# The Effect of Chemotherapy on Aerobic Power and Cardiac Function in Early-stage Breast Cancer Patients

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# BREAST CANCER IN AUSTRALIA

**NUMBER OF WOMEN DIAGNOSED IN 2017**

17,586

**1 IN 8 WILL DEVELOP BREAST CANCER**

**5-YEAR SURVIVAL RATE**


[1] AIHW, 2017

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# Cardiovascular disease in cancer patients is an important public health issue

Cardiovascular disease is the leading cause of non-cancer related death in breast cancer survivors [2-4]

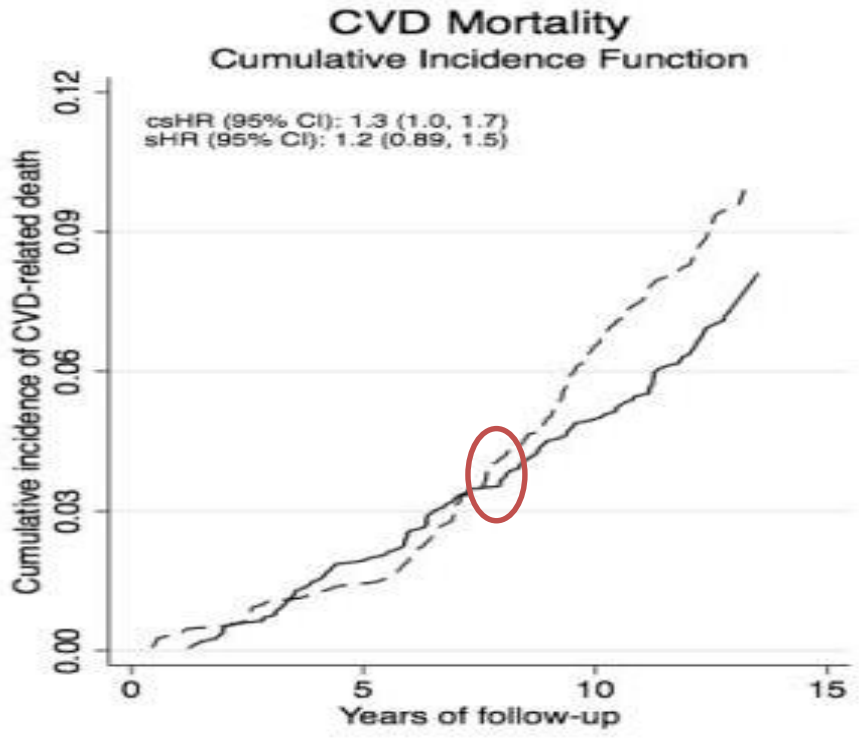


Figure 1: Women with breast cancer (dash), women without breast cancer (solid line)

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[2] Bradshaw et al, 2016 [3] Ewer et al 2010 [4] Ewer et al, 2015

# Chemotherapy may lead to cardiac injury

Anthracycline-chemotherapy is the primary treatment for solid tumours and is associated with cardiotoxicity[5]

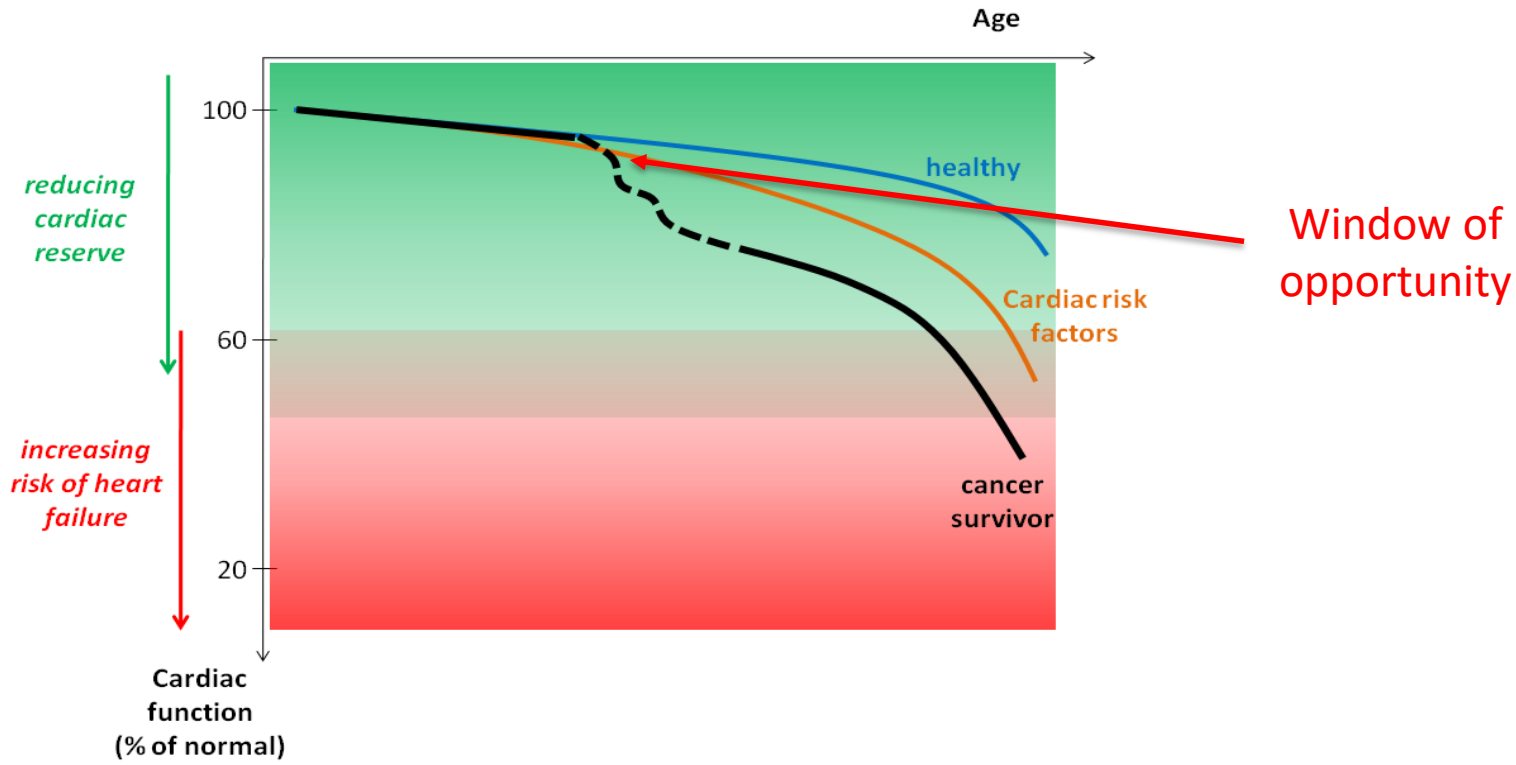


Figure 2: Cardiac reserve decreases with chemotherapy and increases risk of heart failure

[5] Cristietello, La Gerche et al., 2012

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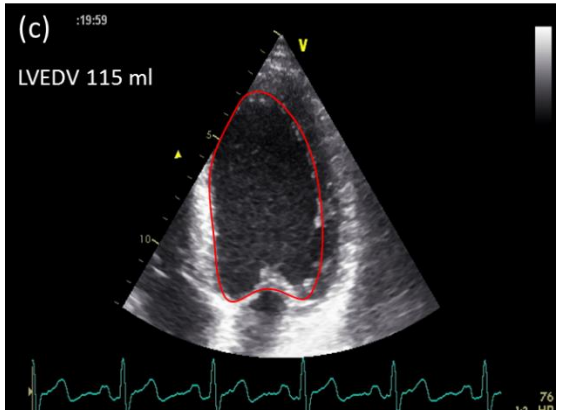
# Cardiac imaging and testing

- Resting echocardiography
  - Left ventricular ejection fraction (LVEF) [5-9]
  - Global longitudinal strain (GLS) [5-9]
- Biochemical markers
  - Troponin[6]
  - B-type Natriuretic Peptide (BNP)[6]
- Cardiopulmonary exercise testing [9-13]




[5] La Gerche et al., 2012, [6] Cardinale et al., 2004, [7] Khouri et al, 2012, [8] Khouri 2014, [9] La Gerche et al., 2013, [10] La Gerche et al., 2013, [12] Scott et al., 2011, [13] Jones et al., 2012

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# Exercise training during chemotherapy

- Exercise training has been proven to be well-tolerated and safe in breast cancer during chemotherapy [13-15]
- One study has demonstrated $VO_2$peak ↑ 11% during chemotherapy but others studies have not. [13-16]
- In patients who do not exercise, $VO_2$peak ↓ ~10% after 12-weeks of chemotherapy treatment [14-17]

[13] Jones et al, 2012, [14] Courneya et al, 2007, [15] Hornsby et al 2014, [16] Courneya et al, 2012, [17] Fitzgerald et al, 1997

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# Research aim and hypotheses

**Aim:** We sought to assess the association between resting cardiac function measures and $VO_2$peak and whether exercise training could attenuate changes in $VO_2$peak during therapy.

**Hypotheses:**

- $VO_2$peak will decrease in early-stage breast cancer patients treated with anthracycline-based chemotherapy
- Changes in cardiac function will not associated with changes in $VO_2$peak
- Exercise will attenuate falls in $VO_2$peak and cardiac function

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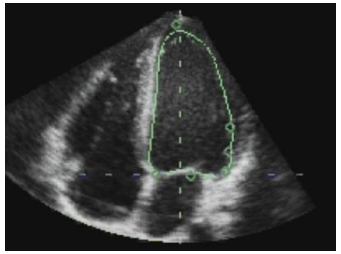
28 early-stage breast cancer patients recruited into a observational non-randomised study

- Scheduled for anthracycline-based chemotherapy
- Aged 18-70 years
- Capable of exercise

Prior to scheduled chemotherapy



**Resting echo**

**CPET**

**Biomarkers**

15 breast cancer patients during chemotherapy -Exercise training

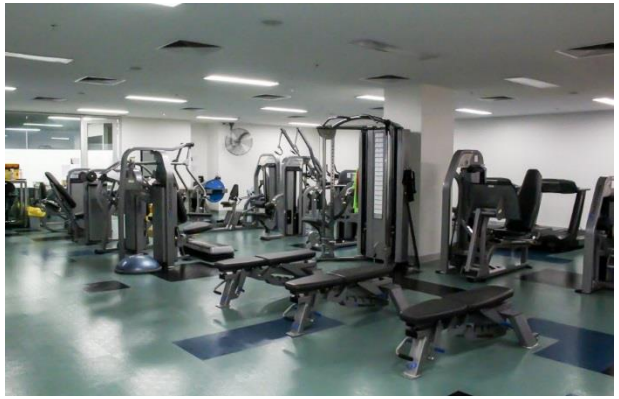
12-week exercise intervention

13 breast cancer patients during chemotherapy - Usual care

~3-weeks after the final (4th) cycle anthracycline-chemotherapy
Repeat outcome measures resting echo, CPET and biomarkers

# Exercise intervention

| Exercise training principles | |
|---|---|
| **Frequency** | Three sessions per week (two supervised, one unsupervised) |
| **Intensity** | Moderately-vigorous - 70-85% exercise intensity |
| **Type** | Mix method of aerobic training (stationary cycling) and resistance training |
| **Time** | 150 minutes per week |
| **Progression/Regression method** | Progressed every 4 weeks using a submaximal progressive exercise test |



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# Baseline characteristics

| | Usual care (n=13) | Exercise training (n=15) | *p* value |
|---|---|---|---|
| Age (y) | 51.8 ± 12.3 | 45.8 ± 9 | 0.15 |
| Height (cm) | 151 ± 8.5 | 152 ± 9.1 | 0.77 |
| Body mass (kg) | 75.4 ± 17.6 | 68.1 ± 20.5 | 0.32 |
| Breast cancer diagnosis | | | |
| • HER2+ | 4 (30%) | 2 (13%) | |
| • ER-, PR-, HER2- | 3 (23%) | 8 (62%) | |
| • Other | 6 (46%) | 5 (33%) | |
| $VO_2$peak ($ml.kg^{-1}.min^{-1}$) | 21.2 ± 5.6 | 26.9 ± 4.9 | 0.007 |
| $VO_2$peak (%predicted) | 65.9± 22.9 | 83.5± 20.7 | 0.04 |

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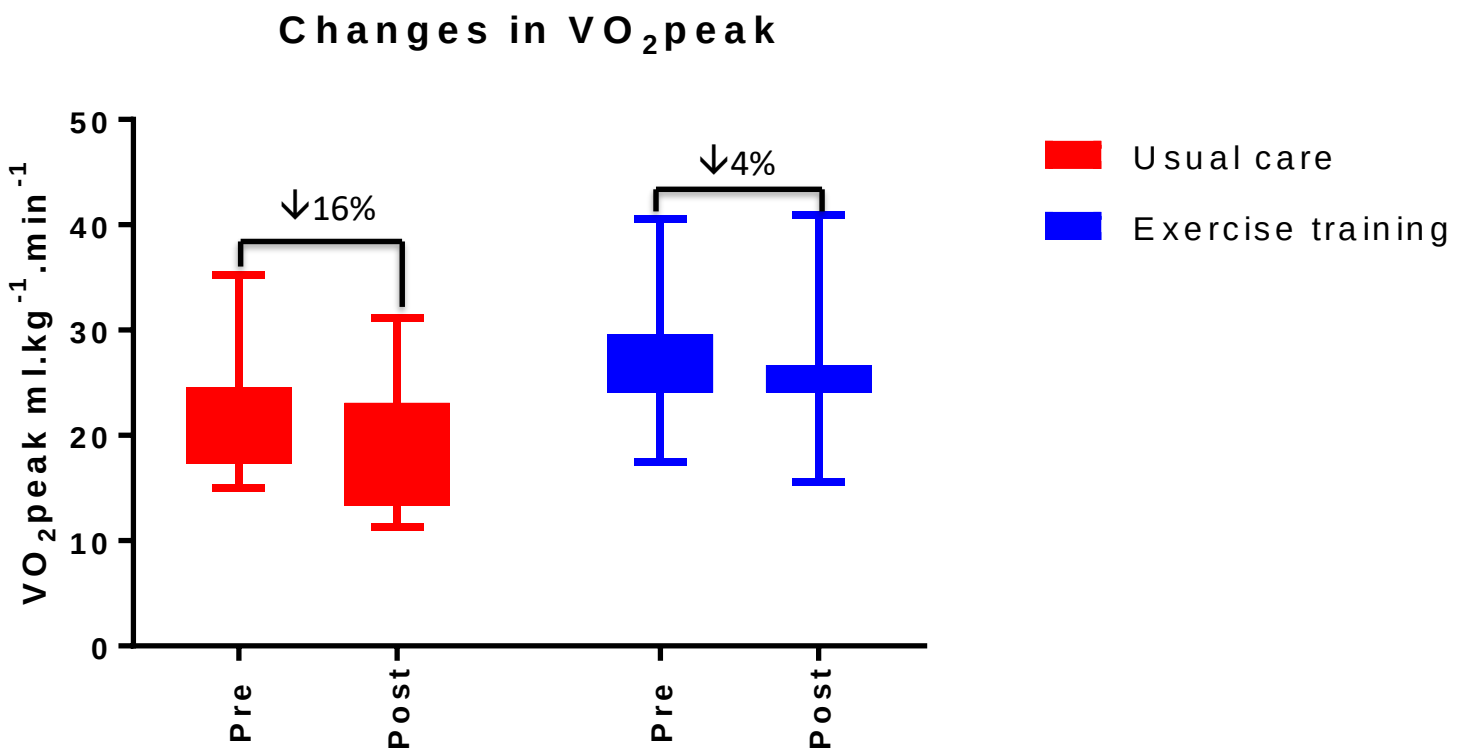
# Exercise training during chemotherapy preserved $VO_2$peak




**Interaction *p* = 0.07**

**Pre to post *p* = 0.002**

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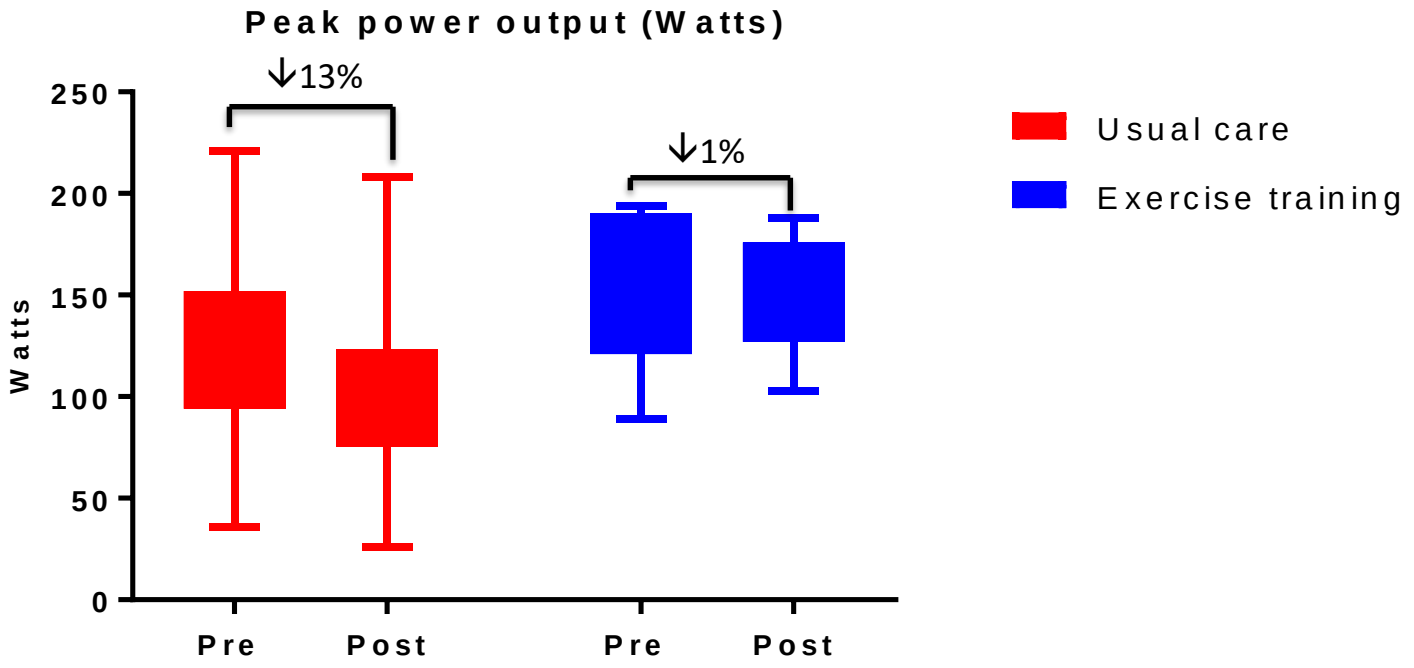
# Exercise training during chemotherapy preserved power output




**Interaction *p* = 0.07**

**Pre to post *p* = 0.03**

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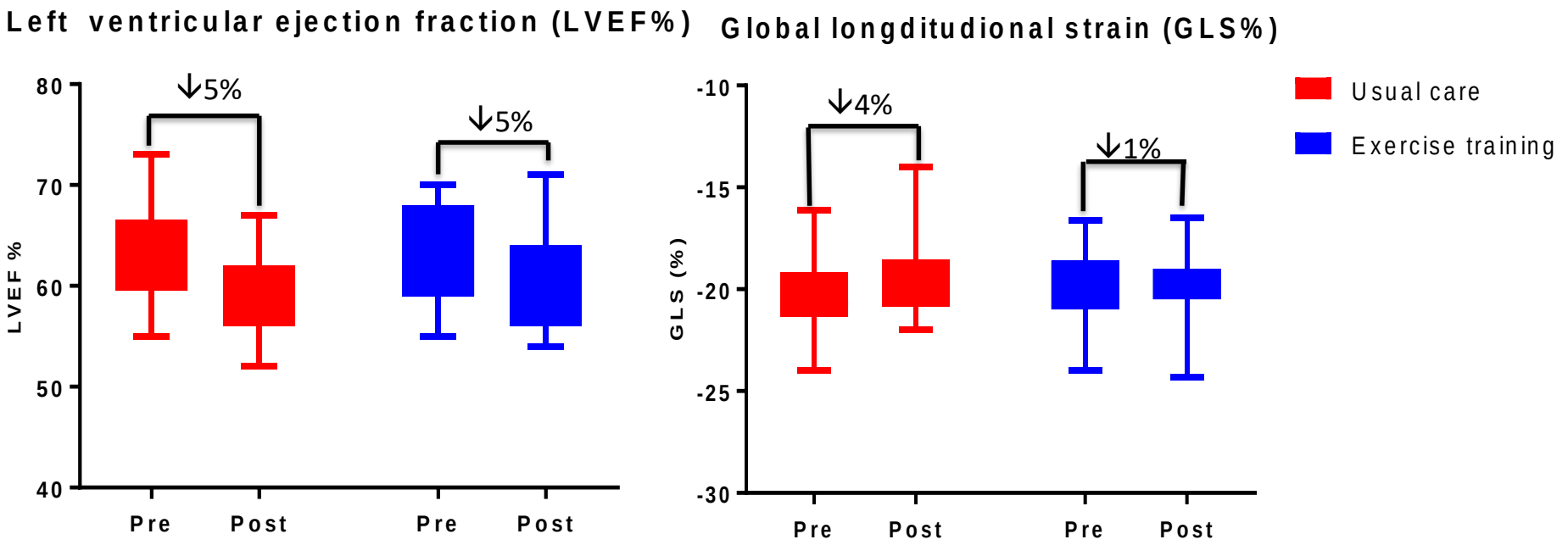
# Cardiac function is reduced during chemotherapy




**Interaction *p* = 0.97**

**Pre to post *p* = 0.02**

**Interaction *p* = 0.33**

**Pre to post *p* = 0.15**

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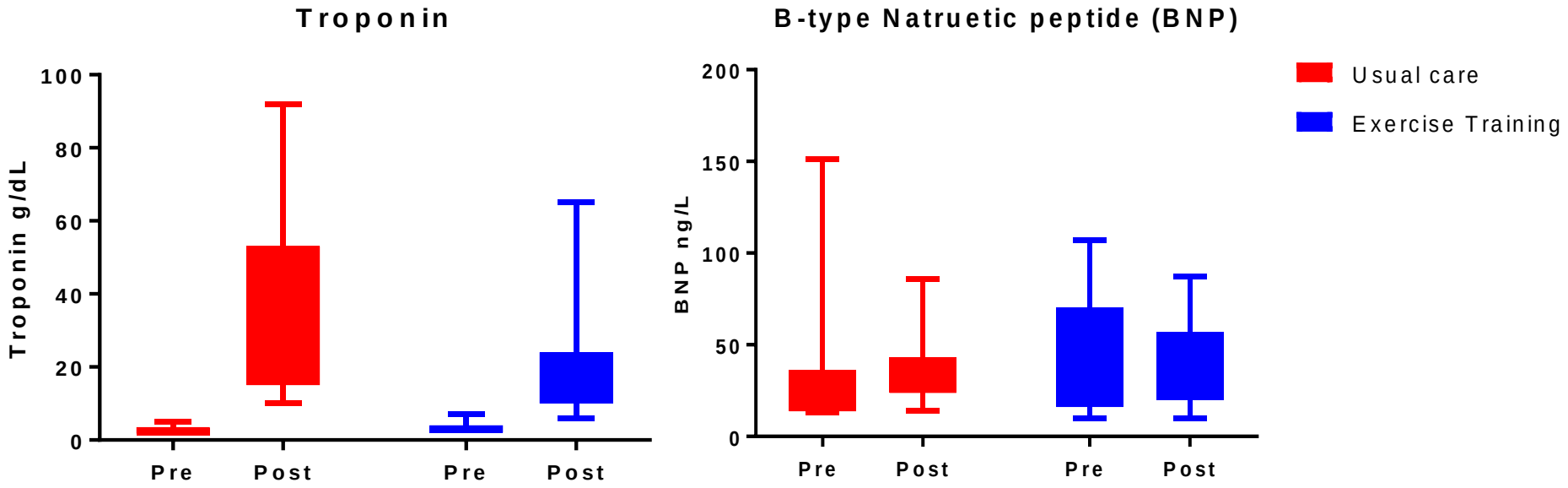
# Biomarkers of cardiac damage increased during chemotherapy




**Interaction $p = 0.04$**

**Pre to post $p < 0.001$**

**Interaction $p = 0.72$**

**Pre to post $p = 0.99$**

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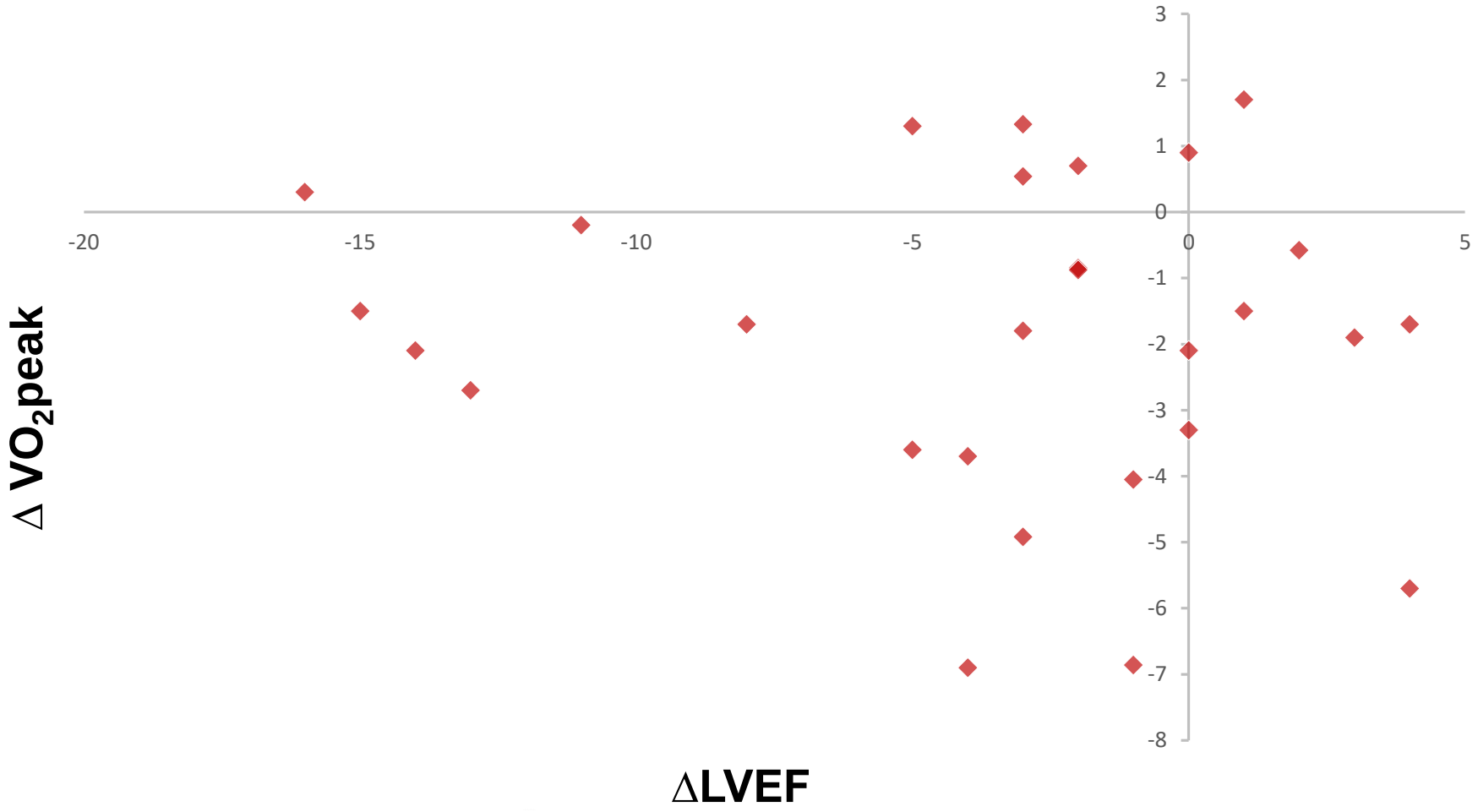
# Linear correlation of LVEF vs $VO_2$peak




$r^2 = 0.001$, $p = 0.86$

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# Study limitations

- The present study was a non-randomised observational with the primary objective of feasibility
- Selection bias
  - Participants allocated to each group by choice
- Other limitations
  - Small proportion of usual care arm completed regular exercise training
  - The single centre study
  - Small sample size (n=28)
  - Short exercise intervention (12-weeks)

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## Conclusion

- Chemotherapy decreased exercise capacity in early-stage breast cancer patients
- Exercise training attenuated the decline in $VO_2$peak during chemotherapy
- A decrease in cardiac function did not predict the decline in $VO_2$peak
- Further studies are planned to test whether changes in $VO_2$peak predicts clinical outcomes

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Special mention to Institute of Health & Ageing, ACU and my PhD supervision team of A/Prof Prue Cormie and A/Prof Michael Baker.







# Thank you!


The fighting heart

Gym aid to cancer patients

BRIGID O'CONNELL

DRAGGING yourself to the gym in the midst of breast cancer treatment may not only improve stamina and strength during treatment, but also reduce heart damage caused by one of the most common anti-cancer drugs.

In the first study of its kind, Melbourne researchers are testing whether exercise during chemotherapy can both help detect early damage to heart muscle caused by anthracycline-based chemotherapy drugs, but also prevent damage decades after treatment has finished.

With more women surviving early-stage breast cancer, studies show they are more likely to die from heart disease than from cancer.

Associate Professor Andre La Gerche, head of sports cardiology at the Baker IDI Heart and Diabetes Institute, is leading a world-first pilot study to measure cardiac function during exercise.

He said while international studies had shown breast cancer patients had up to an 18 per cent higher risk of heart failure later in life, diagnostic tools, such as cardiac ultrasound, only showed measurable heart muscle damage in 1-2 per cent of patients.

Prof La Gerche said this gap suggested diagnostics were not sensitive enough to detect damage, but also that this damage emerged many years after treatment finished.

"We are using exercise to look at the heart and see whether ... it's a more sensitive way of picking up if the muscle is suffering," he said.

Half of the 30 participants in the control group will be advised to follow a healthy lifestyle, including exercise. The rest will undergo two supervised exercise sessions at the Baker IDI gym each week, plus a home-based program for the four months they are receiving chemotherapy.

Study participant Raelle Smit, 40, said while chemotherapy had left her fatigued, exercise had helped increase her strength and stamina during the gruelling treatment.

"We think with exercise it's going to use up all your energy, but it creates energy," Ms Smit said. "If they also find this can protect the heart, that's wonderful, but I've had immediate benefits."

Raelle Smit has found benefits to exercising during her cancer treatment. Picture: NORM OORLOFF

FOR DETAILS ON TAKING PART IN THE STUDY GO TO: bakeridi.edu.au/research/clinical-trials/breast-cancer-trial

**'We think with exercise, it's going to use up all your energy, but it creates energy' – RS - participant**

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| BMI ($kg/m^{-2}$) | 23.1±5.2 | 20.7± 6.2 | 0.27 |
| Breast cancer diagnosis | | | |
| • HER2+ | 4 (30%) | 2 (13%) | |
| • ER-, PR-, HER2- | 3 (23%) | 8 (62%) | |
| • Other | 6 (46%) | 5 (33%) | |
| Treatment | | | |
| • AC | 10 (76%) | 10 (66%) | |
| • AC (dose dense) | 2 (15%) | 3 (20%) | |
| • FED-D | 1 (7%) | 2 (13%) | |
| $VO_2$ ($L/min^{-1}$) | 1.6 ± 0.4 | 1.8 ±.32 | 0.11 |
| $VO_2$peak ($ml.kg^{-1}.min^{-1}$) | 21.2 ± 5.6 | 26.9 ± 4.9 | 0.007 |
| $VO_2$peak (%predicted) | 65.9± 22.9 | 83.5± 20.7 | 0.04 |

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# Fick equation

| Fick equation: $VO_2 = SV \times HR \times [O_2]_{a-v}$ | |
|---|---|
| SV and HR | $\downarrow$SV x $\leftrightarrow$HR |
| $O_2$ arterial (Hb) | $\downarrow$Hb $\Rightarrow$ $\downarrow[O_2]_a$ |
| Skeletal muscle utilisation of $O_2$ | $\downarrow$SV x $\leftrightarrow$HR x $\uparrow[O_2]_{a-v}$ indicated by $\downarrow[O_2]_a$ and $\downarrow\downarrow[O2]_v$ across skeletal muscle |

Abbreviations: $VO_2$ (oxygen consumption), SV (stroke volume), HR (heart rate), $[O_2]_{a-v}$ (arteriovenous oxygen difference across the pulmonary circulation) and Hb (haemoglobin).

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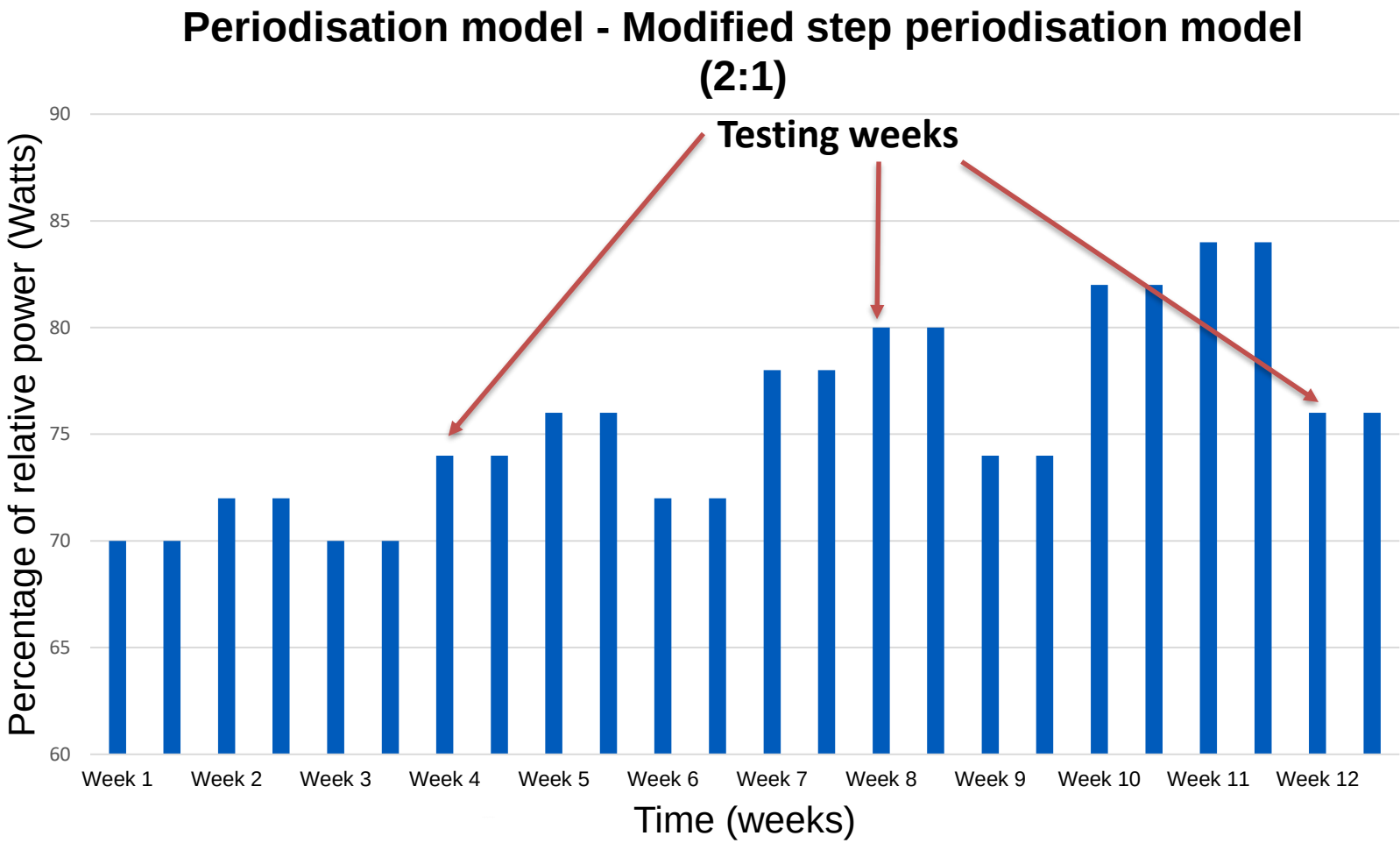
# Exercise intervention model

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