Physical activity and the risks of breast cancer in the Korean Hereditary Breast Cancer Study

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1. Background

Epidemiology of breast cancer

- Female breast cancer is the second leading cause of global cancer incidence in 2022.

- Among women, breast cancer is the most commonly diagnosed cancer, and it is the leading cause of cancer deaths globally and in 157 countries for incidence and in 112 countries for mortality.

Physical activity and the risk of cancer

PHYSICAL ACTIVITY AND THE RISK OF CANCER					
WCRF/AICR GRADING		DECREASES RISK		INCREASES RISK	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing	Physical activity[1]	Colorectum (colon) 2017[2]		
	Probable	Physical activity[1]	Breast (postmenopause) 2017[3]		
			Endometrium 2013		
		Vigorous-intensity physical activity	Breast (premenopause) 2017[3]		
			Breast (postmenopause) 2017[3]		
LIMITED EVIDENCE	Limited – suggestive	Physical activity[1]	Oesophagus 2016[4]	Sedentary behaviours	Endometrium 2013[5]
			Lung 2017		
			Liver 2015		
			Breast (premenopause) 2017[3]		
STRONG EVIDENCE	Substantial effect on risk unlikely	None identified			

1 The exposure of physical activity includes evidence for all types of activity and all intensity levels.

2 The evidence for physical activity and colorectum is for colon cancer only – no conclusion was drawn for rectal cancer.

3 In addition to physical activity, there was sufficient evidence for the Panel to make a separate judgement for vigorous-intensity physical activity and breast cancer (pre and postmenopause).

4 The evidence for physical activity and oesophageal cancer includes unspecified, adenocarcinoma and squamous cell carcinoma.

5 The evidence for sedentary behaviours and endometrial cancer was marked by sitting time.

1. Background

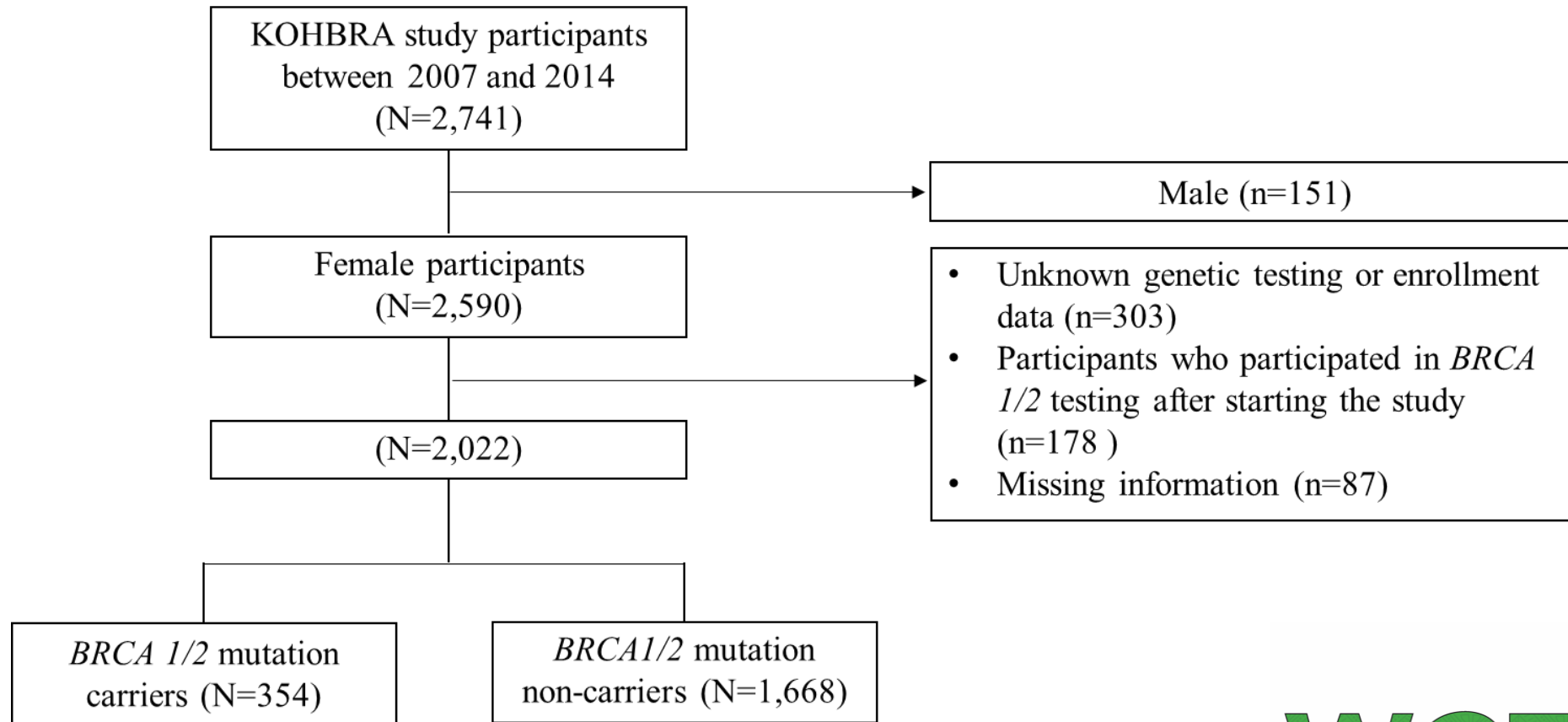- **Physical activity and the risks of cancer**

- A systematic literature review of the relationship between PA and BC concluded that PA is significantly associated with a decrease in the risk of BC. The overall relative risks (ORR) for BC was 0.87 (95% CI=0.84-0.90).

- Also, in subgroup analysis by menopausal status, the ORR was 0.83 (95% CI=0.79-0.87) for premenopausal status and 0.91 (95% CI=0.85-0.97) for postmenopausal women.

- However, a limited number of studies suggests that PA may reduce BC risks among BRCA1/2 carriers.

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2. Objective

- We aimed to examine the association between physical activity and breast cancer risks according to menopause status and BRCA1/2 mutation carrier status, especially with Korean women's population.

3. Materials and Methods

• **Study population**

KOHBRA study participants between 2007 and 2014 (N=2,741)

Male (n=151)

Female participants (N=2,590)

- Unknown genetic testing or enrollment data (n=303)
- Participants who participated in *BRCA 1/2* testing after starting the study (n=178)
- Missing information (n=87)

(N=2,022)

BRCA 1/2 mutation carriers (N=354)

BRCA1/2 mutation non-carriers (N=1,668)
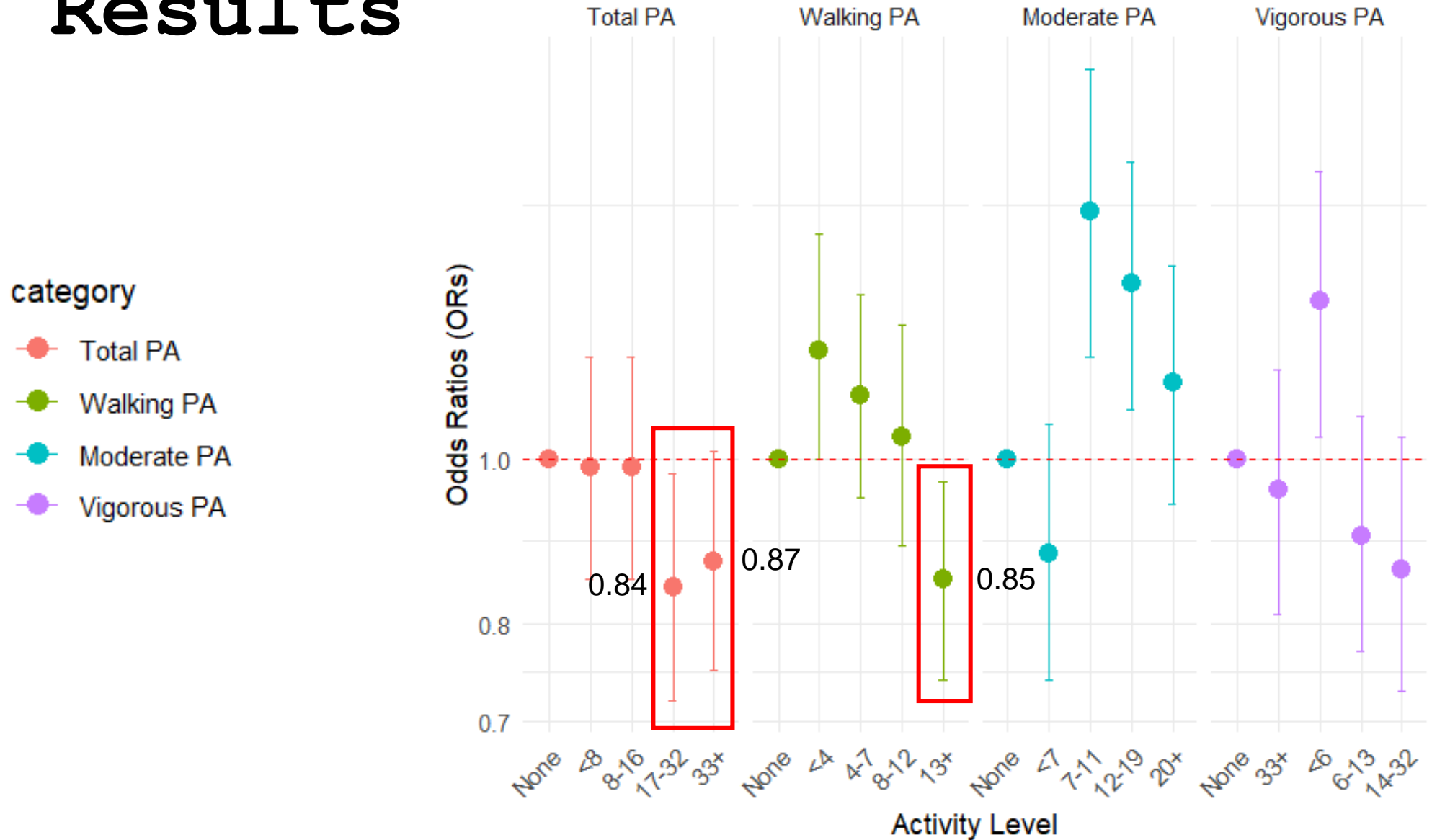
3. Materials and Methods

- **Statistical Analysis**

- To calculate MET hours a week, multiply the MET value given by the hours the activity was carried out and again by the number of days that activity was undertaken. (walking 3.3, moderate 4, vigorous 8)

- Cox's proportional hazard model and 95% CI were used to assess the association between exercise and breast cancer risks, with variables adjusted by marriage status, smoking, BMI, used of HRT, and intake calories (kcal).

- Stratified analysis was performed in menopausal status and BRCA ½ carrier status.
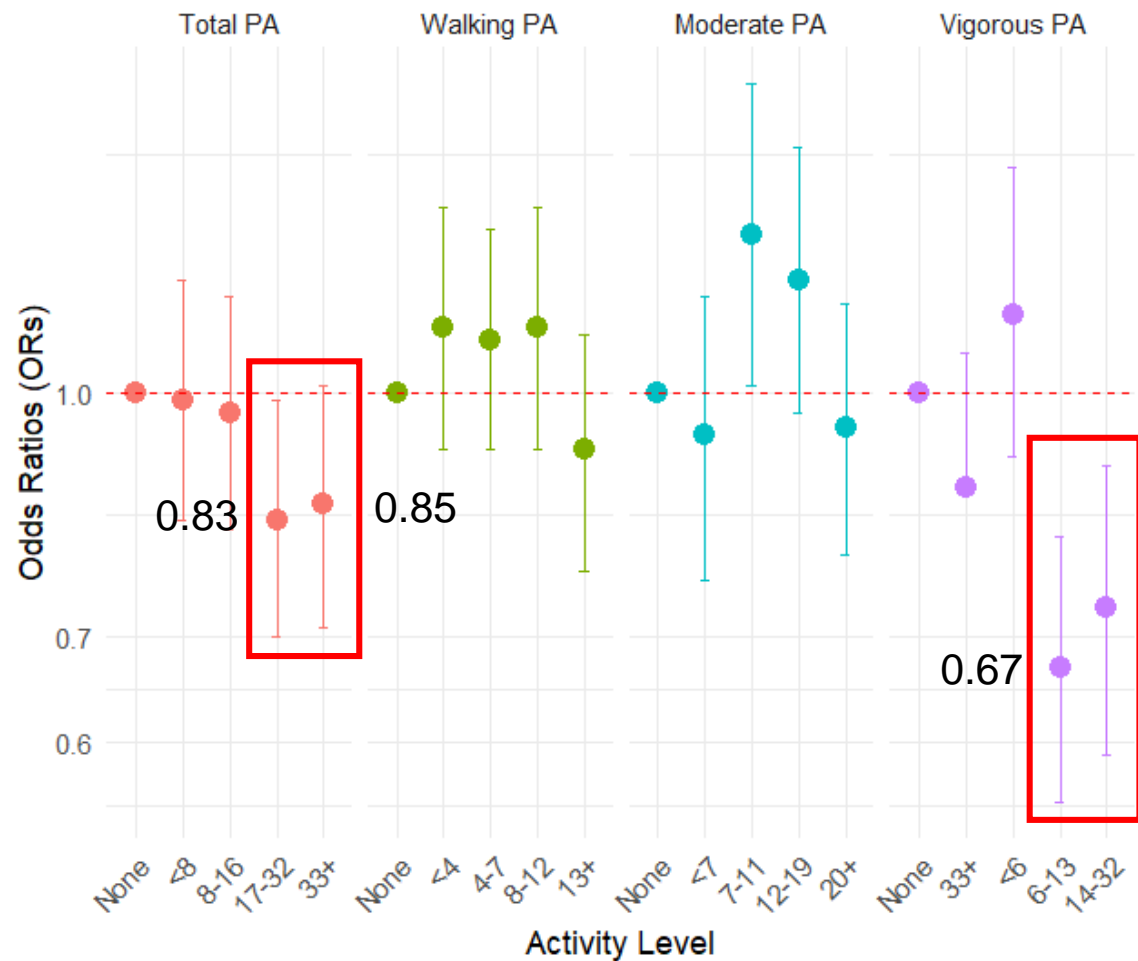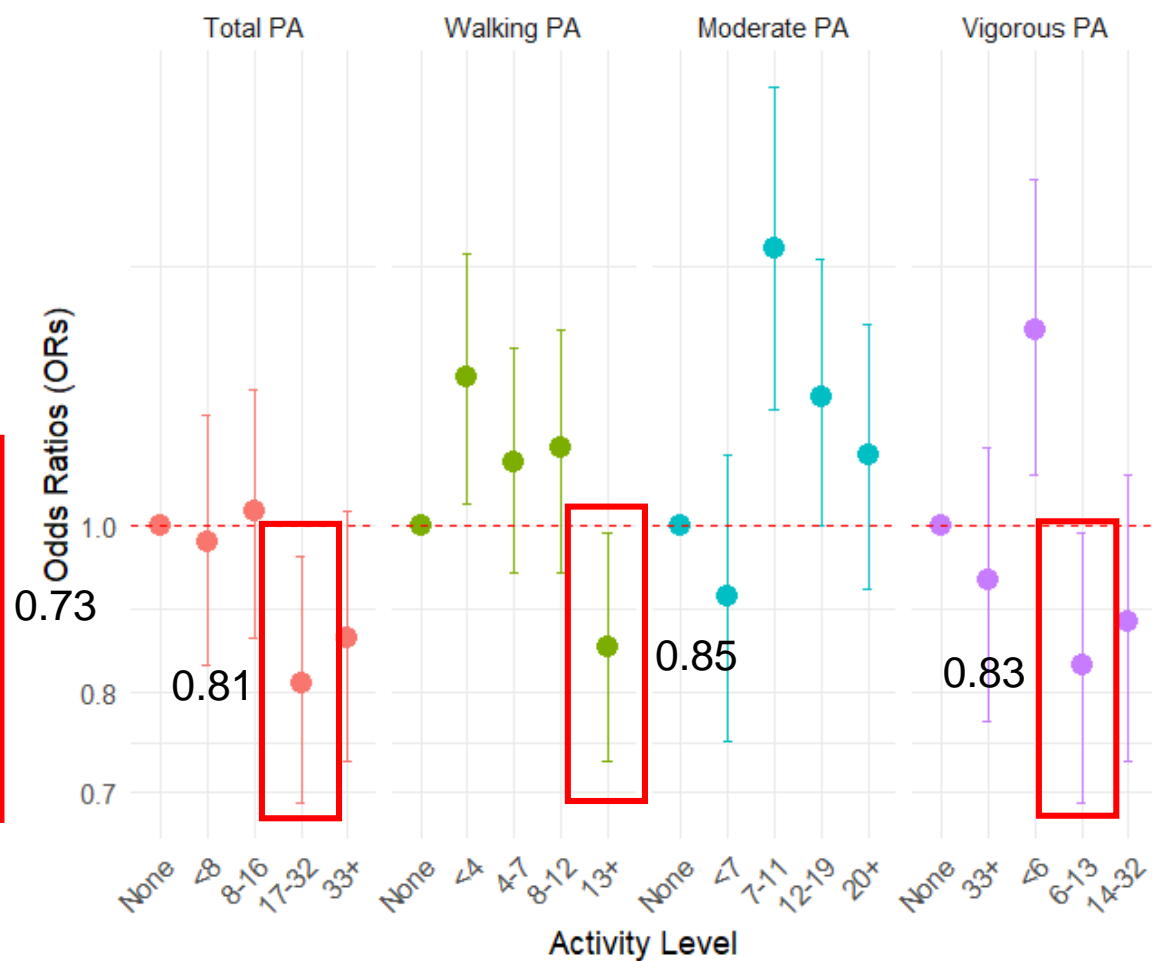
4. Results

Odds Ratios for Different Physical Activities: All cohorts

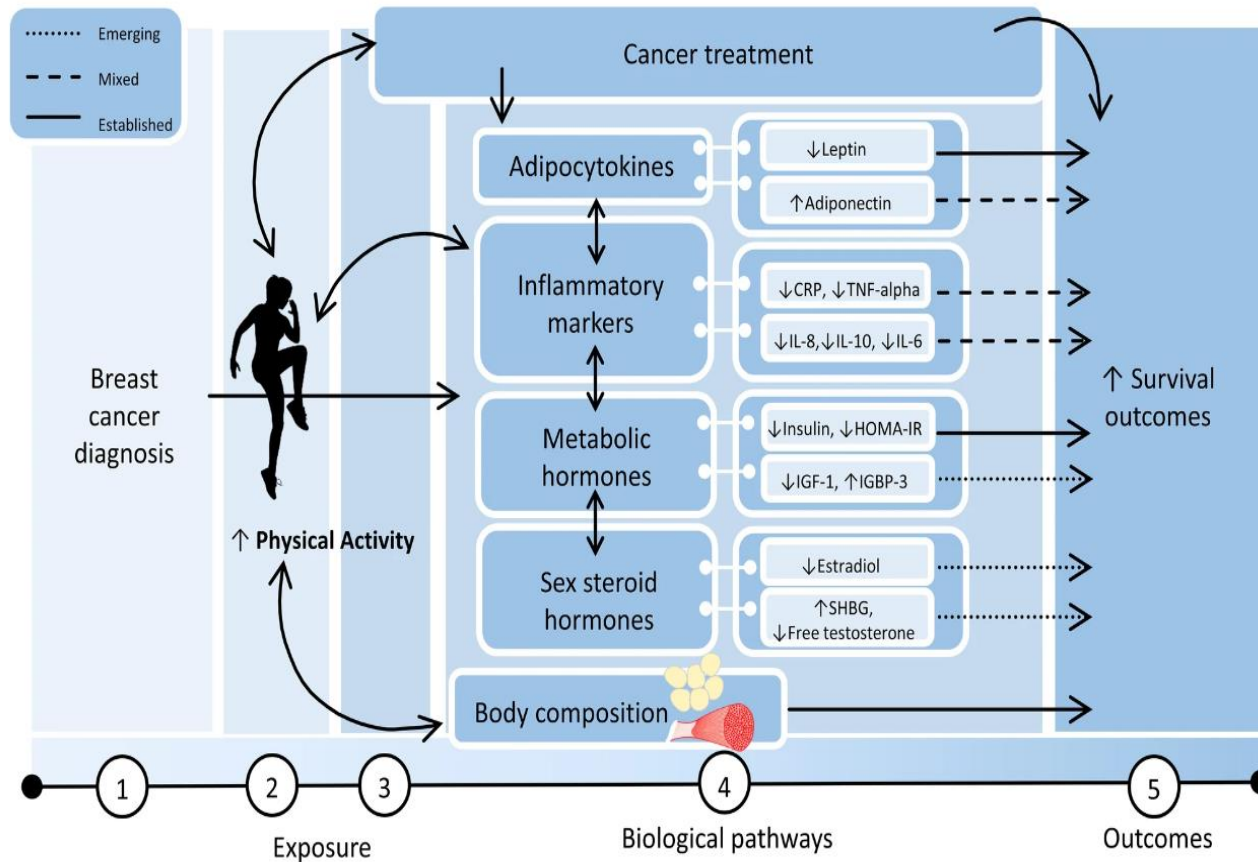**Pre-menopause women**

BRCA ½ Non-carrier

5. Discussion & Conclusion

- **Further considerations**

- The characteristics of the KOHBRA study (Mean: 24.62 MET-hour/week)

- The lack of significant results in post menopausal women → suggested that further analysis stratifying women with high BMI should be considered)

Thank you for listening ☺

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Supplementary Tables

Table 1. Baseline characteristics by total physical activity (MET* hours/week)

	Total participants (n=2,022)				
	Irregular exercise	Regular exercise	p-value		
N. of participants, %	1,248 (61.7)	774 (38.3)			
Age, years (SD)	55.7 (9.80)	59.5 (9.7)	< .0001		
	N (%)	**N (%)**			
Education					
College/graduate degree	662 (53.3)	373 (48.4)	0.09		
Marriage status					
Married	979 (78.6)	647 (83.8)	0.003		
Smoking			0.01		
Never	1,108 (88.9)	718 (92.8)			
Former	103 (8.3)	43 (5.5)			
Current	36 (2.9)	13 (1.7)			
Alcohol			0.74		
Never	760 (61.0)	482 (62.5)			
Former	274 (22.0)	159 (20.6)			
Current	212 (17.0)	130 (16.9)			
Body mass index (kg/m^2)			0.006		
< 18.5	120 (9.7)	50 (6.5)			
18.5-23	648 (52.2)	409 (53.0)			
23-25	231 (18.6)	180 (23.3)			
≥ 25	243 (19.6)	133 (17.2)			
Age at menarche (years)			0.05		
< 12	30 (2.4)	13 (1.7)			
13-14	643 (51.6)	361 (46.7)			
15-16	458 (36.8)	308 (39.9)			
≥ 17	114 (9.2)	90 (11.7)			
Age at menopause (years)			< .0001		
Pre-menopause	966 (83.2)	470 (66.2)			
< 50	127 (10.9)	146 (20.6)			
≥ 50	68 (5.9)	94 (13.2)			
Parity			0.017		
Never	257 (23.0)	125 (18.2)			
Ever	863 (77.0)	561 (81.8)			
Tubal ligation			0.29		
Never	1,170 (93.8)	734 (95.0)			
Ever	77 (6.2)	39 (5.0)			
Oral contraceptives			0.63		
Never	1,105 (88.5)	692 (89.4)			
Ever	142 (11.4)	82 (10.6)			
Hormone replacement therapy			< .0001		
Never	1,221 (97.8)	730 (94.3)			
Ever	27 (2.2)	44 (5.7)			
Breast cancer cases (%)	1,098 (88.0)	677 (87.5)	0.732		
Breast cancer type			0.031		
Luminal A	40 (13.5)	17 (11.0)			
Luminal B	143 (48.3)	72 (46.8)			
HER2 overexpression	88 (29.7)	61 (39.6)			
Triple negative	25 (8.5)	4 (2.6)			

*Total activity=Walking+Moderate physical activity (PA)+Vigorous PA

**Missing variables: smoking (1 participant), alcohol drinking (5 participants), BMI (8 participants), age at menarche (5 participants), age at menopause (151 participants), parity (216 participants), tubal ligation (2), oral contraceptives (1)

1. Performed chi-square test for categorical variables and student t-test for continuous variables (ANOVA for age variables).

Table 2. By menopause status

	Total cohorts (N=2,022)			Pre-menopause women (N=1,436)			Postmenopause women (N=586)		
	Non-BC N (%)	BC cases N (%)	Adjusted HR [3] (95% CI)	Non-BC N (%)	BC cases N (%)	Adjusted HR [3] (95% CI)	Non-BC N (%)	BC cases N (%)	Adjusted HR [3] (95% CI)
Total PA									
None	46 (18.6)	351 (19.8)	1.00	36 (19.9)	260 (20.7)	1.00	10 (15.2)	91 (17.5)	1.00
< 8	45 (18.2)	320 (18.0)	0.99 (0.85-1.15)	38 (21.0)	250 (20.0)	0.99 (0.83-1.18)	7 (10.6)	70 (13.5)	1.02 (0.75-1.41)
8-16	42 (17.0)	377 (21.2)	0.99 (0.85-1.15)	33 (18.2)	261 (20.8)	0.97 (0.82-1.15)	9 (13.6)	116 (22.3)	1.25 (0.94-1.65)
17-32	55 (22.3)	324 (18.2)	0.84 (0.72-0.98)	35 (19.4)	222 (17.6)	0.83 (0.70-0.99)	20 (30.3)	102 (19.6)	1.07 (0.80-1.42)
≥ 33	54 (21.9)	356 (20.1)	0.87 (0.75-1.01)	35 (19.3)	233 (18.5)	0.85 (0.71-1.01)	19 (28.8)	123 (23.6)	1.10 (0.83-1.45)
Missing	5 (2.0)	47 (2.6)		4 (2.2)	29 (2.3)		1 (1.5)	18 (3.5)	
Walking PA									
None	102 (41.3)	661 (37.2)	1.00	76 (42.0)	476 (37.9)	1.00	26 (39.4)	185 (35.6)	1.00
< 4	36 (14.6)	230 (13.0)	1.16 (1.00-1.36)	33 (18.2)	178 (14.2)	1.10 (0.92-1.31)	3 (4.6)	52 (10.0)	1.35 (0.99-1.86)
4-7	35 (14.2)	303 (17.1)	1.09 (0.95-1.25)	26 (14.4)	232 (18.5)	1.08 (0.92-1.27)	9 (13.6)	71 (13.7)	1.14 (0.86-1.52)
8-12	30 (12.1)	252 (14.2)	1.03 (0.89-1.20)	21 (11.6)	172 (13.7)	1.10 (0.92-1.31)	9 (13.6)	80 (15.4)	1.05 (0.80-1.37)
≥ 13	41 (16.6)	306 (17.2)	0.85 (0.74-0.97)	23 (12.7)	182 (14.5)	0.92 (0.77-1.09)	18 (27.3)	124 (23.8)	0.98 (0.78-1.23)
Missing	3 (1.2)	23 (1.3)		2 (1.1)	15 (1.2)		1 (1.5)	8 (1.5)	
Moderate PA									
None	155 (62.7)	1,150 (64.8)	1.00	112 (61.9)	801 (63.8)	1.00	43 (65.1)	349 (67.1)	1.00
< 7	25 (10.1)	149 (8.4)	0.88 (0.74-1.05)	20 (11.0)	108 (8.6)	0.94 (0.76-1.15)	5 (7.6)	41 (7.9)	0.86 (0.62-1.20)
7-11	11 (4.5)	112 (6.3)	1.40 (1.15-1.70)	7 (3.9)	86 (6.8)	1.26 (1.01-1.57)	4 (6.1)	26 (5.0)	1.52 (1.01-2.28)
12-19	21 (8.5)	160 (9.0)	1.27 (1.07-1.50)	16 (8.8)	119 (9.5)	1.18 (0.97-1.43)	5 (7.6)	41 (7.9)	1.35 (0.97-1.87)
≥ 20	33 (13.4)	183 (10.3)	1.11 (0.94-1.30)	24 (13.3)	131 (10.4)	0.95 (0.79-1.14)	9 (13.6)	52 (10.0)	1.43 (1.06-1.93)
Missing	2 (0.8)	21 (1.2)		2 (1.1)	10 (0.8)		0 (0.0)	11 (2.1)	
Vigorous PA									
None	158 (64.0)	1,151 (64.9)	1.00	113 (62.4)	821 (65.4)	1.00	45 (68.2)	330 (63.5)	1.00
< 6	17 (6.9)	134 (7.5)	1.24 (1.03-1.48)	16 (8.8)	95 (7.6)	1.12 (0.91-1.39)	1 (1.5)	39 (7.5)	1.63 (1.16-2.29)
6-13	25 (10.1)	169 (9.5)	0.90 (0.77-1.06)	20 (11.1)	126 (10.0)	0.67 (0.55-0.81)	5 (7.6)	43 (8.3)	1.45 (1.04-2.10)
14-32	26 (10.5)	140 (7.9)	0.86 (0.73-1.03)	17 (9.4)	94 (7.5)	0.73 (0.59-0.90)	9 (13.6)	46 (8.6)	1.24 (0.90-1.70)
≥ 33	21 (8.5)	163 (9.2)	0.96 (0.81-1.13)	15 (8.3)	108 (8.6)	0.87 (0.71-1.06)	6 (9.1)	55 (10.6)	1.16 (0.87-1.56)
Missing	0 (0.0)	18 (1.0)		0 (0.0)	11 (0.9)		0 (0.0)	7 (1.4)	

Table 3. By BRCA ½ carrier status

*The unit for all physical activity is MET-hours/week.
3. Adjusted by marriage status, smoking, BMI, use of HRT, and intake calories (kcal.).

	Total cohorts (N=2,022)			Non-carrier (N=1,668)			BRCA1/2 Carrier (N=354)		
	Non-BC N (%)	BC cases N (%)	Adjusted HR [3] (95% CI)	Non-BC N (%)	BC cases N (%)	Adjusted HR [3] (95% CI)	Non-BC N (%)	BC cases N (%)	Adjusted HR [3] (95% CI)
Total PA									
None	46 (18.6)	351 (19.8)	1.00	38 (17.1)	269 (18.6)	1.00	8 (32.0)	82 (24.9)	1.00
< 8	45 (18.2)	320 (18.0)	0.99 (0.85-1.15)	42 (18.9)	269 (18.6)	0.98 (0.83-1.16)	3 (12.0)	51 (15.5)	1.05 (0.82-1.53)
8-16	42 (17.0)	377 (21.2)	0.99 (0.85-1.15)	37 (16.7)	311 (21.5)	1.02 (0.86-1.20)	5 (20.0)	66 (20.1)	0.87 (0.62-1.21)
17-32	55 (22.3)	324 (18.2)	0.84 (0.72-0.98)	49 (22.1)	264 (18.3)	0.81 (0.69-0.96)	6 (24.0)	60 (18.2)	0.99 (0.70-1.40)
≥ 33	54 (21.9)	356 (20.1)	0.87 (0.75-1.01)	51 (23.0)	295 (20.4)	0.86 (0.73-1.02)	3 (12.0)	61 (18.5)	0.88 (0.62-1.25)
Missing	5 (2.0)	47 (2.6)		5 (2.2)	38 (2.6)		0 (0.0)	9 (2.7)	
Walking PA									
None	102 (41.3)	661 (37.2)	1.00	90 (40.5)	536 (37.0)	1.00	12 (48.0)	127 (38.6)	1.00
< 4	36 (14.6)	230 (13.0)	1.16 (1.00-1.36)	32 (14.4)	197 (13.6)	1.22 (1.03-1.44)	4 (16.0)	33 (10.0)	1.01 (0.68-1.51)
4-7	35 (14.2)	303 (17.1)	1.09 (0.95-1.25)	32 (14.4)	248 (17.1)	1.09 (0.94-1.27)	3 (12.0)	55 (16.7)	1.05 (0.75-1.46)
8-12	30 (12.1)	252 (14.2)	1.03 (0.89-1.20)	29 (13.1)	206 (14.2)	1.11 (0.94-1.30)	1 (4.0)	46 (14.0)	0.79 (0.56-1.12)
≥ 13	41 (16.6)	306 (17.2)	0.85 (0.74-0.97)	36 (16.2)	244 (16.9)	0.85 (0.73-0.99)	5 (20.0)	62 (18.8)	0.75 (0.54-1.03)
Missing	3 (1.2)	23 (1.3)		3 (1.4)	17 (1.2)		0 (0.0)	6 (1.8)	
Moderate PA									
None	155 (62.7)	1,150 (64.8)	1.00	137 (61.7)	923 (63.8)	1.00	18 (72.0)	227 (69.0)	1.00
< 7	25 (10.1)	149 (8.4)	0.88 (0.74-1.05)	24 (10.8)	127 (8.8)	0.91 (0.75-1.10)	1 (4.0)	22 (6.7)	0.78 (0.50-1.24)
7-11	11 (4.5)	112 (6.3)	1.40 (1.15-1.70)	9 (4.1)	93 (6.4)	1.45 (1.17-1.80)	2 (8.0)	19 (5.8)	1.07 (0.66-1.73)
12-19	21 (8.5)	160 (9.0)	1.27 (1.07-1.50)	20 (9.0)	136 (9.4)	1.19 (1.00-1.43)	1 (4.0)	24 (7.3)	2.04 (1.32-3.14)
≥ 20	33 (13.4)	183 (10.3)	1.11 (0.94-1.30)	30 (13.5)	151 (10.4)	1.10 (0.92-1.31)	3 (12.0)	32 (9.7)	1.12 (0.77-1.64)
Missing	2 (0.8)	21 (1.2)		2 (0.9)	16 (1.1)		0 (0.0)	5 (1.5)	
Vigorous PA									
None	158 (64.0)	1,151 (64.9)	1.00	138 (62.2)	930 (64.2)	1.00	20 (80.0)	223 (67.8)	1.00
< 6	17 (6.9)	134 (7.5)	1.24 (1.03-1.48)	17 (7.7)	114 (7.9)	1.30 (1.07-1.59)	0 (0.0)	20 (6.1)	0.99 (0.62-1.58)
6-13	25 (10.1)	169 (9.5)	0.90 (0.77-1.06)	23 (10.4)	138 (9.5)	0.83 (0.69-0.99)	2 (8.0)	31 (9.4)	1.56 (1.06-2.30)
14-32	26 (10.5)	140 (7.9)	0.86 (0.73-1.03)	24 (10.8)	120 (8.3)	0.88 (0.73-1.07)	2 (8.0)	20 (6.1)	0.93 (0.58-1.49)
≥ 33	21 (8.5)	163 (9.2)	0.96 (0.81-1.13)	20 (9.0)	131 (9.1)	0.93 (0.77-1.11)	1 (4.0)	32 (9.7)	1.06 (0.72-1.56)
Missing	0 (0.0)	18 (1.0)		0 (0.0)	15 (1.0)		0 (0.0)	3 (0.9)	