] and the NPI and NPI+[55] are used by clinicians including in New Zealand. Predict 2 gives 5-, 10- and 15-year survival ratings post-surgery to provide an understanding of the additional benefits of different treatment regimens. Very recently a New Zealand specific prognostic nomogram has been developed, which includes ethnicity information and has been shown to be more accurate at predicting outcome in a New Zealand cohort than the NPI[56].

Even with this level of information a need exists to further stratify patients.

Genomic data from tumours

To provide molecular information about an individual's breast tumour, genomic tumour tests have been developed, which measure the levels of specific RNAs. The most well-known are Genomic Health's Oncotype DX, Agendia's Mammaprint, and Nanostring Technologies Prosigna, each able to predict the risk of recurrence and the benefit of treatment options. In contrast to the nomograms described above these have been approved for use in patient groups to assist treatment decisions[57]. They are publicly funded or subsidised in US, Canada, UK as well as Israel, Switzerland, Ireland and Greece and unless funded within our healthcare system, these tests have the potential to increase disparities in New Zealand where they cost approximately $6,000. There are at times discrepancies across these tests however when used in combination with other factors above and below they are proving to assist clinicians tailor care while often saving health systems money and patients' time and wellbeing.

Non-invasive protein biomarkers

Currently there are protein biomarkers which are approved for use in the clinic for breast cancer patients to monitor response to treatment for both early and advanced breast cancer patients, alongside tumour receptor status including cancer antigen CAS 15-3 and carcinoembryonic antigen (CEA). A lift in protein level may be an indicator of relapse. These markers are only recommended for use by the European Group on Tumour Markers[58]. Within the New Zealand healthcare system any new test is more likely to be adopted early if affordable. The work of researchers like Guilford[49] and Lasham et al[58] who both look to produce affordable prognostic blood tests would ensure all women would potentially benefit. Both are looking to develop a test to further improve predictive ability[59], complemented by other assays.

It seems no one test alone is entirely reliable, but a combination of tests performed consistently will ensure that clinicians are better able to stratify patients and ensure they have the information they need when patients fall into the intermediate or moderate risk groups.

For example, in the future women at the time of surgery would have a blood sample taken to measure the level of plasma markers. From this, doctors could tailor their treatment. It

will also influence how much surveillance a patient requires after surgery. If women show an increased risk of recurrence of breast cancer it will help determine the surveillance level required and identify if more aggressive treatment is necessary. It could also assess who does not need chemotherapy with subsequent saving to the New Zealand health system and improvement to the quality of life for New Zealand women.

7.4.2 Recommendation 1: Predictive and prognostic biomarkers, genomic and plasma testing should be standard of care.

7.4.2 Recommendation 2: BCAC recommends continuing to support for local plasma initiatives and funding for genomic testing so that we may better understand whether our population base is as similar to other countries as perceived.

7.5 Treatment

In New Zealand outcomes for those with advanced breast cancer are poor compared to other Western countries (*I'm Still Here*, BCFNZ report)[12].

New Zealand has significant ethnic inequities in cancer care and outcomes.

7.5 Recommendation 1 - BCAC recommends that:

- New Zealand's tumour standards for the treatment of early breast cancer (*Standards of Service Provision for Breast Cancer Patients in New Zealand*) be finalised and implemented
- New Zealand adopts and implements ESMO's Guidelines for the prevention, diagnosis and treatment of advanced breast cancer
- Breast cancer treatment and therapies are evidence-driven and responsive to New Zealand and overseas research findings
- Therapy is locally delivered (Local Delivery of Oncology – LDO) and supported by telehealth to supplement delivery, in some instances from specialist nurses with doctor support
- Senior nurse specialists be enabled to prescribe to reduce doctor involvement where appropriate
- Treatment in NZ should be future-focused, and we should embrace new tools and technologies
- DHBs should work to reduce and remove inequality of service that is race based:
    - Recruitment campaigns to increase the number of ethnicities represented through all roles within DHBs to be more representative of the population
    - Making staff aware that some ethnicities e.g. Māori may prefer not to assert themselves to get the treatment they deserve
    - Improve health literacy for patients, clinicians and care providers together to ensure a clear pathway for proactive detection, diagnosis and care which incorporates a cultural context and is equitable
    - Leadership making it clear that institutional racism exists and is not acceptable
    - Mentoring those who need assistance
    - Introducing standards and guidelines so that it is clear all will receive the same level of treatment including genomic precision oncology and research

- More timely funding of new treatments by PHARMAC through a significantly increased budget and streamlined processes and
- Providing locally delivered treatments where possible.

BCAC has consulted with breast cancer specialists and identified current issues of concern. These include:

- Lack of timely access to medicines and clinical trials
- Lack of access to clinical trials in advanced breast cancer
- Lack of funding for diagnostic biopsies for advanced breast cancer patients
- Lack of timeliness for radiologically guided biopsies due to shortage of radiologists
- A need for Multidisciplinary Meetings (MDM) for advanced breast cancer patients
- Better methods of remuneration for treating advanced breast cancer patients
- Limited ability to be able to assess response to chemotherapy on a timely basis
- Slowness or non-referral of advanced breast cancer patients to medical oncology
- Inadequate staff resource
- Inadequate facilities
- Lack of funding for cancer as a chronic condition
- Inadequate access to radiotherapy
- Waiting times for new patients for medical oncology.

BCAC acknowledges that improving breast cancer outcomes involves a wide spectrum of activities including prompt access to surgeons, radiation oncologists, medical oncologists, medicines, imaging, pathology and haematology services, as well as the facilities, staff and training needed for these. There is a very strong need to increase resources and reduce inequities within the public health system.

The New Zealand Breast Cancer Registers have been especially instructive for understanding inequities in outcomes of breast cancer that affect Māori (Tin Tin, Elwood et al. 2018)[60] and Pasifika (Brown, Lao et al. 2017) women[61].

Recent research has shown alarmingly poor survival for all New Zealanders with advanced breast cancer, compared to those in other countries. In New Zealand the median survival is 16 months, compared to 29.4 months in the Netherlands, 36.8 months in Germany, 25 - 54 months in the USA, 23.1 months in France, and 33 months in Sweden[12]. Overseas expert, Dr Fatima Cardoso, Chair of the ABC Global Alliance and co-author of ESMO guidelines for treatment of advanced breast cancer[62], confirmed our fears about New Zealand's poor outcomes for breast cancer patients by referring to the 'worrisome case of New Zealand' and stating that the outcomes were 'not like those of a developed country' (Cardoso presentations, Auckland, 29 January 2019 and Wellington 'Cancer Care at a Crossroads' conference, 1 February 2019). The adoption of ESMO guidelines will assist DHBs to improve outcomes and remove inequities.

Studies using data from New Zealand's comprehensive Breast Cancer Registers published by researchers based at the University of Waikato have demonstrated serious socio-economic inequities in access to breast cancer detection, treatment and outcomes. Further analysis

presented by the Breast Cancer Foundation NZ reveals ethnic inequities in the number of treatments provided to Māori women with advanced breast cancer and their survival.

To reduce and avoid perpetuation of inequities in the care of New Zealand breast cancer patients, equitable access is required to genomic precision oncology and equitable participation in any research that drives a reduction in incidence, improved detection, reduction of delays in diagnosis, and improvements in future oncology are critical. This view is echoed in Davis and Newman (2018)[63].

There is growing acceptance in the research community (Turner et al. 2017)[64] that advanced breast cancer patients with adequate performance and an interest in clinical trials should all have access to next generation sequencing although clinically there is a need for caution with mixed accessibility to treatments globally and mixed levels of capability to clinically manage these. Turner also asserts that circulating tumour DNA level will be a robust surrogate of drug efficacy with potential to enhance drug development and provides a guide to therapy and intervention studies required now.

7.5 Recommendation 2: BCAC recommends:

- New Zealand researchers work with patients and clinicians locally to grow and develop knowledge and capability through translational research and clinical trials so that advanced breast cancer patients receive care in accordance with measures/targets, guidelines and standards of care yet to be implemented.
- Advanced breast cancer patients in New Zealand receive biopsies/imaging, new treatment regimens, adequately funded palliative care, with a focus on either escalation or de-escalation of treatment guided by genomic precision oncology and an expanded arsenal of targeted therapies.

There is hope for better stratification of therapies using genomic signatures of tumour "immune enablement" (Miller et al. 2016)[65] and New Zealand's long-standing immunology research community is well-placed to take up this challenge.

Breast cancer specialists having identified their issues of concern regarding tertiary care expanded on these issues below:

- **Lack of timely access to medicines and clinical trials**
    - Lack of access to effective drugs especially CDK4/6 inhibitors such as palbociclib and other important medicines including fulvestrant, eribulin, everolimus, nab-paclitaxel, T-DM1 (Kadcyla®) and trastuzumab beyond progression.
    - The tortuous path and time taken prior to these drugs being funded in New Zealand
    - Lack of access to clinical trials in advanced breast cancer (ABC) - often due to being unable to provide the control arm study drugs – a consequence of the above lack of funding and failure to provide the recognised standard of care.

- **Lack of funding for biopsies for breast cancer patients**
    - In some centres, lack of resource for biopsies to tailor and adapt treatments in ABC. This is accompanied by a lack of recognition from other services that this is standard of care and therefore funding is required for it
    - Lack of timeliness for radiologically guided biopsies due to shortage of radiologists.
- **A need for Multidisciplinary Meetings (MDM) for breast cancer patients**
    - A need for MDMs focusing on patients with ABC, with radiology and pathology, doctor and nurse medical oncology specialist input. This is not currently available as MDMs focus primarily on early breast cancer patients.
- **Funding for cancer as a chronic condition**
    - There is a need to recognise that cancer exists for some women as a chronic illness
    - As breast cancer prevalence/ incidence increases, and clinics fill up with patients the current KPI of First Specialist Assessment (FSAs) does not recognise the need for continuity of care for ABC patients and needs to be changed to recognise this along with appropriate funding.
- **Better methods of remuneration to service providers for breast cancer patients**
    - Medical oncology services are not adequately remunerated for patients with cancer under long term follow up. Funding currently focusses on numbers of new patient assessments. Given the chronicity of a patient's disease in the ABC setting, the long duration of their care under oncology and the need for multiple lines of therapy, there should be better and more applicable methods of remuneration to better resource this service.
- **Limited ability to be able to assess response to chemotherapy on a timely basis**
    - Significant problems in some centres with CT imaging in all cancer types/setting which impacts their ability to assess response to chemotherapy in a timely way. More resource for radiology specifically for oncology would relieve this.
    - Lack of re-staging resource – to make sure patients are only on therapy if it is helping them – clinical deterioration occurs often 'too late' to allow for patients to try other active therapy or even stop therapy on a timely basis.
- **Slowness or non-referral of breast cancer patients to medical oncology**
    - There is an issue with slowness of referral to medical oncology and lack of referrals to medical oncology for breast cancer patients New Zealand wide. It will be useful to explore the data generated through the NZ Breast Cancer Registers and investigate this more closely to ascertain why this is the case, although some explanations may lie outside of the register data in its current form.
- **Inadequate staff resource**
    - Staff – in many instances there is a need to improve staff resource shortages by providing funding for medical oncologist senior specialists (MOSS/COS) are not seen as having the capability to manage this work, trained nurses, clinical nurse specialists, pharmacists, radiologists and haematologists are required now.
    - Better resourcing and coverage for when specialist staff take leave.
    - A clinical nurse specialist for ABC would potentially be of benefit, to try to improve uptake of and adherence to endocrine therapy and chemotherapy.
    - Lack of access to pathology time to discuss complex cases.

    - All centres see a pending need for more staff and a risk of further staff shortages as demand grows, and yet there seems to be limited planning for this eventuality.
- **Inadequate facilities -** In many centres there is a need for more chemotherapy chairs and day unit space and time.
    - In some instances, ABC patients are being given lower priority over early breast cancer patients to help manage shortages.
    - Some patients are required to travel to access facilities. These patients may choose non-attendance as they cannot afford the time and cost of travel.
    - For some facilities with inadequate space, patients are being admitted rather than being treated as outpatients.
    - Inadequate space is an ongoing issue which needs to be addressed.
- **Access to radiotherapy**
    - Patients away from the main centres travel distances for prolonged periods of time to receive radiotherapy. As a result, some patients choose other options such as non-attendance or mastectomy.
- **Waiting times for new patients for medical oncology**
    - In some instances, waiting times for a new patient appointment can stretch to several weeks or months during times of annual leave/heavy referral periods. There is also pressure on follow up appointments and clinics are often over-booked and/or patients seen during non-clinical sessions.

Local delivery of care as close to the patient as possible is one of BCAC's recommendations. Breast cancer, being a high volume, complex disease, is ideal for this. For example: utilising subcutaneous trastuzumab to enable PMOs to assume responsibility for this care of HER2+ patients who currently require regular infusions in hospital facilities throughout the country would save resource and time for both the patient and DHBs. Such an initiative would also improve adherence to treatment. It would improve tertiary resource productivity and reduce the time involved for patients. Enabling care closer to home reduces travel time and reduces parking costs. It is in line with New Zealand's Health Strategy.

In addition, enabling Senior Nurse specialists to prescribe would also free up clinician time and enable patients once again to receive their treatment locally. Patients enjoy being treated close to home within their community, it provides a psycho-social benefit as well as an economic benefit.

7.5.1 Access to medicines

Access to new medicines can, to a large extent, account for major improvements in breast cancer survival in the developed world over the last 40 years[66]. As research continues to reveal the multiplicity of sub-types of breast (and other) cancers, the ongoing discovery of new medicines to target each type more precisely is leading to more effective treatments, better quality of life and longer life for cancer patients.

NZ's access to breast cancer medicines (and cancer medicines in general) is poor and has fallen far behind that of other developed countries. This has severe consequences, as evidenced by our shockingly poor outcomes for New Zealanders with advanced breast cancer.

NZ's budget for pharmaceuticals is inadequate and has failed to keep pace with inflation. Economic analysis by NZIER[67] points out that investment in medicines has fallen year on year from 8.1% in real terms in 2007 to only 4.7% in 2017/18. It identifies a $375 million investment gap in government-funded medicines made available through the public health system in New Zealand, in order return to the 2007 level of the Combined Pharmaceuticals Budget, but this would still leave us well below the OECD average.

Our medicines budget represents 0.34% of GDP, while the OECD average is 1.4% of GDP. New Zealand currently spends $199 per person per year on medicines compared to the OECD 2016 average of $951. Of the 36 OECD countries, only Mexico invests less in medicines than New Zealand (PHARMAC, 2017)[68].

Many patients needing high-cost innovative medicines that remain unfunded by PHARMAC are forced to fundraise or miss out on treatment. This creates and compounds socio-economic inequity where the wealthy purchase medicines that will provide longer, healthier lives. Recent research has shown that those treated for breast cancer in NZ's public health system have a 95% higher chance of dying than those treated in the private system (Tin Tin, Elwood et al. 2018)[60].

The pharmaceuticals budget is the only capped budget in NZ's health and disability system. NZ is unacceptably slow to adopt new breast cancer medicines compared to other countries.

Breast cancer medicines which have been funded in NZ have taken nearly three years on average from the time of application to listing.

The ESMO ABC guidelines[62] were agreed by 42 expert authors from 24 different countries: Portugal, Poland, Italy, Cyprus, Switzerland, France, Germany, Mexico, Brazil, Sweden, Netherlands, Spain, Lebanon, Romania, UK, Australia, Israel, India, USA, Uganda, Denmark, Japan, South Africa, and China. To reach the internationally agreed standard of care, New Zealand should implement these guidelines.

7.5.1 Recommendation: BCAC has identified 12 breast cancer medicines and many more indications that are commonplace in other countries which need to be funded in NZ (palbociclib, trastuzumab emtansine (T-DM1), fulvestrant, nab-paclitaxel, everolimus, pertuzumab for patients already being treated with trastuzumab, sub-cutaneous trastuzumab, pegylated doxorubicin, lapatinib for second line use, eribulin, denosumab and trastuzumab for treatment beyond progression). These should be funded in New Zealand. There are 24 different medicine treatments in combinations and sequences recommended in the ESMO Guidelines for Advanced Breast Cancer for the different sub-types of advanced breast cancer medicines that are not funded in New Zealand. The absence of a toolkit of funded treatment options that can be tailored to individual patients, so that when one stops working another is started, means those unable to pay high costs are simply denied further treatment and die earlier. These guidelines should be urgently implemented in New Zealand.

As well as the societal impacts, these delays in funding cost-effective medicines result in health system costs such as hospitalisations, as well as higher mortality, more productivity loss and greater loss of quality of life[69].

7.6 Support and care

A diagnosis of cancer has a huge impact on an individual and their family/whānau. A patient-centred approach provides for the emotional, psychological, social, cultural, economic and spiritual requirements of the individual and their family/whānau, along with their physical needs.

Most women affected by breast cancer experience some form of distress. For most women, this resolves with time and general support, without the need for specialised interventions.

Many women and their families will need additional support to help them cope. Assessment of women and their family/whānau support needs should be undertaken at key points along the breast cancer care pathway.

For some, the distress can be significant and enduring, and may lead to depression, an anxiety disorder or other problems requiring specialist intervention. It is estimated that up to 30 percent of women diagnosed with breast cancer develop psychological morbidity within one year of diagnosis (NZGG 2009).[70]

Support from everyone surrounding the woman with cancer – especially providers of cancer services – is crucial. Evidence suggests that when women with cancer receive good social, psychological and cultural support the quality of their life improves.

Health professionals as a group are proven to be poor at identifying cancer-related distress in women and their family/whānau without use of a formal tool.

Women with breast cancer are often reluctant to discuss their distress with health professionals for fear of judgement, or they may perceive staff to be too busy. Some minimise their issues, believing 'others are worse off than me'.

An accurate assessment is more likely if information is gathered from a variety of sources including the use of a validated tool and a consideration of the risk factors, or vulnerability for distress.

Between 15 and 55 percent of cancer patients may require specialised assessment and intervention (Howell et al 2009).[71]

BCAC notes that excellent suggestions for improving supportive care for cancer patients were made in the provisional 'Standards of Service Provision for Breast Cancer Patients in New Zealand' produced in 2013 by the National Breast Cancer Tumour Standards Working Group. There has been no progress in implementing these standards and so we repeat them here.

BCAC recommends:

7.6 Recommendation 1: Women with breast cancer are screened with a validated tool to identify psychological and social needs at key points of their breast cancer experience.

('Validated tools' include the 'Distress Thermometer' or a cancer-related distress self-assessment tool [e.g. see Appendix 4 in 72]. 'Key points' include at diagnosis; at the start, during and at the end of treatments; during follow-up; and in the event of relapse or terminal disease.)

1.1 All health and social care professionals offer women and their family/whānau (including children) supportive care throughout their cancer journey.

1.2 Care professionals acknowledge each woman's individual supportive care needs, depending on her ethnicity, culture, religion, sexuality, region (rural/urban), education, family circumstances, employment status, economic status and tumour stage.

1.3 Care professionals maintain a high level of cultural competence and understanding of the Māori world view.

1.4 Care professionals make women with breast cancer and their family/whānau aware of all their support entitlements, provide current good quality information about them, and if they choose, guide women through the process of accessing them in a timely manner.

1.5 Up-to-date supportive care services directories are accessible by all staff and people affected by cancer.

1.6 Staff are trained on the use of screening tools and appropriate referral pathways.

1.7 When a woman's distress score meets the threshold for an assessment (eg, ≥4 on a distress thermometer), she is assessed by a health professional who has undertaken relevant training.

1.8 Services develop criteria and pathways for an intervention approach to ensure women are efficiently referred to relevant social or specialist psychological support services (modified Baken and Sutcliffe 2012).[73]

7.6 Recommendation 2: Women or their family/whānau found to have significant psychological distress or facing particularly difficult treatment decisions are offered prompt referral to a specialist psychological service, as part of an integrated cancer service.

2.1 All major cancer units employ a clinical psychologist specialising in psycho-oncology, available to women and their family/whānau.

2.2 Service delivery models provide a tiered approach to supportive care for women and their supporters: that is, provision for psycho-education for many; and one-to-one counselling, cognitive behaviour therapy, short-term group therapy or psychiatric care for a few, where required (modified Baken and Sutcliffe 2012).[73]

2.3 Health care providers are particularly aware of factors associated with an increased risk of psychosocial problems among women diagnosed with breast cancer (NHMRC 2003[74]; expert opinion).

7.6 Recommendation 3: Women may have difficulty accessing cultural and/or spiritual support unless health professionals have appropriate knowledge and training to advise how to seek such support.

3.1 Health and social care professionals help women and their family/whānau (including children) access cultural and spiritual support.

3.2 All women with breast cancer who identify as Māori are asked if they would like to be referred to their local Māori support provider at key points in their journey.

3.3 All women who identify as an ethnicity other than European or Māori are asked if they would like to be referred to specific support services or providers.

3.4 All health care providers are aware of, acknowledge and where possible incorporate specific cultural norms into their practice.

3.5 All women are made aware of available spiritual supportive care services and asked if they would like a referral at key points in the journey.

The suggestions made in the 2013 Standards of Service provision are supported both in the ABC report from BCFNZ (**Appendix 4, ref. 12**) and in the ABC Global Charter published by the ABC Global Alliance.[75]

In addition, the ABC Global Charter highlights the importance of protecting the right to work and providing flexible working conditions and supportive workplaces for patients, including patients with metastatic disease (10 Actions for Change, Action 10). Many cancer patients in New Zealand continue to work throughout their treatment. Many women with breast cancer, including metastatic cancer continue to support their family/whanau during treatment and report the social and health benefits, as well as the financial benefits of doing so.

New Zealand already has flexible working legislation in place which allows for employees to request flexible working hours on a short-term or long-term basis and many supportive workplaces.[76]

BCAC recommends therefore:

7.6 Recommendation 4:

4.1 Health services and information providers include information in their online and other resources to inform patients of their rights to request flexible working conditions to accommodate treatment periods.

4.2 Health services and MBIE work together to ensure greater awareness of flexible working provisions and availability for people living long-term with health conditions such as cancer – and also to improve public understanding of such conditions.

7.7 Clinical trial research

The New Zealand clinical trial research sector generates $384 M in GDP per annum (Medicines NZ, 2017), with 340 trials in 2015 (MOH, HRC, ANZCTR) whereas the Australian sector is worth $1.1 billion and generates 1,306 trials and 6,900 jobs (LEK Consulting, 2015).[77] To compete New Zealand needs to establish an innovation fund for co-sponsoring clinical trials with therapeutic product and pharmaceutical companies and DHBs funded to undertake clinical research as a front-line activity. New Zealand's 10-year R&D spend aspiration is set at 2% of GDP; we support the New Zealanders for Health Research recommendation of 3.3% and tax incentives of 35% in line with Australia. We also recommend an extension of ACC coverage for harm resulting from a clinical trial.[77]

7.7 Recommendation 1: BCAC recommends:

- the establishment of a national framework for clinical trial research at DHBs, PHOs and other publicly funded health service entities.
- Specific health research/clinical trial investment benchmarks and targets.
- Clinical trials investment strategies which will enable New Zealand to be competitive with Australian public health providers and other countries as a place to conduct clinical trials.
- Set targets and develop strategies which will result in public providers including DHBs attracting increased industry investment in trials particularly drug trials.
- DHBs and other publicly funded service providers be funded to undertake clinical research as a front-line activity. They are currently regarded as lacking capacity and slow (6-9 months to establish a trial), and this is having an impact.
- Establish a single accessible register of clinical trials in New Zealand with enough utility, including fields to enable key elements of clinical trial trends to be reliably analysed and monitored.
- Improve funding of the sector (PHARMAC, DHBs etc) as poor funding impacts on clinical trials.
- The reimbursement model (PHARMAC) has caused some suppliers of pharmaceuticals to lose interest in New Zealand as they do not believe their participation here is viable.
- Promote participation in clinical trials through public and physician awareness.

Such initiatives have already shown benefits for New Zealand for example: Hepatitis C Case Study showed the economic benefit of providing a vaccine with 99% cure and $200M savings and the cost savings achieved. Likewise, a New Zealand case study in the use of Saline instead of Albumin saved 137M per annum (Sullivan, 2019)[78].

Clinical trials generate export revenues, avoid public healthcare costs, provide access to new medicines at no cost to the health system, save lives and provide productivity gains. New Zealand's advantages include high quality research facilities, efficient ethics and regulatory framework, and we can accommodate seasonal differences and a diverse participant pool (clinicaltrials.health.nz).

Therefore, BCAC recommends:

7.7 Recommendation 2: More clinical trials are made available to New Zealanders with breast cancer, right across the breast cancer pathway.

At New Zealand Society of Oncology (NZSO) 2017 Mark McKeage described how just 2% of Auckland cancer and blood patients are involved in clinical trials. Over the last twenty years breast cancer translational research, especially genomics, has produced numerous clinically-relevant insights into breast cancer (Low, Zembutsu et al. 2017)[79].

Associate Professor Ian Campbell (2017)[80] views trials as a basic pathway to treatment however he identifies barriers affecting the ease with which a trial participant can move from one region to another and whether trials in New Zealand are adequately administered and resourced.

7.7 Recommendation 3: New Zealanders' participation in clinical trials (an important means for some patients to gain access to new medicines and to contribute to research) is facilitated by full access to treatments that are the current international standard of care, i.e. New Zealanders are no longer excluded from trials aimed at testing the addition of a new

treatment because we cannot participate in the control arm of the study (as medicines that are the global standard of care are not funded in New Zealand) let alone the experimental one.

Changes in the clinical trial environment have seen a noticeable shift to accelerated approvals in the US and a trend to adaptive approval trial designs and combined phases (SABCS, 2017)[81]. These designated approval trials recruit very quickly and now may in some instances be tissue site agnostic, i.e. not dependent on the original site of the cancer such as breast, lung or gastrointestinal, but be "basket –registration" trials in which recruitment eligibility is based on specific genomic alterations.

7.7 Recommendation 4: New Zealand nimbly works to include designated approval trials to bring an advantage to patients and other stakeholders.

7.8 Systems and technology

At an Auckland Medical School public lecture in February 2018, Professor Eric Topol from Scripps in the US, said it is important to put in place systems and technology which will support and not hinder change. He described a range of tools which will help the move towards individualised medicine. How smartphones, big data, and technology are combining to democratize health care assisted by artificial intelligence to process information. The future as described by Professor Topol will require a high level of motivation and commitment from patients and doctors with support from new technologies for such a transformation to occur.

There will be an increasing role for artificial intelligence and other types of computational technology in both breast cancer research and in clinical diagnostic testing. This may include interpretation of imaging (Fusco, Sansone et al. 2016)[82], cytology (Saha, Mukherjee et al. 2016)[83] and histology data (Robertson, Azizpour et al. 2017)[84] and integration of genomic data with protein information (Borrebaeck 2017)[85], (Muthukaruppan, Lasham et al. 2017)[86], clinic-pathological data (Low, Zembutsu et al. 2017)[87] and digital pathology and imaging to personalised biopsies (McKinsey, 2016)[88]. The expectation is that use of machine learning technologies is and will support scientists, clinicians and patients to make well considered decisions on a timely basis with improved patient outcomes.

We hear constantly that sound initiatives are stalled because the systems in place do not and cannot support them and yet we are not aware that MOH are planning to avert the risk of critical systems failing e.g. Breast Screen Aotearoa and GHSNZ. Lack of action is hampering opportunities for improvement in diagnosis and monitoring across a range of age groups. Poor monitoring of high-risk groups results in invasive breast cancer and the resultant advanced disease and higher treatment costs.

7.8 Recommendation 1: New Zealand increases the use of new technologies including telehealth, apps, artificial intelligence and deep learning so that patients, doctors, clinicians, scientists and regulators may more easily play their role in a cost-effective manner to turn breast cancer into a chronic as distinct from a terminal condition. That existing systems are updated and supported to enable these initiatives.

Future technological change will make provision of the information needed by patients more important than ever. There is a need for greater links between patients/consumers and both clinicians and researchers – ideally translational breast cancer research will be a three-way partnership between these groups as will clinical trials and ultimately the introduction of outcomes from both to create new standards of care.

McKinsey wrote about these changes in 2016[88] and again in January 2018[89] suggesting that technological advances are coming in a range of forms, for example: patient data (vital signs, behavioural data, patient reported outcomes), saying there will be a need to structure, integrate and interpret this data to inform care decisions as well as research and development.

The key will be to focus on initiatives and technologies that can improve outcomes and provide benefit in the longer term, as well as those that will improve treatment stratification and reduce costs in the shorter term – we need to get this balance right.

7.8 Recommendation 2: New technologies are used to monitor early breast cancer patients beyond 5 years and that different forms of care are considered, for example, an online specialist support service.

This is not done today, often on the premise that patients will worry. Recent presentations to the Health Select Committee[90] by patients with advanced breast cancer demonstrate that there are failings in the current system. Patients need to remain vigilant and there needs to be a specialist at the end of a phone who can organise a test without the refrain "there is nothing to worry about". It is important to identify symptoms of advanced disease. Access to specialised telehealth specialists supported by access to diagnostic tools would not result in constant fear but earlier diagnosis and less advanced disease with a greater opportunity to treat the advanced cancer as a chronic condition.

7.8 Recommendation 3: The New Zealand Breast Cancer Registers be extended from 60-70% coverage to 100%.

The Registers are a vital tool in enabling us to understand and better manage breast cancer in New Zealand. The data they collect is entirely relevant to New Zealand as it is sourced directly from the New Zealand population. They allow analysis of the disease by factors including ethnicity, age, public vs private providers, treatments delivered and outcomes and have an important role to play in understanding what we are doing well and what we need to improve.

7.8 Recommendation 4: New Zealand should consider "living tissue banks" of breast cancer cells grown as 'organoids' (Sachs, de Ligt et al. 2018)[91] and build on Christchurch and Auckland tissue banks.

As genome wide association studies (GWAS) expand in numbers, we will be able to more accurately identify the epistatic roles of variants in genes associated with low-penetrance breast cancer risk SNPs (Li, Rowley et al. 2018)[92]. There is a need to build on the Cancer Society Tissue Bank in Christchurch (driven by Professor Robinson) and the newly developed breast cancer collection in the Auckland Regional Tissue Bank (driven by Dr Ramsaroop).

8. **What are the top priorities for system level change that would make the biggest difference to New Zealanders?**

Our scientists, clinicians, health professionals, policy makers, consumers, communities and New Zealand's four largest breast cancer charities need to continue to collaborate and provide leadership to:

a. Enhance prevention by better informing people earlier in their lives about breast cancer risks.
b. Understand risk and more effectively differentiate lethal from non-lethal disease, so that those at higher risk will gain early access to tailored treatment to ensure their cancer is caught early and will be less likely to recur. In addition, more conservative treatment could be offered to those at lower risk of cancer or at lower risk of a lethal cancer.
c. Improve the use of new technologies, artificial intelligence and deep learning so that NZ patients, doctors, clinicians, scientists and regulators may more easily play their role in turning breast cancer into a chronic condition.
d. Provide evidence-based targeted support and resource where it is needed so we can improve detection and interventions, in order to reduce inequities and mortality.
e. Implement national Standards and Guidelines for all elements of the breast cancer pathway including the prevention, risk assessment, early diagnosis, predictive and prognostic support for neoadjuvant, adjuvant treatment, advanced treatment, continuing monitoring, biopsy and diagnosis as well as support and palliative care for cancer patients.
f. Invest in cancer research and clinical trials which investigate and optimise risk assessment to tailor screening and therapies, suited to New Zealanders' needs.
g. Provide timely and transparent funding of new evidence-based treatments through an improved, better funded medicines access system.
h. Enable all key stakeholders to work together towards a common goal of improved healthcare for all, in line with developed country expectations including addressing inequities for Māori and Pasifika women within and across the public health system in both what is provided and how it is provided
i. Ensure that governance of the Health & Disability System incorporates a truly independent body that is tasked with questioning and checking the performance of Departments and Institutions within the system. This organisation would incorporate a group of representative stakeholders including authentic consumer representatives.
j. Where a gap in the health system has been identified, describe a vision of what is possible and develop a plan for its rapid implementation. Develop a plan for a transition as we implement each aspect of the plan that incorporates regular monitoring, evaluation and input of new information to determine progress and success while continually tailoring and adapting what is delivered over time.
k. Ensure that transparency, openness and honesty are values underpinning the whole health system and that these are demonstrated by employees from senior leaders to the lowest levels across all health system entities.
l. Continually strive to problem solve, improve and achieve culturally competent local delivery of high-quality healthcare.

9. **Is there anything else you wish to add?**

There is a clear need to provide adequate reimbursement for existing structures: MOH, PHARMAC, DHBs, Primary and Community care, which will require a significant increase in the health budget. This is a political decision. We request that the panel clearly inform the Government of the critical need to properly resource all elements of the health system, with a particular focus on cancer control and care, and with medicines funding an urgent priority. By investing now, we will save time, resources and lives in the longer term.

Notes and References

1. Developed countries have advanced technological infrastructure and have diverse industrial and service sectors. Their citizens typically enjoy access to *quality* health care and higher education. (emphasis added) - https://www.bdc.ca/en/articles-tools/entrepreneur-toolkit/templates-business-guides/glossary/pages/developed-country.aspx?type=Def&order=1&intlnk=rightbox
2. Lawrenson R, Blackmore T, Campbell I, Scott N. How to Improve Outcomes for Women with Breast Cancer in New Zealand. Health Research Council of NZ and the University of Waikato; 2018. Health Research Council Reference: 14/484
3. BCAC acknowledges a small number of women are receiving treatment in a pilot programme.
4. https://www.partnershipagainstcancer.ca/about-us/our-mandate/
5. http://www.pbs.gov.au/info/industry/listing/participants/pbac; http://www.scottishmedicines.org.uk/Public_Involvement/Public_Partners; http://www.scottishmedicines.org.uk/Public_Involvement/Public_Involvement_Network_Advisory_Group ; https://www.nice.org.uk/media/default/About/NICE-Communities/Public-involvement/Patient-and-public-involvement-policy/Patient-and-public-involvement-policy-November-2013.pdf; https://www.cadth.ca/collaboration-and-outreach/advisory-bodies/pcodr-expert-review-committee-perc.
6. Tin Tin S, Elwood MJ, Lawrenson R, Campbell I, Harvey V, Seneviratne S. Differences in breast cancer survival between public and private care in New Zealand: which factors contribute? PLOS One, 2016. DOI:10.1371/journal.pone. 0153206, April 7, 2016.
7. https://www.nsu.govt.nz/news/screening-matters-issue-38-february-2013/pleasing-improvement-pacific-breast-screening-rates
8. Lawrenson R, Blackmore T, Campbell I, Scott N. How to Improve Outcomes for Women with Breast Cancer in New Zealand. Health Research Council of NZ and the University of Waikato; 2018. Health Research Council Reference: 14/484
9. https://www.health.govt.nz/publication/selected-cancers-2014-2015-2016
10. How to Improve Outcomes for Women with Breast Cancer, Health Research Council 14/484, Ross Lawrenson et al, The University of Waikato, 2018.
11. Voduc KD, Cheung MC, Tyldesley S, Gelmon K, Nielson TO, Kennecke H: Breast Cancer Subtypes and the risk of local and regional relapse. J Clin Oncol 2010, 28 (10): 1684-1691.
12. "I'm still here" – Insights into living – and dying – with Advanced Breast Cancer in New Zealand. Breast Cancer Foundation NZ. September 2018. http://breastcancerfoundation.org.nz/Images/Assets/21893/1/BCFNZ-ABC-Report-2018.pdf
13. https://www.ncbi.nlm.nih.gov/pubmed/29246526
14. ISBN Print: 978-1-74127-336-6 ISBN Online: 978-1-74127-337
15. Professor Cliona Ni Mhurchu et al, OL@-OR@ World Conference of Health Promotion, Rotorua April 2019 (in press).
16. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5773773/
17. https://jamanetwork.com/journals/jamaoncology/fullarticle/2677301
18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6143016/; B-0915 - Impact of the use of a breast cancer risk assessment tool on the intensive screening of women clinically referred to as intermediate to high risk; S. Woussen1, H. Westerlinck2, M. Keupers3, R. M. A. Prevos4, T. Thywissen5, C. Van Ongeval3; 1Harelbeke/BE 2Heverlee/BE 3Leuven/BE 4Meerssen/NL 5Diepenbeek/BE
19. From the US Preventative Services Task Force Report - https://www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/breast-cancer-medications-for-risk-reduction1

20. https://www.nature.com/articles/s41436-018-0406-9

21. https://www.nature.com/articles/s41436-018-0406-9

22. Breast and Ovarian Special Interest Group meeting 28 February, 2019

23. https://www.health.govt.nz/system/files/documents/pages/standards-of-service-provision-breast-cancer-patients-jan14.doc

24. Tin Tin, S., J. M. Elwood, C. Brown, D. Sarfati, I. Campbell, N. Scott, R. Ramsaroop, S. Seneviratne, V. Harvey and R. Lawrenson (2018). "Ethnic disparities in breast cancer survival in New Zealand: which factors contribute?" BMC Cancer **18**(1): 58.

25. https://breastcancernow.org/news-and-blogs/news/annual-screening-detects-breast-cancers-earlier-for-women-aged-35-39-with-a-family-history-major-uk-trial-finds

26. https://www.breastcancerfoundation.org.nz/news-and-events/news-articles/article/extension-of-breast-screening-programme-will-certainly-save-lives-breast-cancer-foundation-nz

27. https://www.ncbi.nim.nih.gov/pubmed/23940285

28. ECR Online 2019 - Additional MRI screening in women with extremely dense breasts: primary outcome of the first round of the randomised DENSE trial; M. F. Bakker1, S. Lange1, R. M. Pijnappel1, R. M. Mann2, C. Loo3, B. Bisschops4, M. Lobbes5, M. D. F. De Jong6, K. M. Duvivier3, J. Veltman7, W. B. Veldhuis1, C. Van Gils1, O. DENSE Trial Study Group
1; 1Utrecht/NL 2Nijmegen/NL 3Amsterdam/NL 4Dordrecht/NL 5Maastricht/NL 6's Hertogenbosch/NL 7Almelo/NL

29. Improving participation in breast screening in a rural general practice with a predominately Māori population Rachel M Thomson, Sue Crengle, Ross Lawrenson. NZMJ 13 March 2009, Vol 122 No 1291; ISSN 1175 8716 p.39

30. Breast Cancer Foundation NZ submission to the Health Select Committee, 2019

31. https://tiromedical.com/

32. https://www.nzherald.co.nz/lifestyle/news/article.cfm?c_id=6&objectid=11815123

33. https://breastcancernow.org/news-and-blogs/news/annual-screening-detects-breast-cancers-earlier-for-women-aged-35-39-with-a-family-history-major-uk-trial-finds

34. https://www.ncbi.nim.nih.gov/pubmed/23940285

35. MRI vs mammography screening for high-risk women: an RCT - the influence of density and effectiveness. A. Geuzinge1, S. Saadatmand1, E. J. J. Rutgers2, R. M. Mann3, D. de Roy van Zuidewijn4, H. Zonderland2, R. Tollenaar5, M. Lobbes6, M. Ausems7, M. van 't Riet8, M. Hooning1, I. Mares-Engelberts1, E. Luiten9, E. Heijnsdijk1, C. Verhoef1, N. Karssemeijer3, J. Oosterwijk10, I.-M. Obdeijn1, H. de Koning1, M. Tilanus-Linthorst1; 1Rotterdam/NL 2Amsterdam/NL 3Nijmegen/NL 4Leeuwarden/NL 5Leiden/NL 6Maastricht/NL 7Utrecht/NL 8Delft/NL 9Breda/NL 10Groningen/NL

36. ECR Online 2019 - Additional MRI screening in women with extremely dense breasts: primary outcome of the first round of the randomised DENSE trial. M. F. Bakker1, S. Lange1, R. M. Pijnappel1, R. M. Mann2, C. Loo3, B. Bisschops4, M. Lobbes5, M. D. F. De Jong[6], K. M. Duvivier[3], J. Veltman[7], W. B. Veldhuis[1], C. Van Gils[1], O. DENSE Trial Study Group[1]; [1]Utrecht/NL [2]Nijmegen/NL [3]Amsterdam/NL [4]Dordrecht/NL [5]Maastricht/NL [6]'s Hertogenbosch/NL [7]Almelo/NL

37. https://breastcancernow.org/news-and-blogs/news/annual-screening-detects-breast-cancers-earlier-for-women-aged-35-39-with-a-family-history-major-uk-trial-finds

38. https://www.ncbi.nim.nih.gov/pubmed/23940285

39. C-2270-Validation of Volumetric breast density software using 3D printed single-material breast phantom, C.Feedon, M.L. Hill, H. Bosmans, D.R., Dance, R.E. vvan Engen, U.Mader, S.Schopphoven, I. Srchopoulos, Nijimegen/NLIssy Les Moulineux/FR Leuven/BE Guilford/UK GieBen/DE Marburg/DR, ECR online 2019.

40. Abbreviated breast MRI protocols: the newcomer in breast imaging. S. A. H. Hassanein, R. Habib; Shibin El Kom/EG

41. https://breastcancernow.org/news-and-blogs/news/annual-screening-detects-breast-cancers-earlier-for-women-aged-35-39-with-a-family-history-major-uk-trial-finds

42. Ellison-Loschmann L, McKenzie F, Highnam R, Cave A, Walker J, Jeffreys M. 2013. Age and ethnic differences in volumetric breast density in New Zealand women: A cross-sectional study. PLoS ONE 8(7): e70217. https://doi.org/10.1371/journal.pone.0070217

43. Improving participation in breast screening in a rural general practice with a predominately Māori population Rachel M Thomson, Sue Crengle, Ross Lawrenson. NZMJ 13 March 2009, Vol 122 No 1291; ISSN 1175 8716 p.39

44. https://www.researchgate.net/publication/296055503_Breast_cancer_inequities_between_Maori_and_non-Maori_women_in_AotearoaNew_Zealand

45. https://www.mdedge.com/oncologypractice/article/155789/breast-cancer/modeling-study-screening-treatment-effects-breast

46. https://www.ncbi.nlm.nih.gov/pubmed/29497091

47. http://journals.sagepub.com/doi/10.1177/1010428317731511

48. Professor Parry Guilford, NZ Herald 2.4.2019

49. https://healthierlives.co.nz/research/circulating-tumour-dna-for-better-cancer-management/

50. https://www.ncbi.nlm.nih.gov/pubmed/29348365

51. https://www.bjs.co.uk/article/minimizing-inequality-in-access-to-precision-medicine-in-breast-cancer-by-real-time-population-based-molecular-analysis-in-the-scan-b-initiative/

52. Abdel-Fatah TMA, Broom RJ, Lu J, Moseley PM, Huang B, Li L, Liu S, Chen L, Ma RZ, Cao W, Wang X, Li Y, Perry JK, Aleskandarany M, Nolan CC, Rakha EA, Lobie PE, Chan SYT, Ellis IO, Hwang LA, Lane DP, Green AR, **Liu DX**. SHON expression predicts response and relapse risk of breast cancer patients after anthracycline-based combination chemotherapy or tamoxifen treatment. ***British Journal of Cancer*** 2019. (in press)

53. https://scienceblog.cancerresearchuk.org/2019/03/13/rewriting-the-breast-cancer-rulebook/

54. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2879556/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5440946/

55. https://www.ncbi.nlm.nih.gov/pubmed/24619074

56. https://www.ncbi.nlm.nih.gov/pubmed/30223800

57. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5790421/

58. Lasham, A., et al, 2019, A predictor of early disease recurrence in breast cancer patients using a cell free RNA and protein liquid biopsy – submitted but unpublished.

59. https://www.nature.com/articles/s41523-018-0063-9, https://www.ncbi.nlm.nih.gov/pubmed/27130929

60. Tin Tin, S., J. M. Elwood, C. Brown, D. Sarfati, I. Campbell, N. Scott, R. Ramsaroop, S. Seneviratne, V. Harvey and R. Lawrenson (2018). "Ethnic disparities in breast cancer survival in New Zealand: which factors contribute?" BMC Cancer **18**(1): 58.

61. https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2017/vol-130-no-1467-15-december-2017/7444 . Lawrenson, S. Tin Tin, M. Schaaf, J. Kidd, A. Allan-Moetaua, J. Herman, R. Raamsroop, I. Campbell and M. Elwood (2017). "Characteristics of and differences between Pasifika women and New Zealand European women diagnosed with breast cancer in New Zealand." N Z Med J **130** (1467): 50-61.

62. Cardoso F. et al. 4th ESO–ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4), *Annals of Oncology*, Volume 29, Issue 8, 1 August 2018, Pages 1634–1657, https://doi.org/10.1093/annonc/mdy192; Also Senkus E, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E, Zackrisson S, Cardoso F, on behalf of the ESMO Guidelines Committee. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 26 (Supplement 5): v8–v30, 2015 doi:10.1093/annonc/mdv298

63. https://www.pharmaceutical-journal.com/news-and-analysis/features/genomic-medicine-is-going-mainstream-and-pharmacists-need-to-be-prepared/20203321.article

64. Turner, Neven, Loibl, Andre, Lancet Oncology 2017. https://www.ncbi.nlm.nih.gov/pubmed/27939057

65. Miller, L. D., J. A. Chou, M. A. Black, C. Print, J. Chifman, A. Alistar, T. Putti, X. Zhou, D. Bedognetti, W. Hendrickx, A. Pullikuth, J. Rennhack, E. R. Andrechek, S. Demaria, E. Wang and F. M. Marincola (2016). "Immunogenic Subtypes of Breast cancer Delineated by Gene Classifiers of Immune Responsiveness." Cancer Immunol Res **4**(7): 600-610.

66. 5. Sledge GW, Mamounas EP, Hortobagyi GN, Burstein HJ, Goodwin PJ, Wolff AC. Past, present, and future challenges in breast cancer treatment. J Clin Oncol. 2014; 32(19):1979-86.,

67. NZIER. Community pharmaceuticals. Expenditure trends. NZIER report to Medicines New Zealand. December 2018. https://nzier.org.nz/static/media/filer_public/01/08/010883de-26d3-432d-9dde-0bc0d1f59dd9/community_pharmaceutical_expenditure_nzier_to_medicines_nz_december_2018_update_final.pdf

68. PHARMAC. Briefing to the incoming Minister of Health. 8 November 2017. https://www.pharmac.govt.nz/assets/briefing-to-incoming-minister-2017-11.pdf

69. NZIER. PHARMAC economic analysis and "savings" claims. Background notes. Produced for Medicines New Zealand, October 2018. https://nzier.org.nz/static/media/filer_public/a0/e1/a0e1043d-93dd-491c-b8fe-f3f474acbce0/pharmac_savings_background_note.pdf

70. Management of Early Breast Cancer. Evidence-based best practice guideline. New Zealand Guidelines Group. Ministry of Health 2009.

71. Howell D, Currie S, Jones G, et al. 2009. *A Pan-Canadian Clinical Practice Guideline: Assessment of Psychosocial Health Care Needs of the Adult Cancer Patient*. Toronto: Canadian Partnership Against Cancer (Cancer Journey Action Group) and the Canadian Association of Psychosocial Oncology.

72. Standards of service provision for breast cancer patients in New Zealand – Provisional. National Breast Cancer Tumour Standards Working Group. NZ Government, 2013.

73. Baken D, Sutcliffe S. 2012. *National Standards for Supportive Care*. Unpublished.

74. NHMRC. 2003. *Clinical Practice Guidelines for the Psychosocial Care of Adults with Cancer*. Canberra: National Health and Medical Research Council.

75. https://www.abcglobalalliance.org/wp-content/uploads/2019/02/ABC-Global-Charter-_EN.pdf

76. https://www.employment.govt.nz/workplace-policies/productive-workplaces/flexible-work/

77. https://www.nz4healthresearch.org.nz/wp-content/uploads/2019/04/NZHR-clinical-trials-workshop-22nd-March-summary-010419-002.pdf

78. Sullivan, M. 2019. The Benefits of Clinical Research. Presentation at "Health and Prosperity through Clinical Trials" workshop.

79. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5834810/

80. What do Breast Cancer Patients in NZ need? Associate Professor, University of Auckland, Ian Campbell – Breast Cancer Summit, Auckland New Zealand, October, 2017.

81. SABCS, 2017

82. https://link.springer.com/article/10.1007/s40846-016-0163-7

83. http://biomarkers.imedpub.com/sputum-cytological-changes-in-rural-women-of-west-bengal-chronically-exposed-to-low-level-groundwater-arsenic-contamination.php?aid=8371

84. https://www.ncbi.nlm.nih.gov/pubmed/29175265

85. https://www.ncbi.nlm.nih.gov/pubmed/28154374

86. https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2017/vol-130-no-1464-27-october-2017/7396

87. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5834810/

88. https://www.mckinsey.com/~/media/McKinsey/Industries/Healthcare%20Systems%20and%20Services/Our%20Insights/The%20next%20wave%20of%20innovation%20in%20oncology/The-next-wave-of-innovation-in-oncology.ashx

89. https://www.mckinsey.com/industries/healthcare-systems-and-services/our-insights/why-the-evolving-healthcare-services-and-technology-market-matters

90. https://bit.ly/2TZ6cME and https://www.facebook.com/hescnz/videos/372288133374707/UzpfSTE0NTUyNDEyMTQ6Vks6MjI1OTE5OTY4NzYzNTkzNQ/

91. https://www.ncbi.nlm.nih.gov/pubmed/29224780

92. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5761188/

93. Solinas, C., A. Gombos, S. Latifyan, M. Piccart-Gebhart, M. Kok and L. Buisseret (2017). "Targeting immune checkpoints in breast cancer: an update of early results." ESMO Open **2**(5): e000255.