

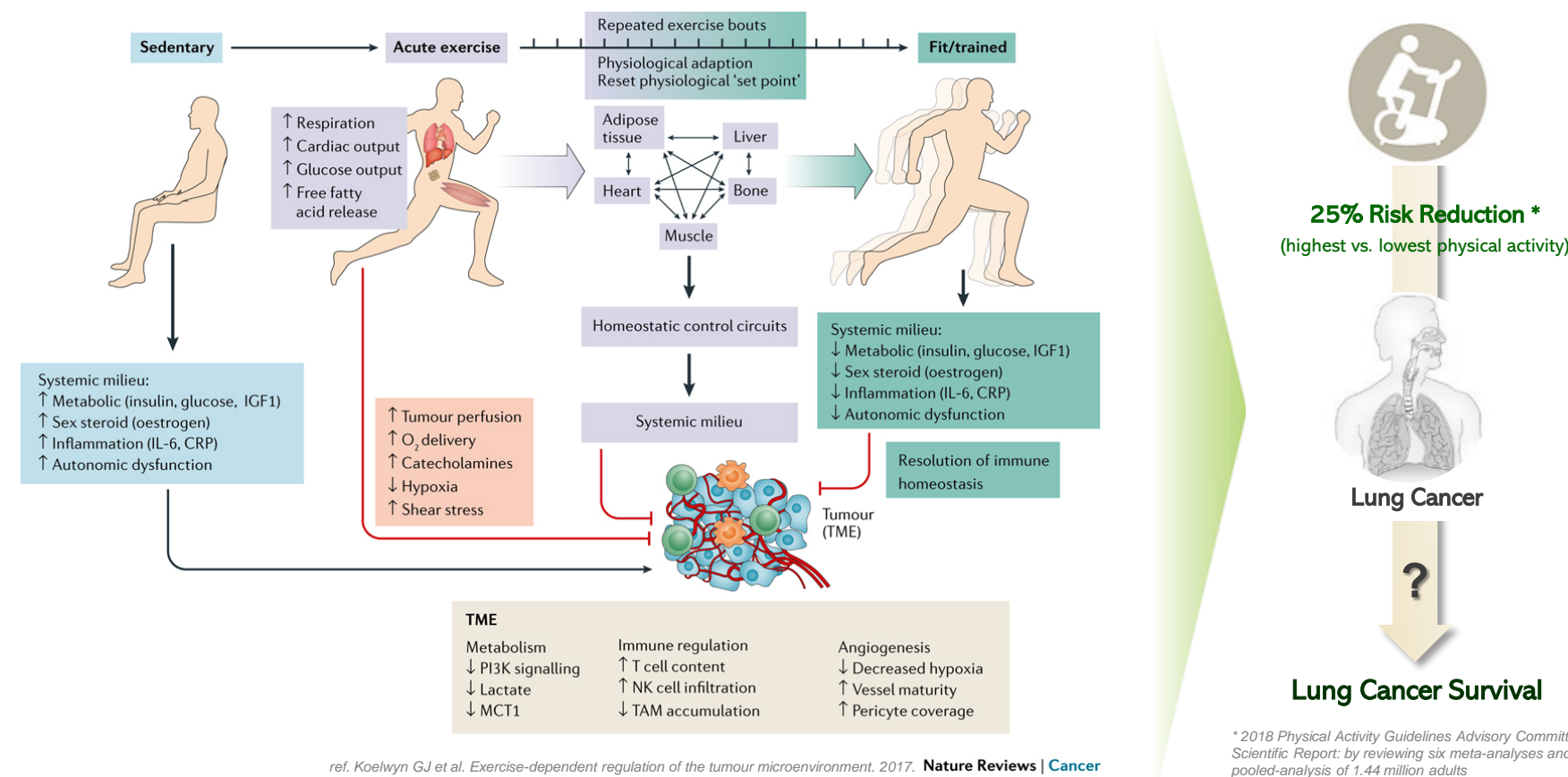
PRE-DIAGNOSTIC PHYSICAL ACTIVITY AND LUNG CANCER SURVIVAL : A POOLED ANALYSIS OF 11 COHORT STUDIES

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INTRODUCTION

- Emerging evidence has indicated a protective role of physical activity in the development and progression of various cancers, including lung.
- Habitual physical activity such as leisure-time physical activity (LTPA) before cancer diagnosis may link to better prognosis or lower mortality among lung cancer patients.



Objectives

- To evaluate the potential effect of pre-diagnostic LTPA on lung cancer survival among more than 20,000 incident primary lung cancer cases ascertained in 11 cohort studies from the US, Europe, and Asia.
- To investigate potential effect modifications by individual's demographic factors, lung cancer risk factors (e.g., smoking and other lifestyle), and prognostic factors (i.e., histologic types and tumor stage and grade).

METHODS

- Based on the de-identified individual-participants data from 11 prospective cohort studies participating in the Lung Cancer Calcium Intake Pooling Project
- LTPA and outcome assessment
 - Total metabolic equivalent hours per week (MET-h/week) : measured by using validated cohort-specific questionnaires at baseline survey
 - : no LTPA (reference group; the lowest LTPA)
 - : >0 to <8.3 MET-h/week;
 - : ≥8.3 MET-h/week (the recommended level for substantial health benefits)
 - Incident lung cancer and vital status: data linkage to cancer/death registries, active follow-up survey, and medical record reviews
- Cox proportional hazard model - to estimate multivariable-adjusted hazard ratios

CONCLUSIONS

- Adherence to the physical activity guidelines, i.e., LTPA ≥8.3 MET-h/week, may confer beneficial effects on lung cancer survival, especially for localized and regional lung cancer cases.
- Physical activity even engaged before cancer diagnosis may improve lung cancer survivorship, indicating a possible long-term benefit of physical activity for cancer progression.

RESULTS

Table 1. Participating Cohorts: the Pooled Analysis of LTPA and Lung Cancer Survival

	No. Cases ^a	Mean Age ^b	≥ 8.3 MET-hr/wk (%)	Smoker (%)	No. Deaths	5-year Survival Rate (95% CI)
United States						
NIH-AARP Diet and Health Study	9,684	68.6	39.2	93.1	8,407	20.1 (19.3-20.9)
Health Professionals Follow-up Study	983	72.9	51.5	88.8	885	22.5 (20.0-25.2)
Nurses' Health Study	1,542	69.4	40.4	90.8	1,257	27.3 (25.0-29.6)
Iowa Women's Health Study	1,017	73.9	41.9	82.3	914	16.1 (13.9-18.4)
Prostate, Lung, Colorectal & Ovarian Cancer Screening Trial	666	71.2	34.1	89.6	263	53.8 (49.5-57.9)
Southern Community Cohort Study	815	60.2	17.2	94.8	585	18.9 (16.1-21.8)
VITamins And Lifestyle Study	1,029	71.1	32.7	92.5	764	21.1 (18.6-23.8)
Europe						
European Prospective Investigation into Cancer & Nutrition	2,540	64.9	81.5	90.0	2,081	15.0 (13.6-16.5)
Helseundersøkelsen i Nord-Trøndelag	474	68.9	25.5	94.1	432	10.4 (7.85-13.4)
Asia						
Shanghai Men's Health Study	918	67.0	30.3	85.8	706	16.5 (14.1-19.1)
Shanghai Women's Health Study	826	67.2	26.4	8.0	570	26.0 (22.9-29.2)
Total study populations	20,494	68.5	42.6	88.0	16,864	20.9 (20.3-21.5)

a. Including primary lung cancer cases who were eligible for the current pooled analysis. b. Mean age at lung cancer diagnosis.

Table 2. Association of Leisure-time Physical Activity and Lung Cancer Survival

	Leisure-time Physical Activity (MET-hr/wk)			P _{trend}
	None, n=3,519	< 8.3, n=7,866	8.3 - 16.6, n=5,171	
All-cause Mortality (Overall Survival)				
No. deaths/cases	2,380/3,008	7,297/8,749	7,187/8,737	
Overall 5-yr survival rate (95% CI)	18.1 (16.7-19.6)	21.1 (20.2-22.0)	21.2 (20.3-22.1)	
Total lung cancer cases, HR (95% CI)	1 (ref.)	0.97 (0.91-1.02)	0.93 (0.88-0.99)	0.01
Localized lung cancer cases, HR (95% CI)	1 (ref.)	0.93 (0.78-1.12)	0.80 (0.67-0.97)	0.004
Regional lung cancer cases, HR (95% CI)	1 (ref.)	0.94 (0.82-1.09)	0.89 (0.77-1.02)	0.07
Distant lung cancer cases, HR (95% CI)	1 (ref.)	0.98 (0.90-1.08)	0.98 (0.89-1.07)	0.73
Lung Cancer Mortality (Disease Free Survival)				
No. deaths/cases	1,965/2,822	5,764/8,267	5,867/8,328	
Overall 5-yr survival rate (95% CI)	23.7 (22.0-25.4)	28.5 (27.5-29.5)	27.4 (26.4-28.4)	
Total lung cancer cases, HR (95% CI)	1 (ref.)	0.98 (0.92-1.04)	0.96 (0.90-1.02)	0.17
Localized lung cancer cases, HR (95% CI)	1 (ref.)	0.86 (0.69-1.08)	0.80 (0.64-1.00)	0.13
Regional lung cancer cases, HR (95% CI)	1 (ref.)	0.94 (0.81-1.10)	0.89 (0.76-1.03)	0.10
Distant lung cancer cases, HR (95% CI)	1 (ref.)	1.00 (0.91-1.10)	1.00 (0.91-1.11)	0.92

a. HRs (95% CIs) were adjusted for age at diagnosis, sex, smoking status, smoking pack-years, race/ethnicity, education, alcohol consumption, history of diabetes, BMI levels, hormone therapy in women, and histological type, tumor stage, and grade of lung cancer; and stratified by cohort, year of lung cancer diagnosis, and time interval from LTPA assessment to lung cancer diagnosis

Stratified Analysis among Localized/Regional Cases: All-cause Mortality

≥ 8.3 MET-hours/week vs. none	No. of Deaths	Adjusted HR (95% CI)	P for Interaction
Histology			
Adenocarcinoma	1567	0.79 (0.66-0.95)	0.47
Squamous cell carcinoma	1085	0.84 (0.67-1.06)	
Other non-small cell carcinoma	689	0.90 (0.68-1.19)	
Small cell carcinoma	502	0.93 (0.65-1.32)	
Grade			
Well/moderately differentiated	911	0.82 (0.62-1.07)	0.75
Poorly & undifferentiated	1485	0.92 (0.74-1.13)	
Time from baseline to diagnosis			
< 5 years	2061	0.87 (0.74-1.01)	0.13
5-9 years	1789	0.80 (0.67-0.96)	
≥ 10 years	408	1.10 (0.75-1.60)	
Age at lung cancer diagnosis			
<70 years	2340	0.77 (0.66-0.89)	0.05
≥70 years	1918	0.99 (0.83-1.18)	
Sex			
Men	2500	0.86 (0.74-1.00)	0.83
Women	1758	0.87 (0.74-1.03)	
Race			
White	3707	0.86 (0.75-0.98)	0.54
Black	200	0.68 (0.44-1.06)	
Asian	311	0.91 (0.67-1.22)	
Smoking status			
Never	404	0.76 (0.55-1.06)	0.19
Former	1820	0.80 (0.66-0.97)	
Current	2034	0.92 (0.79-1.07)	
Alcohol consumption			
None	1279	0.91 (0.77-1.09)	0.37
Moderate	2060	0.86 (0.71-1.04)	
Heavy	919	0.77 (0.60-0.98)	
Obesity status			
≤Normal weight, BMI<25	1804	0.83 (0.70-0.98)	0.94
Overweight, 25≤BMI<30	1714	0.93 (0.77-1.12)	
Obese, BMI≥30	740	0.78 (0.60-1.02)	
Education			
≤High school graduation	2048	0.94 (0.81-1.08)	0.14
>High school graduation	2210	0.76 (0.64-0.91)	
History of diabetes			
No	3866	0.86 (0.77-0.97)	0.92
Yes	392	0.95 (0.60-1.50)	
Hormone therapy in women			
No	1003	0.88 (0.72-1.08)	0.82
Yes	755	0.94 (0.70-1.26)	

Adjusted for age at diagnosis, sex, smoking status, smoking pack-years, race, education, alcohol consumption, history of DM, BMI, hormone therapy, and histological type, tumor stage, and grade of lung cancer; and stratified by cohort, year of lung cancer diagnosis, and time interval from LTPA assessment to lung cancer diagnosis

Stratified Analysis among Localized/Regional Cases: Lung Cancer Mortality

≥ 8.3 MET-hours/week vs. none	No. of Deaths	Adjusted HR (95% CI)	P for Interaction
Histology			
Adenocarcinoma	1202	0.82 (0.66-1.01)	0.41
Squamous cell carcinoma	787	0.81 (0.63-1.06)	
Other non-small cell carcinoma	523	0.91 (0.66-1.25)	
Small cell carcinoma	422	0.91 (0.62-1.32)	
Grade			
Well/moderately differentiated	622	0.85 (0.61-1.16)	0.25
Poorly & undifferentiated	1145	0.86 (0.68-1.09)	
Time from baseline to diagnosis			
< 5 years	1556	0.91 (0.76-1.08)	0.50
5-9 years	1399	0.81 (0.66-0.99)	
≥ 10 years	279	0.95 (0.61-1.48)	
Age at lung cancer diagnosis			
<70 years	1841	0.77 (0.65-0.90)	0.11
≥70 years	1393	1.01 (0.82-1.24)	
Sex			
Men	1905	0.88 (0.74-1.05)	0.96
Women	1329	0.87 (0.72-1.05)	
Race			
White	2768	0.86 (0.74-0.99)	0.60
Black	143	0.53 (0.31-0.91)	
Asian	294	0.91 (0.67-1.24)	
Smoking status			
Never	325	0.76 (0.53-1.09)	0.23
Former	1323	0.81 (0.65-1.02)	
Current	1586	0.91 (0.77-1.08)	
Alcohol consumption			
None	970	0.94 (0.77-1.15)	0.26
Moderate	1562	0.87 (0.70-1.08)	
Heavy	702	0.73 (0.56-0.96)	
Obesity status			
≤Normal weight, BMI<25	1396	0.88 (0.72-1.06)	0.57
Overweight, 25≤BMI<30	1305	0.87 (0.70-1.07)	
Obese, BMI≥30	533	0.81 (0.59-1.11)	
Education			
≤High school graduation	1598	0.93 (0.79-1.09)	0.51
>High school graduation	1636	0.73 (0.59-0.89)	
History of diabetes			
No	2956	0.86 (0.75-0.98)	0.39
Yes	278	1.01 (0.59-1.73)	
Hormone therapy in women			
No	771	0.89 (0.71-1.12)	0.97
Yes	559	0.86 (0.60-1.22)	

Adjusted for age at diagnosis, sex, smoking status, smoking pack-years, race, education, alcohol consumption, history of DM, BMI, hormone therapy, and histological type, tumor stage, and grade of lung cancer; and stratified by cohort, year of lung cancer diagnosis, and time interval from LTPA assessment to lung cancer diagnosis