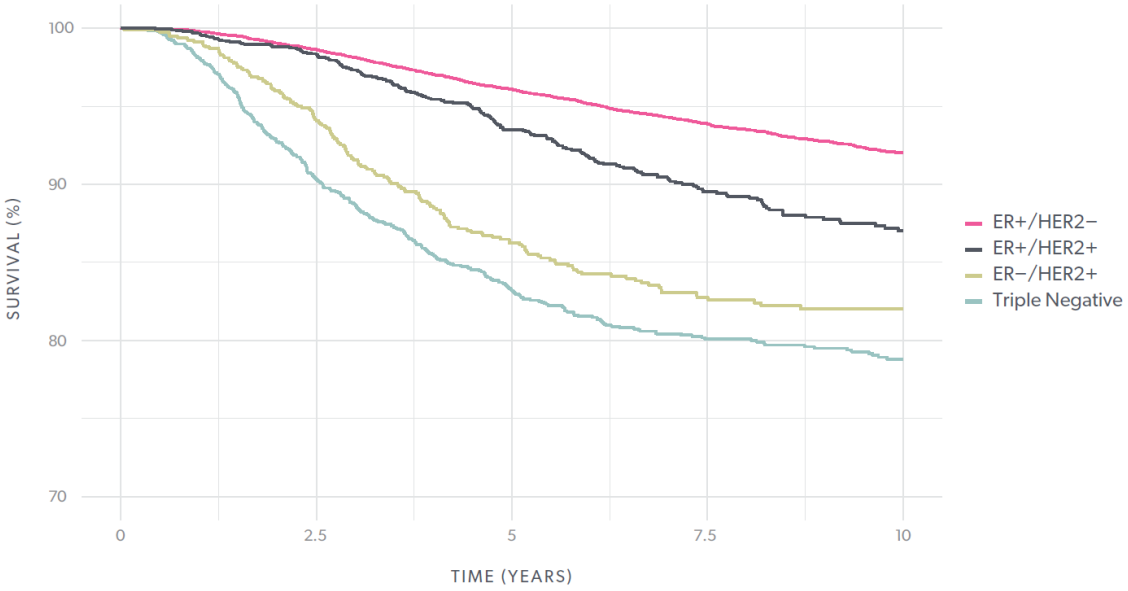
Please provide an overview of the disease that would be treated by the proposed pharmaceutical.

Eribulin would be used to treat patients with advanced or metastatic breast cancer who have progressed after two prior regimens for advanced disease. A report by the New Zealand Breast Cancer Foundation in 2018 found that median survival after a diagnosis of metastatic/advanced breast cancer in New Zealand is 16 months, considerably worse than overseas. For example, this compares with 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. Therefore, although there have been improvements in rates of survival for breast cancer over the past decades, New Zealand still lags behind equivalent countries, for survival of people with metastatic breast cancer (Breast Cancer Foundation New Zealand 2018).

Breast cancer treatment is individualised based on tumour characteristics, patient characteristics and treatment history. Survival with metastatic disease varies greatly by subtype, from 27.3 months for Luminal A patients down to 6.6 months for triple negative breast cancer. Five-year survival after metastatic diagnosis is only 5% in Māori populations, compared to 15% in non-Māori populations (Breast Cancer Foundation New Zealand 2018).

In particular need are patients with triple negative breast cancer. Triple negative breast cancer (TNBC) is a subtype of breast cancer that lacks expression of the three primary breast tumour markers: oestrogen receptor (ER), progesterone receptor (PR) and HER2 protein. Triple-negative (ER-negative, PR-negative, HER2/neu not overexpressed) breast cancer has distinct clinical and pathologic features, and is a clinical problem because of its relatively poor prognosis, aggressive behaviour and lack of targeted therapies. About 10 to 20 per cent of all breast cancers are classified as triple negative. This type of breast cancer often affects younger women and those with the breast cancer gene BRAC1. Triple negative breast cancer also tends to be more aggressive than other forms of breast cancer.

A recent report by BCFNZ from the Breast Cancer Register reinforced that women with triple negative breast cancer (TNBC) have the poorest rates of 5-year and 10-year survival as shown below.



SUBTYPE	5-YEAR SURVIVAL	10-YEAR SURVIVAL
ER+/HER2−	96% (96-96)	92% (91-93)
ER+/HER2+	94% (92-95)	87% (85-89)
ER−/HER2+	86% (84-88)	82% (80-85)
Triple Negative	83% (82-85)	79% (77-81)

Fig. 5.2-6. *Breast cancer-specific survival by receptor status of invasive tumours. Proportion of women surviving invasive breast cancer to 10 years by their tumour receptor status. Table: Proportion of women surviving to five and 10 years, (95% CI).*

Source: (Breast Cancer Foundation New Zealand 2022)

ESMO guidelines recommend the use of chemotherapy (including eribulin) in triple negative metastatic breast cancer (mTNBC). The treatment algorithm is shown in the graphic below (Figure 5 from the 2021 ESMO Guidelines).

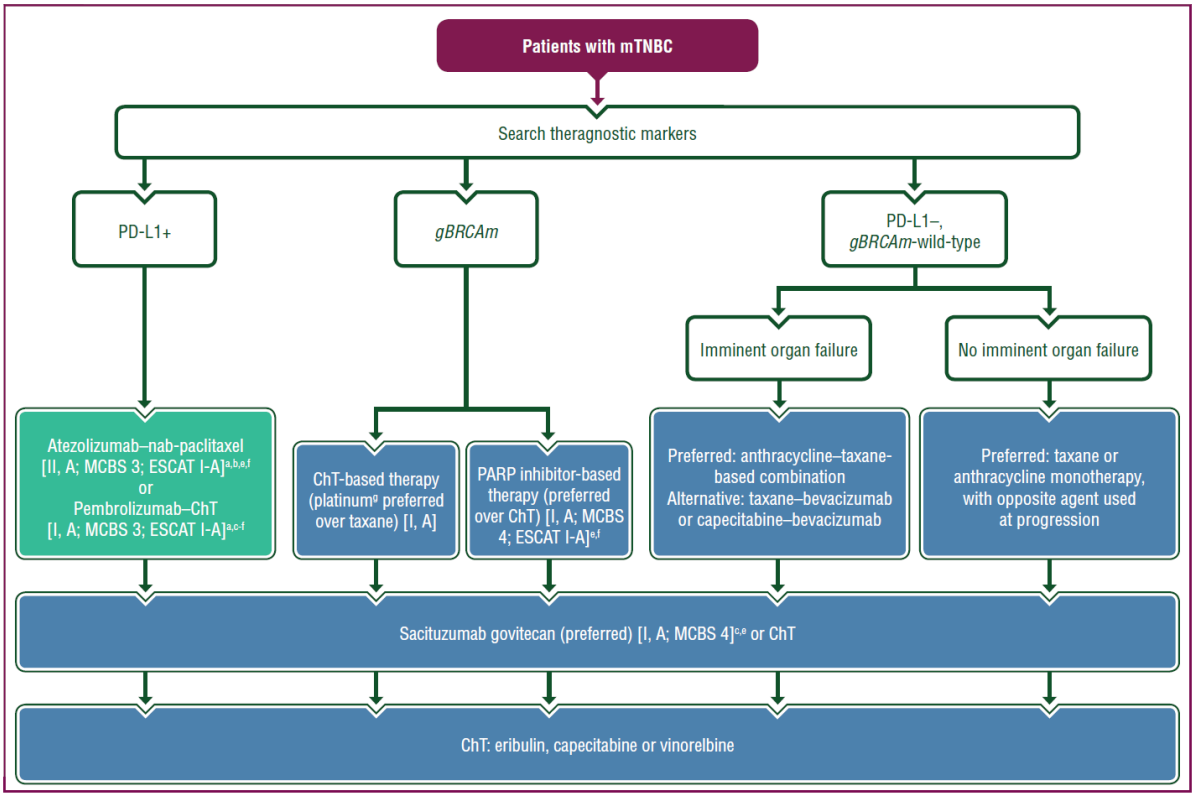


Figure 5. Treatment of mTNBC.
Purple: general categories or stratification; turquoise: combination of treatments or other systemic treatments; white: other aspects of management; blue: systemic anticancer therapy.
ChT, chemotherapy; EMA, European Medicines Agency; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; FDA, Food and Drug Administration; *gBRCAm*, germline *BRCA1/2* mutation; ICI, immune checkpoint inhibitor; MCBS, ESMO-Magnitude of Clinical Benefit Scale; mTNBC, metastatic triple-negative breast cancer; PARP, poly (ADP-ribose) polymerase; PD-L1, programmed death-ligand 1.
[a] May be considered as monotherapy in further lines in case of high PD-L1 positivity and no previous exposure to ICI.
[b] EMA approved, not FDA approved.
[c] FDA approved, not EMA approved.
[d] ChT physician's choice of nab-paclitaxel, paclitaxel or gemcitabine/carboplatin.
[e] ESMO-MCBS v1.1[93] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1/scale-evaluation-forms-v1.1).
[f] ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[89]
[g] If not used previously.

It needs to be emphasised that most of the agents recommended for treatment of mTNBC such as PARP-inhibitors, atezolizumab, bevacizumab, pembrolizumab and sacituzumab govitecan) are not available (funded) for this population in New Zealand. Therefore, the options for New Zealand patients with this type of breast cancer are very limited indeed compared with their counterparts elsewhere.

Eribulin would also be available as chemotherapy in other types of breast cancer, particularly ER+/HER2 negative cancers where existing treatment options have been exhausted. This is also consistent with ESMO Guidelines recommendations for ER+/HER- metastatic breast cancer, where other options have failed and chemotherapy (ChT) is indicated (as shown in the figure below). It should also be noted that there are several options in the treatment algorithm shown that are not available funded in New Zealand (e.g. everolimus, alpesilib and PARP inhibitor). Eribulin monotherapy would be a choice amongst other chemotherapies, based on patient history and other

characteristics.

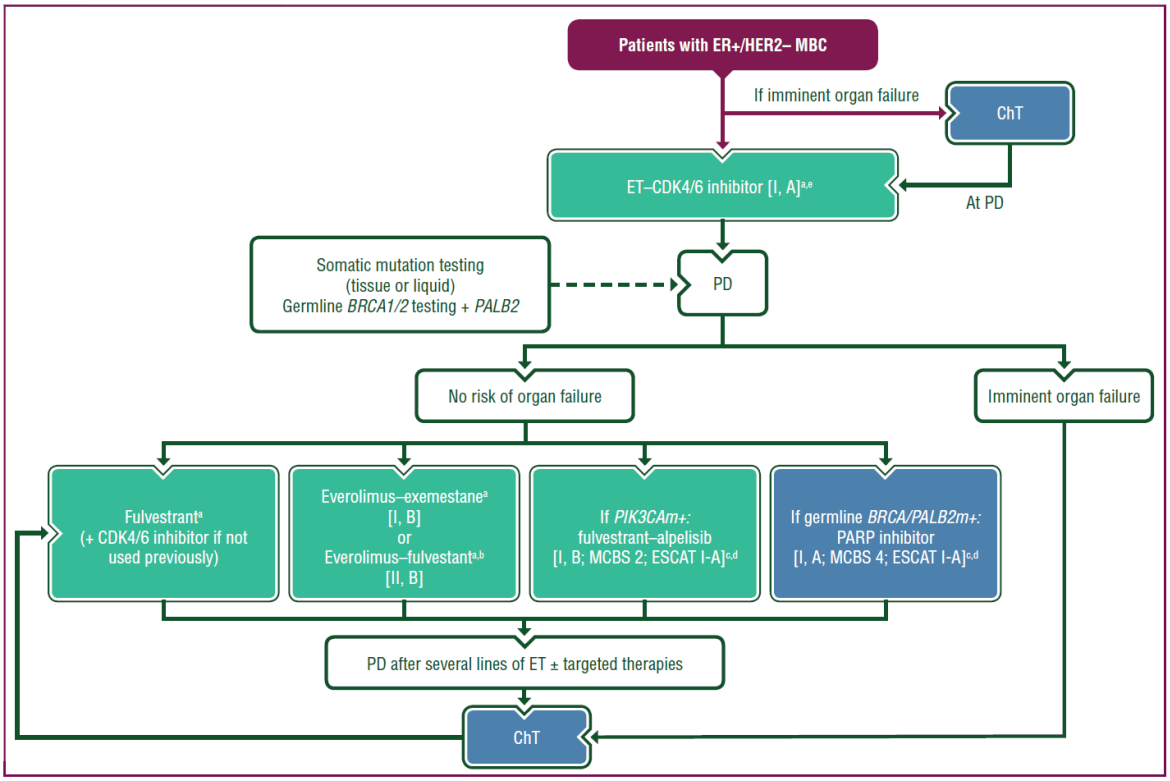


Figure 2. Treatment of ER-positive/HER2-negative MBC.
Purple: general categories or stratification; turquoise: combination of treatments or other systemic treatments; white: other aspects of management; blue: systemic anticancer therapy.
AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4 and 6; ChT, chemotherapy; EMA, European Medicines Agency; ER, estrogen receptor; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; ESR1, estrogen receptor 1; ET, endocrine therapy; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; m, mutation; MBC, metastatic breast cancer; MCBS, ESMO-Magnitude of Clinical Benefit Scale; OFS, ovarian function suppression; *PALB2, partner and localiser of BRCA2*; PARP, poly (ADP-ribose) polymerase; PD, progressive disease; *PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.*
[a] OFS if the patient is premenopausal.
[b] Preferred if the patient is *ESR1* mutation positive [ESCAT score: II-A].[d]
[c] ESMO-MCBS v1.1[93] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1/scale-evaluation-forms-v1.1).
[d] ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[89]
[e] If relapse <12 months after end of adjuvant AI: fulvestrant—CDK4/6 inhibitor[a]; if relapse >12 months after end of adjuvant AI: AI—CDK4/6 inhibitor[a].

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Does the disease impact on the health of the patient's family, whānau or wider society? Please explain and provide sources of information.

Breast cancer is diagnosed in about 3,500 people annually in New Zealand. The latest Ministry of Health mortality report shows nearly 700 deaths in 2019. It is therefore an important health issue in terms of physical and mental health and has a significant social and economic impact on society, families, and whānau. Despite the perception that cancer is an older person's disease, breast cancer is the number one cause of death for New Zealand women under 65.

Receiving a diagnosis of advanced breast cancer is devastating for the patient and has deep impacts on colleagues, communities and whānau. Having a relative living with or dying of breast cancer affects other family members significantly both emotionally and financially. Women aged 44 years and younger have the highest rate of diagnosis of triple negative breast cancer (14.4%) (Breast Cancer Foundation NZ 2022). This group is most likely to contain young mothers whose time with dependent children is precious.

Women undertake many vital roles in our society, both professional and unpaid. These include caring for elderly parents, children and other family members, keeping households fed and running effectively and providing emotional support for friends and whānau. Keeping women alive with a good quality of life has huge benefits for families and society.

To provide insight into the realities of advanced breast cancer and the need for additional treatment options we include some statements from women who are members of the Metavivors NZ, a group for women with advanced breast cancer, who will be eligible for treatment with eribulin.

I was diagnosed with Stage IV Breast Cancer in April 2018 – with no prior history of disease. Believe me – it was a shock. Mean lifespan from diagnosis 13 – 15 months. The shocks were not to end there. I was told that there was a possible medicine available for me – but unfunded. Ibrance – at a cost of $8750 per 28 day cycle. We managed to find the money – to pay for this modern, effective drug for 11 months before Pharmac funded it. It keeps me well – and with a combination of this and surgery, I am today without Evidence of Disease. I regard myself as fit and healthy. I am a mother and grandmother, wife and farmer – and still productively working full time.

I am not naïve enough to think myself 'cured' and know that it is very likely for this to again become a problem – and given my subtype of cancer - there are very few options available. Eribulin is a medicine that my oncologist has told me will be a future treatment if I can afford it. A 6-month course would cost around $80,000 and a year $160,000. I dread the thought of having to pay for more new technology drugs – and quite frankly – after already forking out $96,250 for Ibrance to date – how can anyone afford it?

Please Pharmac, fund eribulin and do your best for New Zealanders like me! We're worth the investment in this important medicine so we can continue working, caring for our families and contributing to society for as long as possible.

I am 53 and I have advanced breast cancer. I was first diagnosed at age 44 and then given the grim metastatic diagnosis it had spread to my bones in 2021. I was 51, mother of two teenage daughters, owner of a prospering SME, fit, healthy (or so I thought), and clean living. Why did this happen to me? It is likely attributable to a genetic mutation called PALB2. Bad luck. I am Er3+, PR-, HER2-, and I currently on my third line of treatment, Vinorelbine. Vinorelbine seems to be working quite well at the moment and long may that last. But the number of "nicer" future options as my Oncologist puts it, are limited. By nicer, she means those with little or tolerable side effects, those that enable me to have a reasonable quality of life, continue to do some of the things that I enjoy, that make life meaningful, to support and parent my girls (still teens). Having another tool in the treatment box is huge but the proposed cost of Eribulin (Halaven) is prohibitive. A year's treatment at $160k would completely wipe out our family financially, leaving nothing left for when things go wrong, family holidays, supporting kids through tertiary education. And no inheritance for my kids who will be left without a mother far too soon in life. Eribulin (Halaven) is fully funded by many other countries (including Australia since 2013). It has the potential to have a positive impact on my future and I wholeheartedly support BCAC's submission to have this medication fully funded by Pharmac.

I'm a single 66 year old woman receiving the pension. I am a Mother of 4 sons and Grandmother to 3 Grandchildren. It is my dearest wish to enjoy time with my family and friends and see my Grandchildren grow up. I have worked as a Librarian, Receptionist and Teacher Aide. Also have been involved on a voluntary basis on committees of the local Playcentre, Kindergarten, PTA of the Primary school and Swimming Club over a period of 25 years.

I have always kept fit, watched my diet and looked after my health. I had regular mammograms. It came as a great shock to me 2 years ago when I was diagnosed with Triple Negative Breast Cancer, Grade 3, Stage 4. PDL-1 positive. The breast cancer did not show up on either a Mammogram or ultrasound but was found after a PET Scan.

I have had 4 different types of chemotherapy and will soon start my fifth. The previous chemotherapy drugs have failed to halt the progress of the cancer in my lymph nodes. I have been told that I am running out of options of free chemotherapy drugs. As Triple Negative is a rarer form of breast cancer, that already means there are less chemotherapy drugs available to me.

The next suggested drug for me is Eribulin which has to be obtained in the Private system and is extremely costly. I can't afford to pay for it. This is a great worry for me. I don't want to be put in the position of begging family members for financial help, resorting to Give A Little or trying to borrow funds to stay alive. No women should have to do this!

I still endeavour to keep fit and walk daily. On good days I walk 5 to 6 kms. I am worth being kept alive for a longer period of time. I, along with other women need hope, it keeps us going through all the treatments and pain. Please help women like me stay alive for longer by making Eribulin available as soon as possible in the Public Health system. Please don't take too long to do this

BCAC and its member groups are extremely concerned about the poor access to treatments in New Zealand for people with metastatic breast cancer. The group of women with triple negative breast cancer are of particular concern as they have few specific treatment options available. Although the treatment goals in advanced breast cancer remain palliative in nature, access to a wider range of treatments, that are aimed at controlling symptoms, improving or maintaining quality of life, and prolonging survival is needed in New Zealand. BCAC has lobbied the manufacturer of eribulin to apply for registration with MEDSAFE and an application was made for this treatment in 2022. It has been approved in Australia, Europe, and the USA for over a decade.

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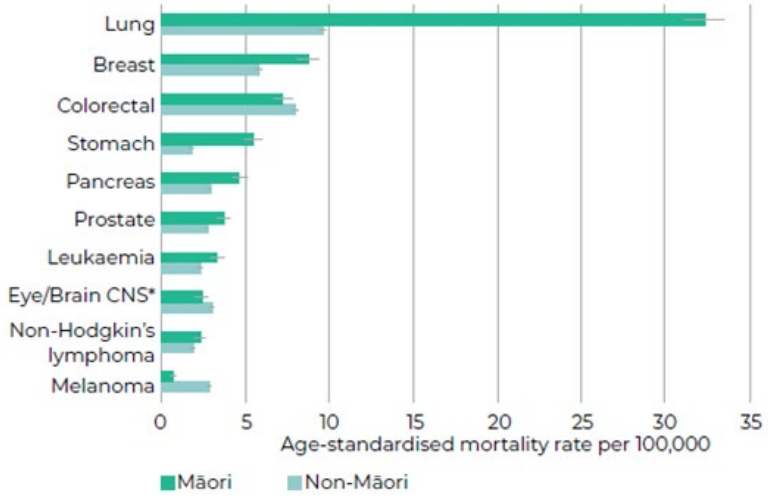
What is the impact of the disease on Māori health outcomes? Please explain and provide sources of information.

In recent years, approximately 3,500 have been diagnosed with breast cancer annually in Aotearoa New Zealand; this number has steadily increased over time in line with our growing and aging population. The actual rate of diagnoses (per 100,000 women) has increased slightly over the past 20 years for both wāhine Māori and non-Māori women (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021). In 2018, the incidence of breast cancer per 100,000 women was 124.9 for Māori and 97.4 for non-Māori (Ministry of Health 2020). It is therefore of significant concern that Māori health outcomes, particularly for wāhine Māori are being impacted by poor access to treatments for breast cancer.

Wāhine Māori are more likely to be diagnosed with advanced disease and are more likely to die from breast cancer than non-Māori/non-Pacific women. Pacific women are also more likely to be diagnosed with advanced disease and more likely to die of breast cancer than non-Māori/non-Pacific women.

Age- and sex-standardised cancer-related mortality 2007–2017



* CNS = central nervous system

Source: (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021)

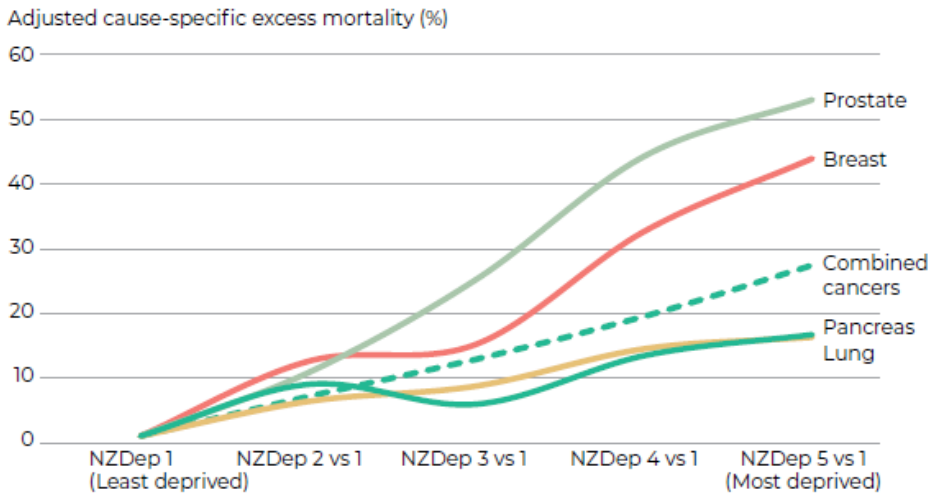
Does the disease disproportionately affect population groups that may already be experiencing a health disparity?

People who are economically deprived are already in poorer health in New Zealand. Overall, cancer incidence is higher among those living in the more deprived areas – although this varies depending on the type of cancer. Poverty is a barrier to accessing early diagnosis and best-practice treatment for cancers, leading to inequities in cancer survival between the poor and the affluent. This is particularly important for highly treatable cancers, where finding a cancer early and treating it

quickly can significantly improve survival outcomes (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021).

The figure below (from Te Aho), shows the impact of economic deprivation on survival

Impact of deprivation on cancer survival, 2007–2016



Source: (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021)

The fact that many New Zealanders must personally pay to gain access to cancer medicines that are evidence-based and recommended by their oncologists is creating a two-tiered health system in which those who can pay will live longer. Families are being forced to cash in retirement savings, sell properties, set up 'Give a Little' pages and fundraise to gain benefits in quality of life, progression free survival and overall survival. This situation is lamentable and does not contribute to the notion of equity within health care. The Ministry of Health's definition of equity is: "In Aotearoa New Zealand, people have differences in health that are not only avoidable but unfair and unjust. Equity recognises different people with different levels of advantage require different approaches and resources to get equitable health outcomes."

People living with mental health and addiction issues have significantly reduced life expectancy compared with the general population, mainly due to dying early from physical illnesses, such as heart disease and cancers. Access to and quality of health care are major contributors, including access to cancer screening, timely diagnosis, and treatment. Research in Aotearoa has found that, among people diagnosed with breast or colorectal cancers, survival is much poorer for those with a history of recent contact with specialist mental health services (Te Aho o Te Kahu Cancer Control Agency He Pūrongo Mate Pukupuku o Aotearoa 2021).

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