The effectiveness of physical activity on psychological and physical well-being in older breast cancer patients: A systematic review and meta-analysis

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- Breast Cancer (BC) is the most frequent cancer worldwide and the most common among women (DeDantis et al., 2014).
- It is also the second cause of cancer death among women in developed and the first in undeveloped countries (Lahart et al., 2018).
- BC patients suffer adverse physical and psychological effects, including social isolation, depression and anxiety as well as body image concerns (González-Hernandez et al., 2018; Sherman et al. 2018). Patients also experience fatigue, weight gain and chronic distress (Feng et al., 2018).
- Our interest in BC research started with our work in the EC project IMPORTANT.

- Although the causes of BC are unknown, research suggests that engaging in **physical exercise** (Mokhtari-Herasi & Montazeri, 2020) and **mindfulness compassion-based interventions (IMPORTANT EU Project)** produced several benefits on psychological health.

- Among these benefits are improvements on mental health, emotion regulation, and social relations (Kirby et al., 2017; Millard et al., 2023).

- Higher levels of **fatigue** are associated with **worse Quality of life** (QoL), more depression and anxiety symptoms, and lower levels of physical activity (Abrahams et al., 2018) in these patients.

- The **IMPORTANT EU project** (Coord. Dr. Antonis Velachis, Orebro University, Sweden) aims to conduct a pragmatic clinical study with older patients with refractory advanced HR+/HER2-negative BC, focusing on achieving a high level of evidence (level I) and introducing innovative approaches.

- As part of our work in **IMPORTANT**, our UNED group in collaboration with Prof. Flicker and his team (FHNW, Switzerland) are developing an "***Online Mindful Self-Compassion Intervention for older BC patients*** ".

- **IMPORTANT** is a 5-year project that has received funding from **the European Union's Horizon 2020 Research and Innovation programme** under Grant Agreement No. 101104589.

Main Objective of this Systematic Review and Meta-Analysis

- To explore and update the evidence on the effectiveness of **physical exercise**, including aerobics, strength, and combined interventions **in improving QoL and reducing fatigue, anxiety, and depression in BCS.**

- The findings from this **systematic review** will be helpful to develop effective exercise programs to improve quality of life in BCS.

Five Main Research Questions

1. To what extent does exercise improve QoL and reduce fatigue in BC patients? (the global effect)?
2. Do different types of exercise (aerobic, strength training, or combined exercise training) have a different impact on QoL of women suffering BC?
3. Are duration and intensity of the exercise moderators of the effect of regular exercise on the investigated domains?
4. Is the type of control group (active *vs* passive) a moderator of the changes in the investigated domains?
5. Is age a moderator of the effect of exercise on the investigated components of well-being and quality of life?

Eligibility Criteria

❖ We followed the **PICO** framework (Population, Intervention, Comparators, Outcomes

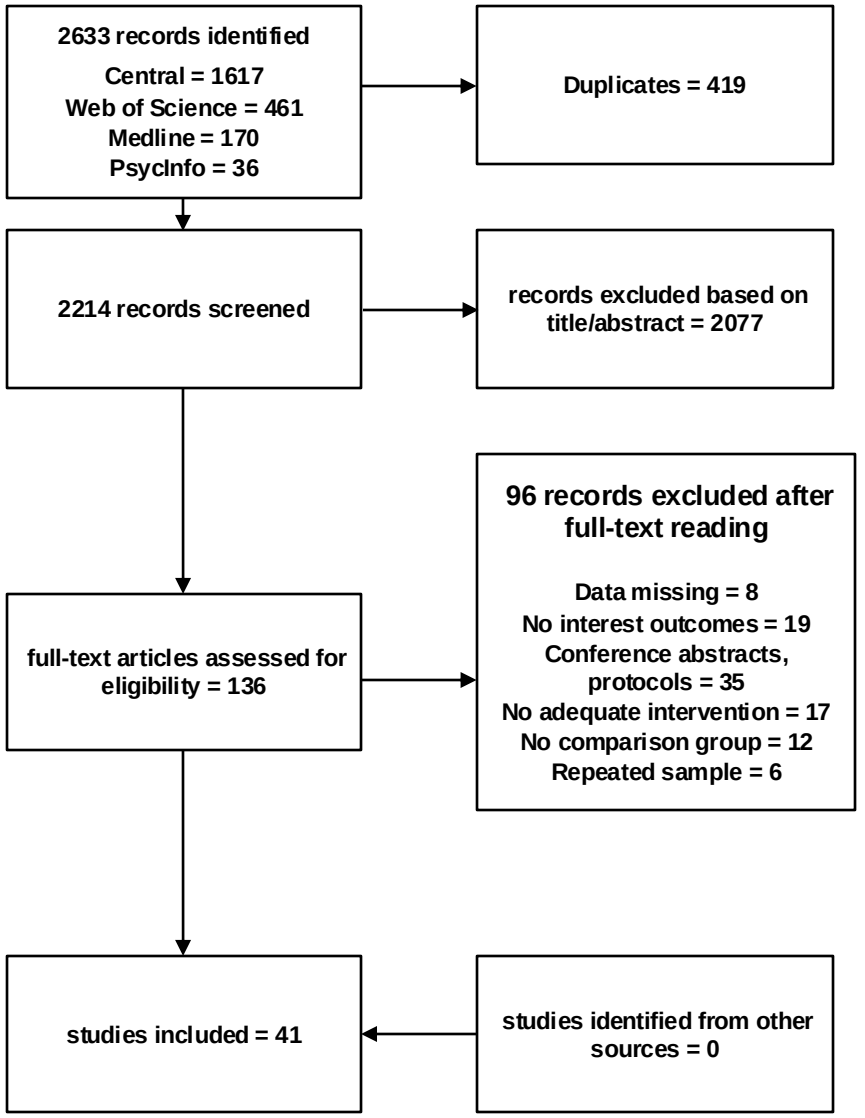
- Population. BC patients with a mean age of 40 years or older.
- Intervention. RCTs focusing on the effects of physical exercise have been screened.
- Comparators. Comparators included active control groups (light exercise, stretching, relaxation) and/or passive control groups (waiting list, usual care, and habitual activities).
- Outcomes. QoL, fatigue, anxiety, depression, and cognitive functions, assessed at baseline and at the end of the intervention through well-validated questionnaires or psychological tests.

Literature search strategy

- ❑ A systematic electronic database search was conducted in PsycInfo, MEDLINE, Web of Science and CENTRAL to identify relevant studies published up to January 2024.

- Keywords used: Breast cancer, physical exercise, physical activity, exercise, walking, strength training, weight training, resistance training, fitness, randomized controlled trial (RCT), older adults, elderly, qualitive of life, fatigue, anxiety, depression, body image, cognition.

Flowchart of the search strategy



Risk of Bias

- The risk of bias (RoB) of the studies is assessed with the Cochrane RoB 2 tool (Higgins & Green, 2006; Sterne et al., 2019).

- Biases are assessed across five areas: bias from the randomization process, deviations from the intended interventions, bias due to missing outcome data, bias in the measurement of the outcomes, and bias in selection of the reported results

- The risk of bias of each study was assessed based on a series of questions provided for each of the five areas and the possible answers in the following 5 categories: "Yes", "Probably yes", "No", "Probably no", and "No information". Finally, the risk of bias in each area will be assessed as “Low risk of bias”, “Some concerns”, or “High risk of bias”.

Statistical Analysis

- **The effects sizes** have been modeled using a three-level structure:

- **Statistical analysis**. Was conducted using the rma.mv function (metaphor package-version 2.4) (Viechtbauer, 2010) within the R software environment (version 4.0.1; R Core Team, 2021). Dot-plot figures were depicted using Mathematica (version 10.4) with software developed specifically for the present study.

- After completing the selection stages, 41 studies were included (flow chart) in the review and meta-analysis. Then, the relevant information contained in these included studies was extracted in an Excel spreadsheet.

DESCRIPTIVE RESULTS: Participants characteristics and type of EX

- A total of 4065 BC patients participated in the 40 articles (41 studies) with a mean age of 53,69 years.
- The studies were published since 2003 up to 2021. The largest number of studies was in 2019 with **7 studies**, followed by 2018 with **5**, 2014, 2015, and 2016 with **4** articles each year; **3** articles in 2013, and 2020, **2** articles in 2011 and 2021, and just **one** article per year in 2003, 2007- 2010 and 2017.
- The countries with the largest number of studies were Australia and Canada with **6** articles each, followed by USA with **5**, Spain with **4.** Then, United Kingdom with **3**, Germany, Sweden and Taiwan with **2** articles each, and Denmark, Latvia, Brazil, Turkey, Korea, Belgium, Kosovo, Ukraine, Iran and The Netherlands with **one** article each.
- Regarding the type of exercise, 16 articles trained aerobics, 11 trained strength, and 13 combined (aerobics and strength) training.
- The total duration of the intervention varied from 8 weeks in 3 studies to 48 weeks in another 3 studies with most intervention lasting 12 weeks (20 studies).

Preliminary results

Effects of exercise on Fatigue

- The analysis of Hedges' g for Fatigue (random model) showed a significant heterogeneity

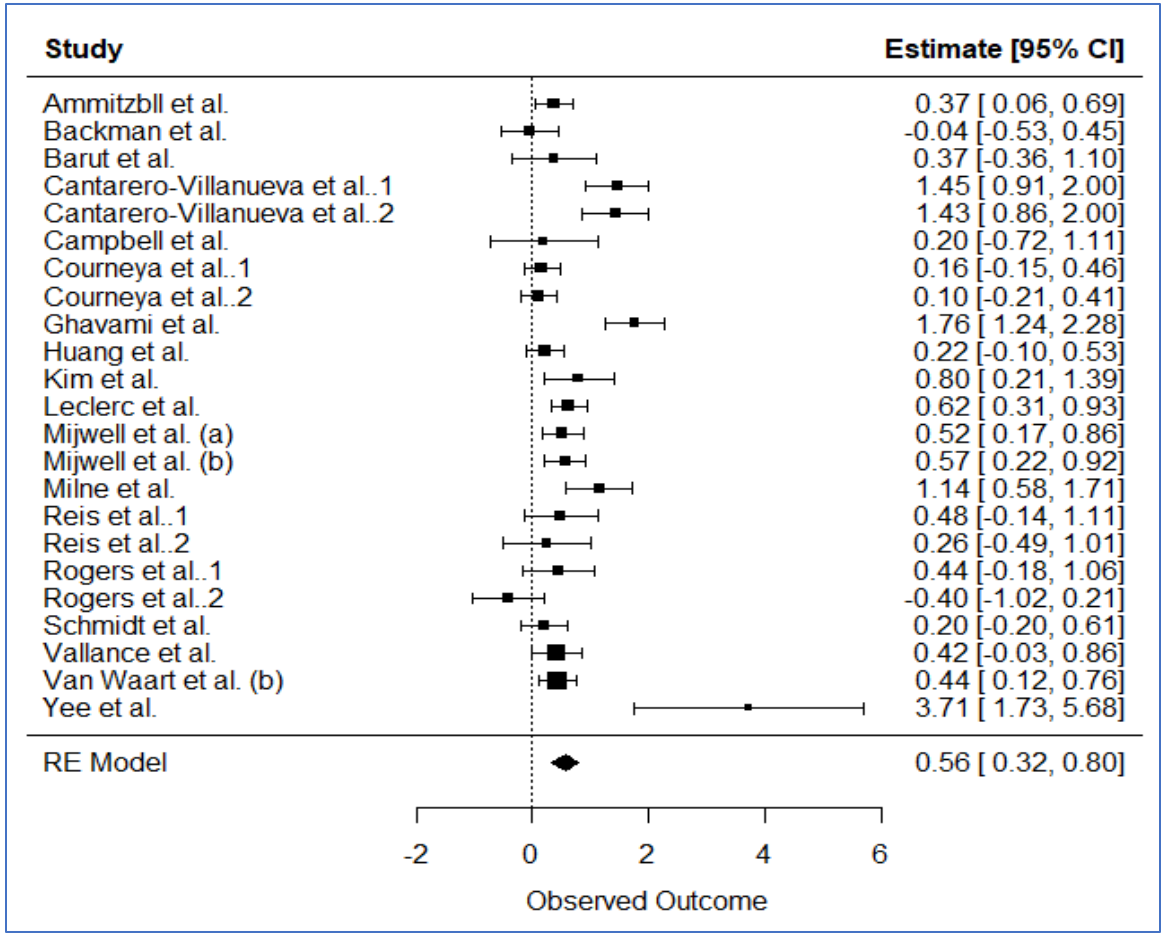
Between-study heterogeneity was significant	**Q(22) = 91.99, *p* < .0001**

Conclusion:

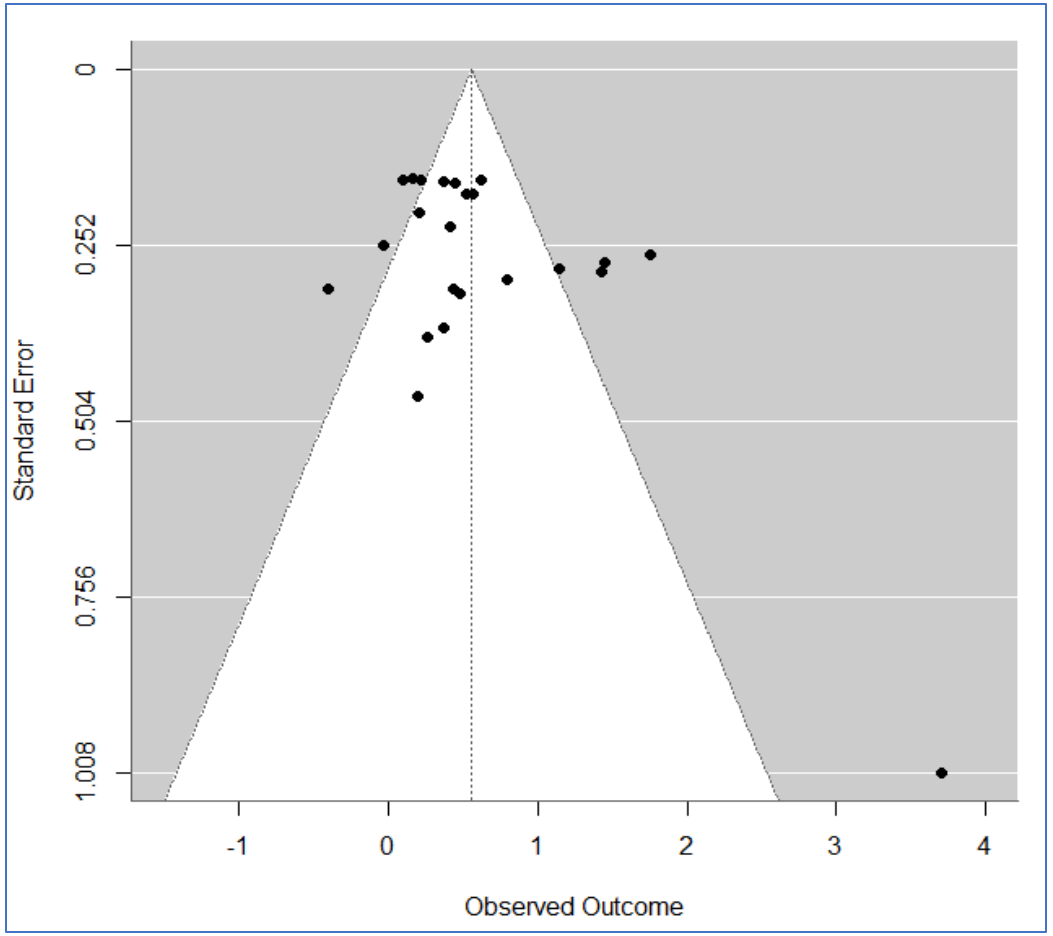
- Our data has more variation than can be expected from sampling error alone.
- Sampling error variance comes from random sampling of participants in every study.
- There is variation due to between-study heterogeneity, as expected in a random model.

Estimate of the ES for fatigue	Standard error	T-value	Degrees of freedom	P-value	Inferior limit	Superior limit
0.5585	0.1163	4.8005	22	< .0001	0.3172	0.7998

Forest Plot: Effect Sizes for Fatigue



Fannel Plot for the Summary Effects



Pre-post comparison (g = 0.56, p < 0.001, 95% CI [0.32, 0.80])
Summary effects for Fatigue (k = 23), Method: REML

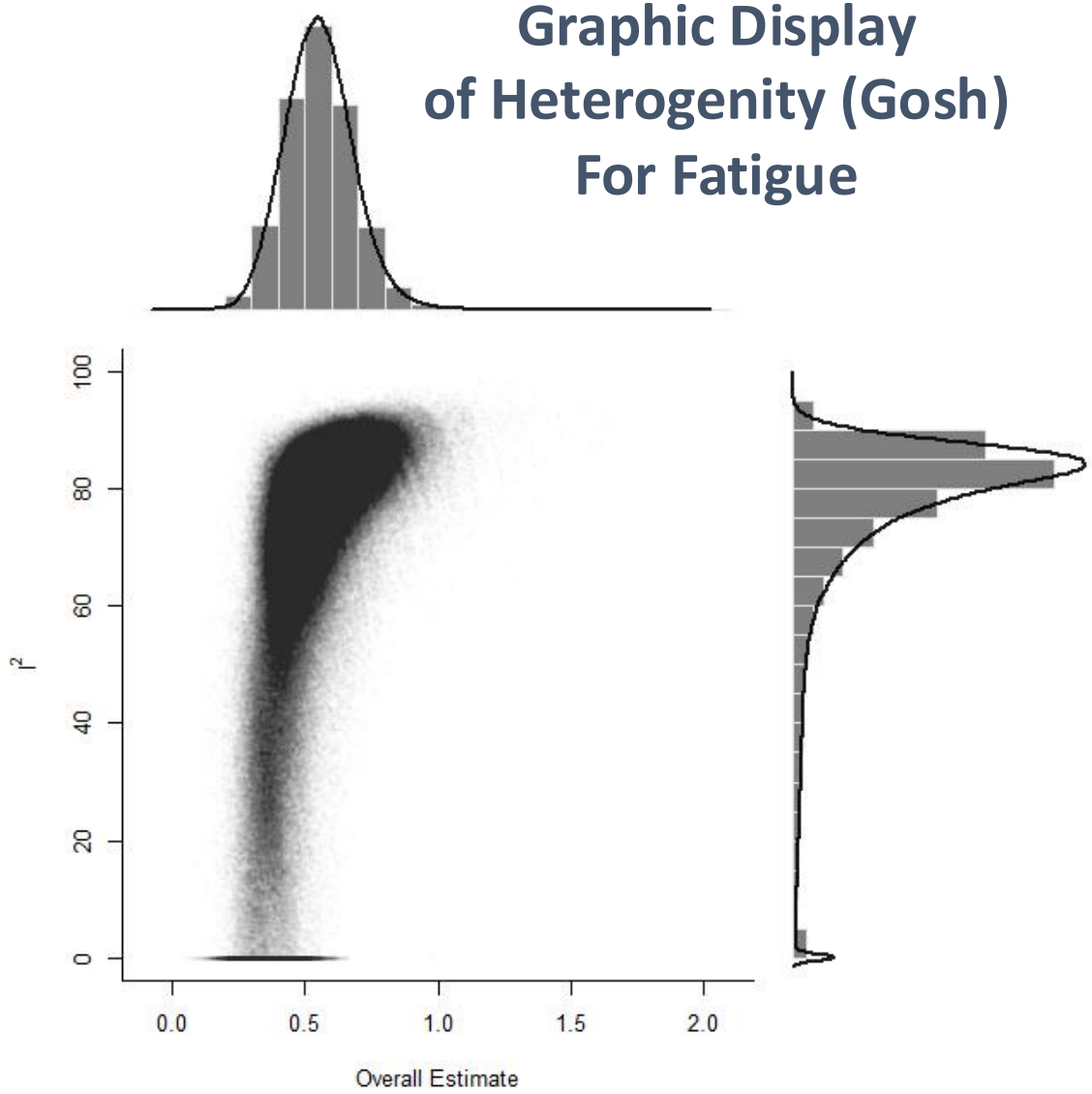
Outliers and influence analysis not performed yet!

Gosh: A fitting of the same meta-analysis model to all possible subsets of the included studies.
Pooled effect size on the x-axis and the between-study heterogeneity on the y-axis.

- Most values are concentrated in a cluster with relatively high effects and high heterogeneity.
- The distribution of I^2 values is heavily right-skewed and bimodal.
- Some study combinations showed low heterogeneity but with pooled effect sizes also smaller.

- I^2 = Percentage of variability in the Effect Sizes not caused by sampling error.

Graphic Display of Heterogenity (Gosh) For Fatigue



Exercise effects on Quality of Life (Global Score)

- The analysis of Hedges' g for QoL global (random model) showed a significant

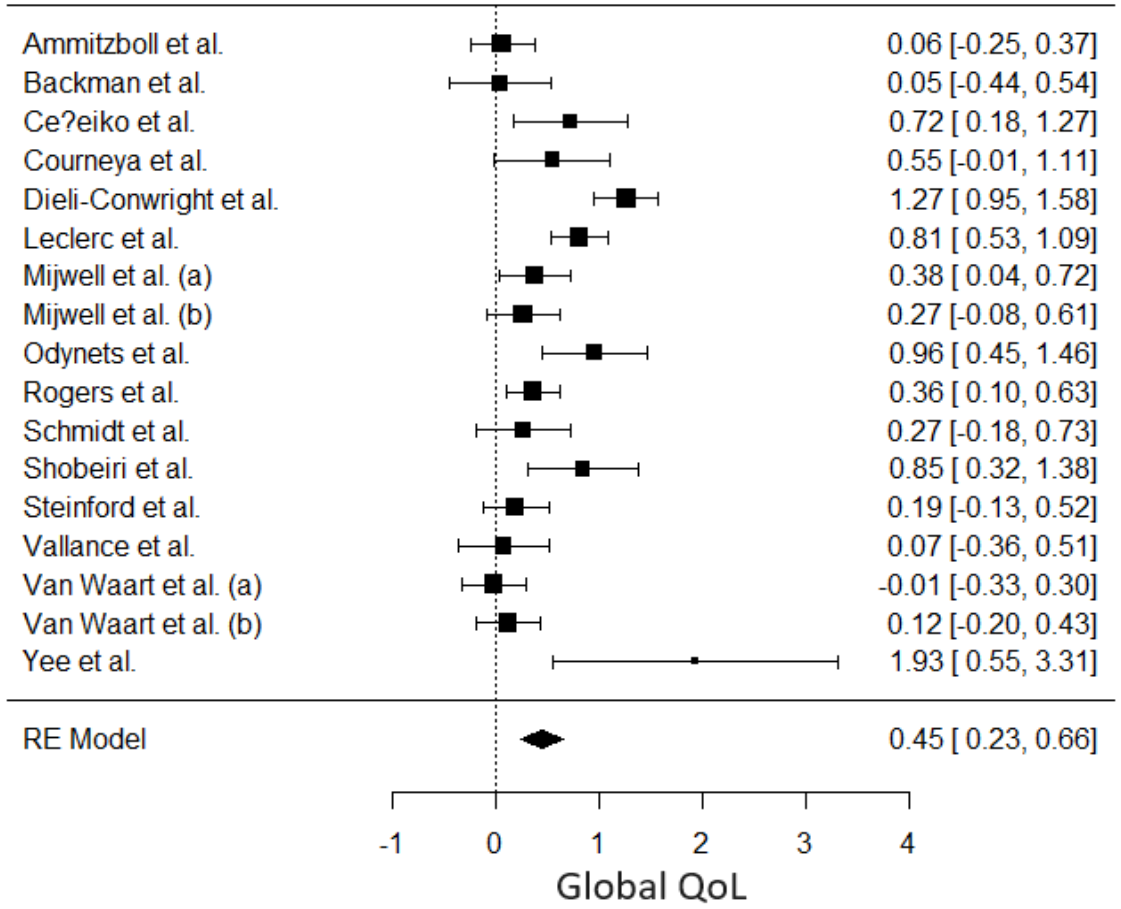
Between-study heterogeneity significant	**Q(16) = 72.2054, p < .0001**

Results: Our data has more variation than can be expected from sampling error alone. Sampling error variance comes from random sampling of participants in every study. There is variation due to between-study heterogeneity.

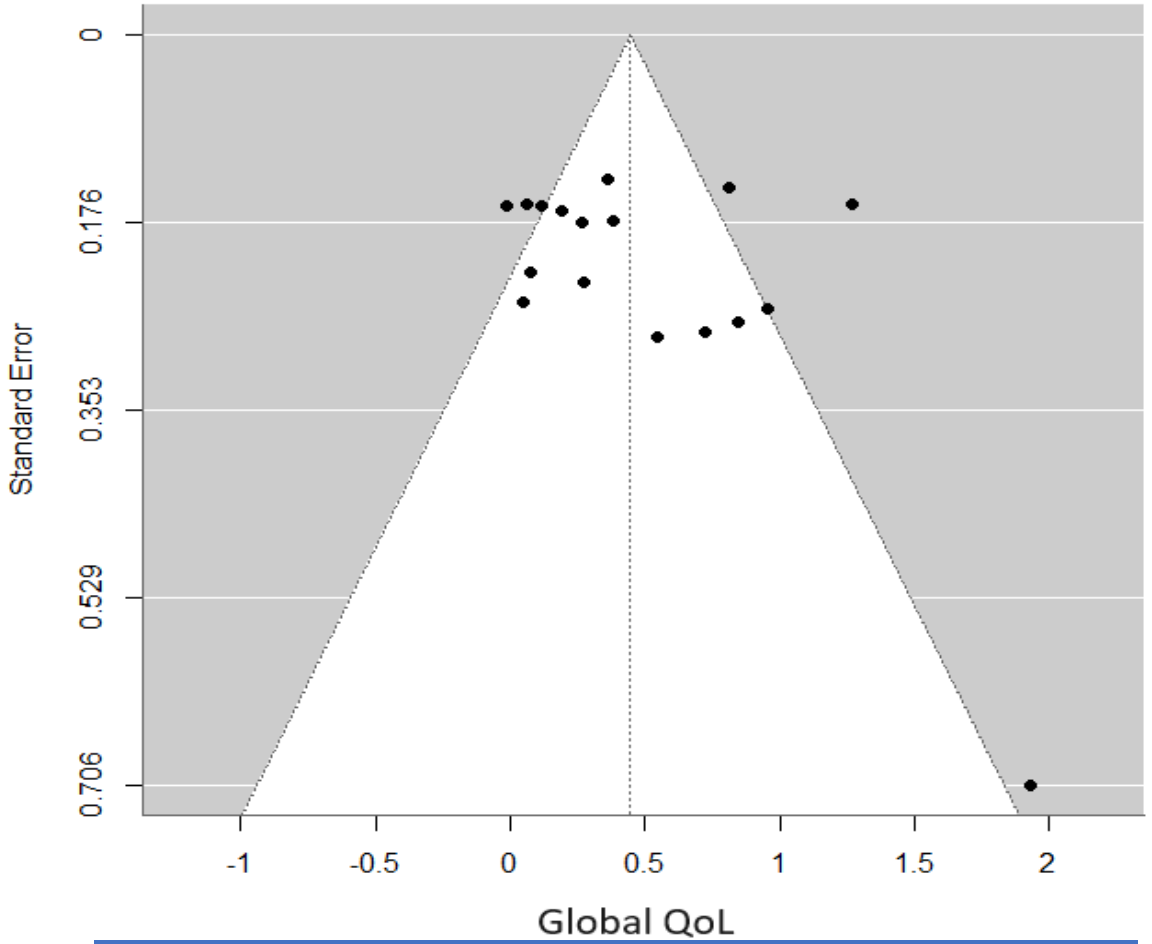
Medium positive effect of exercise on global score of QoL in BC patients.

Estimate ES for QoL	Standard error	T-value	Degrees of freedom		Inferior limit	Superior limit
0.4466	0.0999	4.4689	16	0.0004	0.2348	0.6585

Forest Plot: Effect Sizes QoL (Global)



Fannel Plot for the Summary Effects

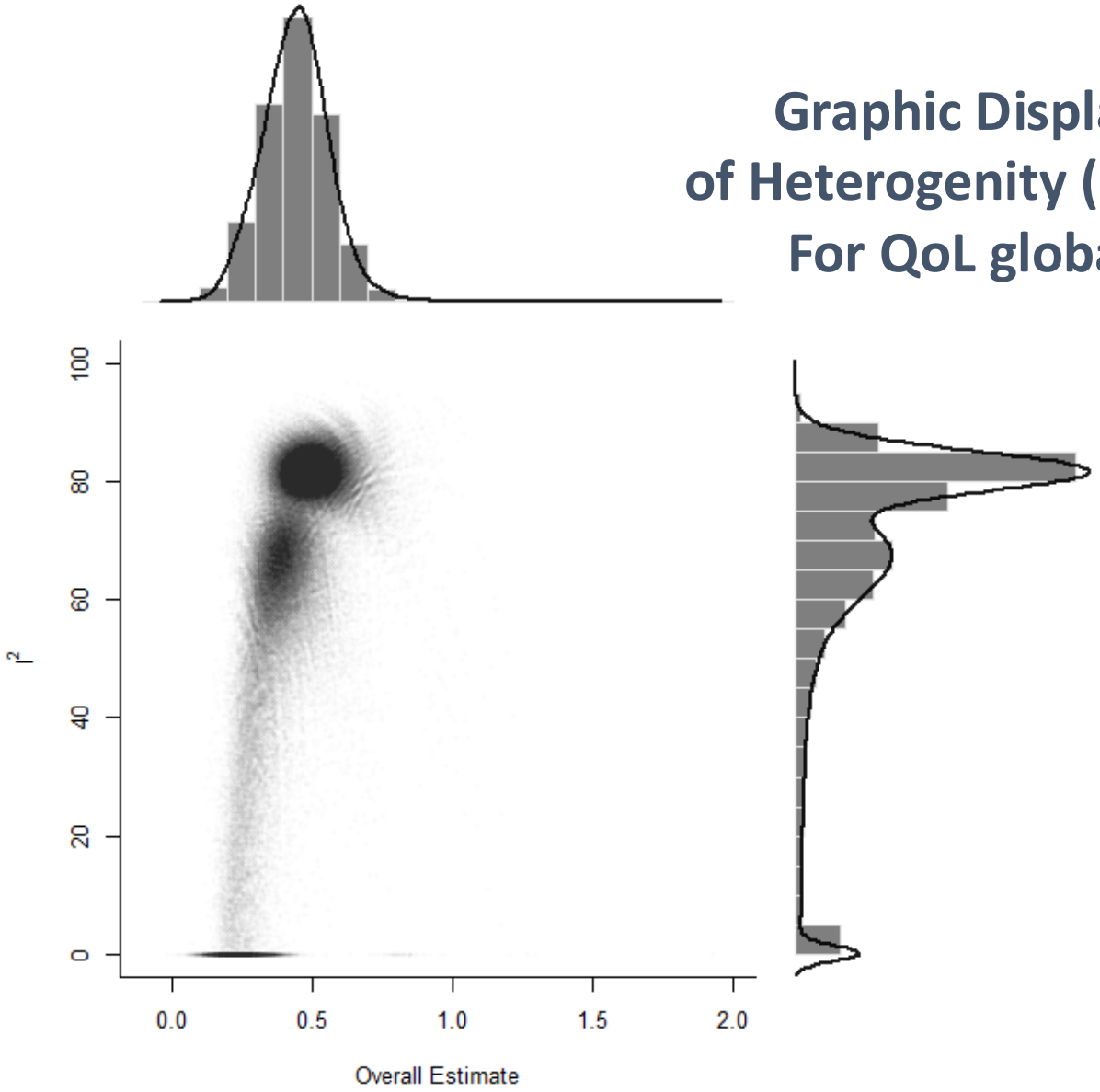


Pre-post comparison (g = 0.45, p < 0.001, 95% CI [0.23, 0.66])
Summary effects for QoL Global (k = 17), Method: REML

Outliers and influence analysis not performed yet!

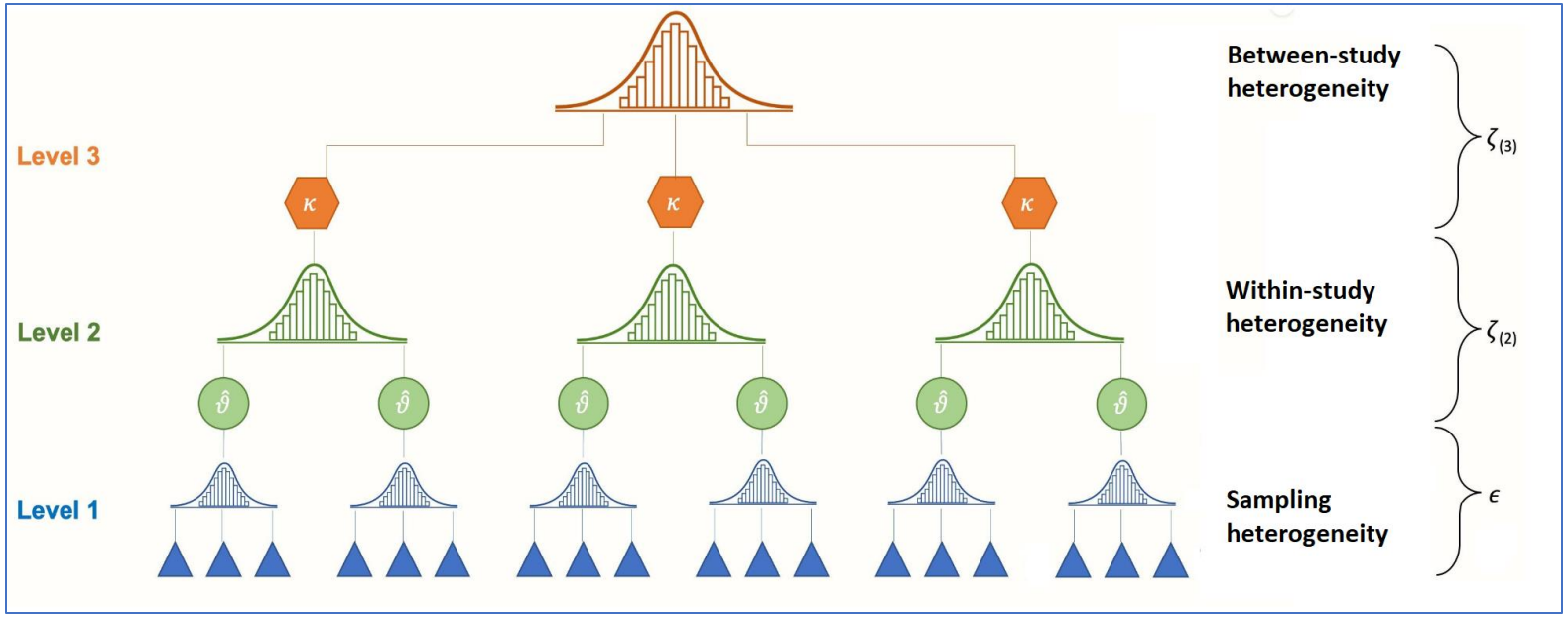
Graphic Display of Heterogenity (Gosh) For QoL global

- Most values are concentrated in a cluster with relatively high effects and high heterogeneity.
- The distribution of I^2 values is heavily right-skewed and tri-modal.
- Some study combinations showed low heterogeneity but with pooled effect sizes also smaller.



Quality of Life (multilevel analysis)

- As studies informed about several effect sizes (EF) for QoL (physical, role, emotional, social cognitive, mental, functional and fatigue QoL), the scores were dependent. We applied a three-level structure to the meta-analytic analysis to assess the within-study and between study heterogeneity (Cheung, 2014).



Results: most of the variability is due to level three

21.14 % of the total variance attributed to variance at level 1.

25.97 % of the total variance attributed to variance at level 2

52.88 % of the total variance attributed to variance at level 3

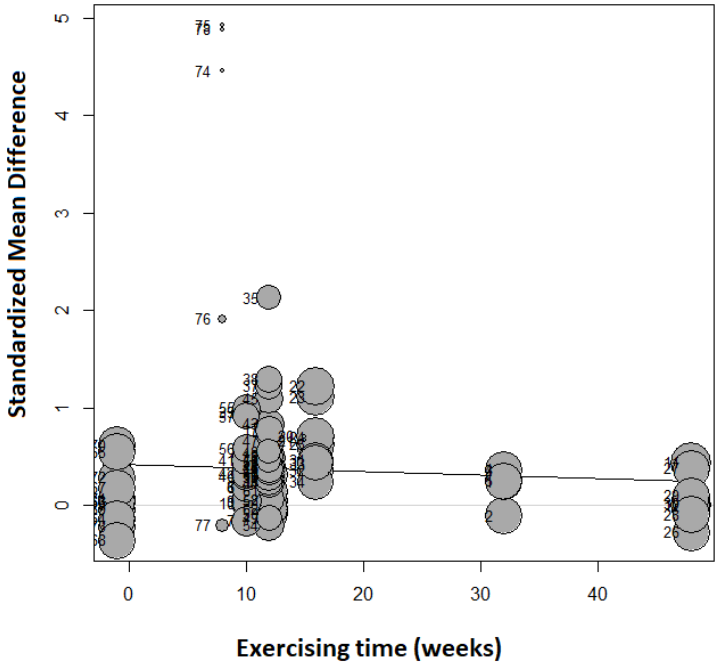
Does Quality of Life (QoL) depend on type of exercise or on the mean age?

§ It seems that aerobic exercise shows larger effect on QoL
§ The mean age of the participants is not significant (but not far from significance).

	Estimate	Standard error	T-value	Degrees of freedom	P-value	Inferior limit	Superior limit
Intercept	0.2525	0.1051	2.4019	74	0.0188	0.0430	0.4620
Strength	0.0707	0.1045	0.6767	74	0.5007	-0.1375	0.2789
Aerobic	0.1821	0.0778	2.3400	74	**0.0220**	0.0270	0.3372
Mean Age	0.0012	0.0007	1.6387	74	0.1055	-0.0003	0.0026

Does Quality of Life (QoL) depend on length of training?

- There is no evidence of the effect of the variable length of training on QoL



	Estimate	Standard error	T-value	Degrees of freedom	P-value	Inferior limit	Superior limit
Intercept	0.4216	0.0883	4.7761	76	< .0001	0.2458	0.5975
Training weeks	-0.0036	0.0042	-0.8371	76	**0.4052**	-0.0120	0.0049

DISCUSSION AND CONCLUSION

- This review and meta-analysis included 41 physical EX intervention studies (with 4065 BC patients; mean age 54 years) that investigated the effectiveness of exercise training in improving fatigue and quality of life of BCS.
- Although the results are very preliminary, the overall effect sizes revealed **medium positive effects of exercise** interventions on **fatigue** and **quality of life** in BC patients.
- Only "**aerobic exercise**" seems to moderate the effect on QoL, and mean age appears promising as a moderator factor, but not significant. Practice time does not seem to affect QoL.
- The variability due to differences between labs explains 50% of the variance on QoL.
- In agreement with previous meta-analyses (Dorri et al, 2020; Goldschmidt et al., 2023; Lee, 2018), our preliminary analysis suggest that exercise interventions had beneficial effects in BC patients.