

Impact of **Exercise** and **Nutrition** on the Immune System and Outcomes in NSCLC



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1. Effect on cancer Immune
 - Molecular and biological mechanism
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 - Advanced lung cancer
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Nutrition

1. Lung cancer prevention
2. Sarcopenia
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Exercise and physical activity

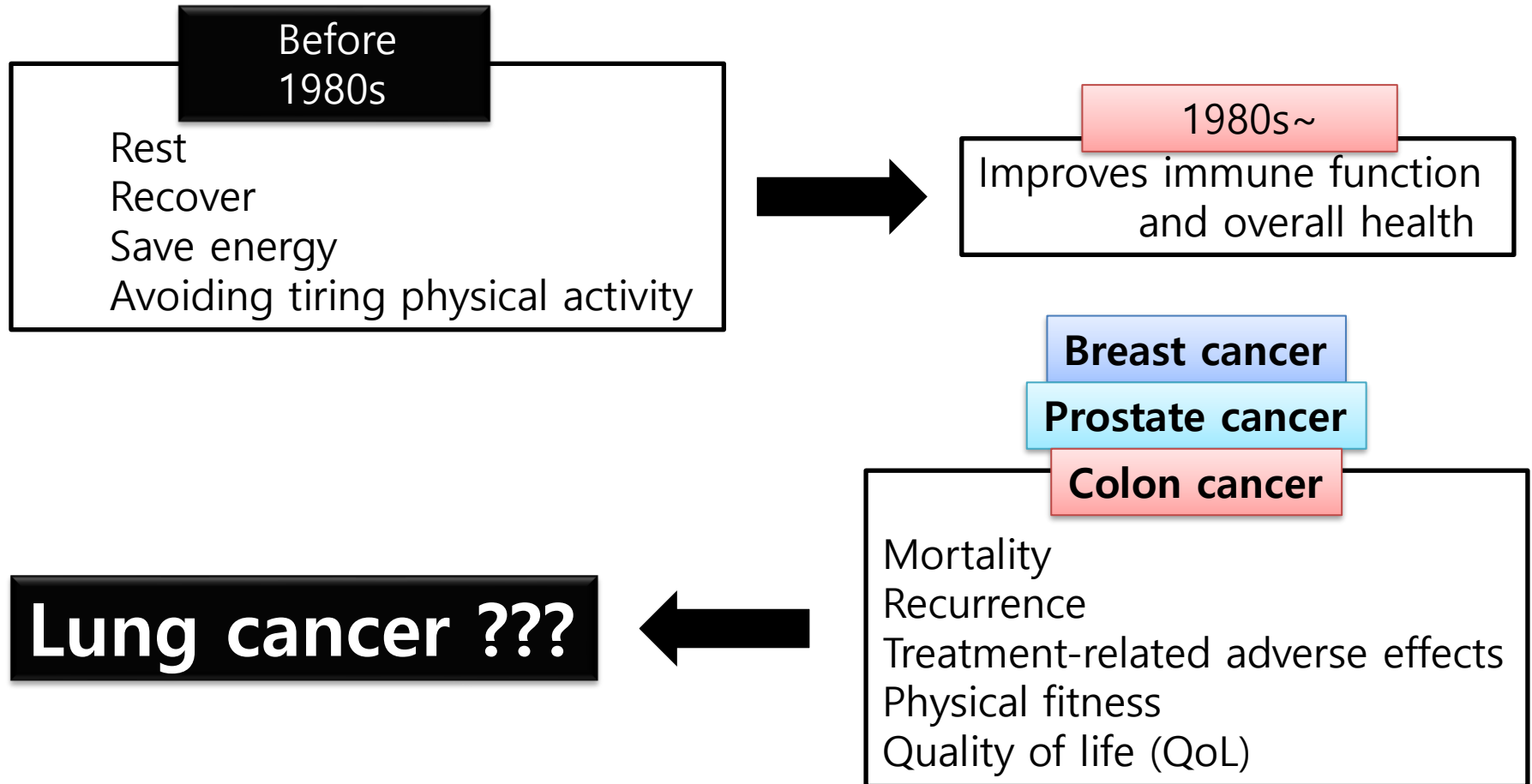
Physical activity

ANY BODILY MOVEMENT produced by **SKELETAL MUSCLES** that results in **ENERGY EXPENDITURE**

Exercise

PLANNED, STRUCTURED, AND REPETITIVE activities aimed at improving or maintaining one or more components of **PHYSICAL FITNESS**

Exercise and physical activity



Lung cancer

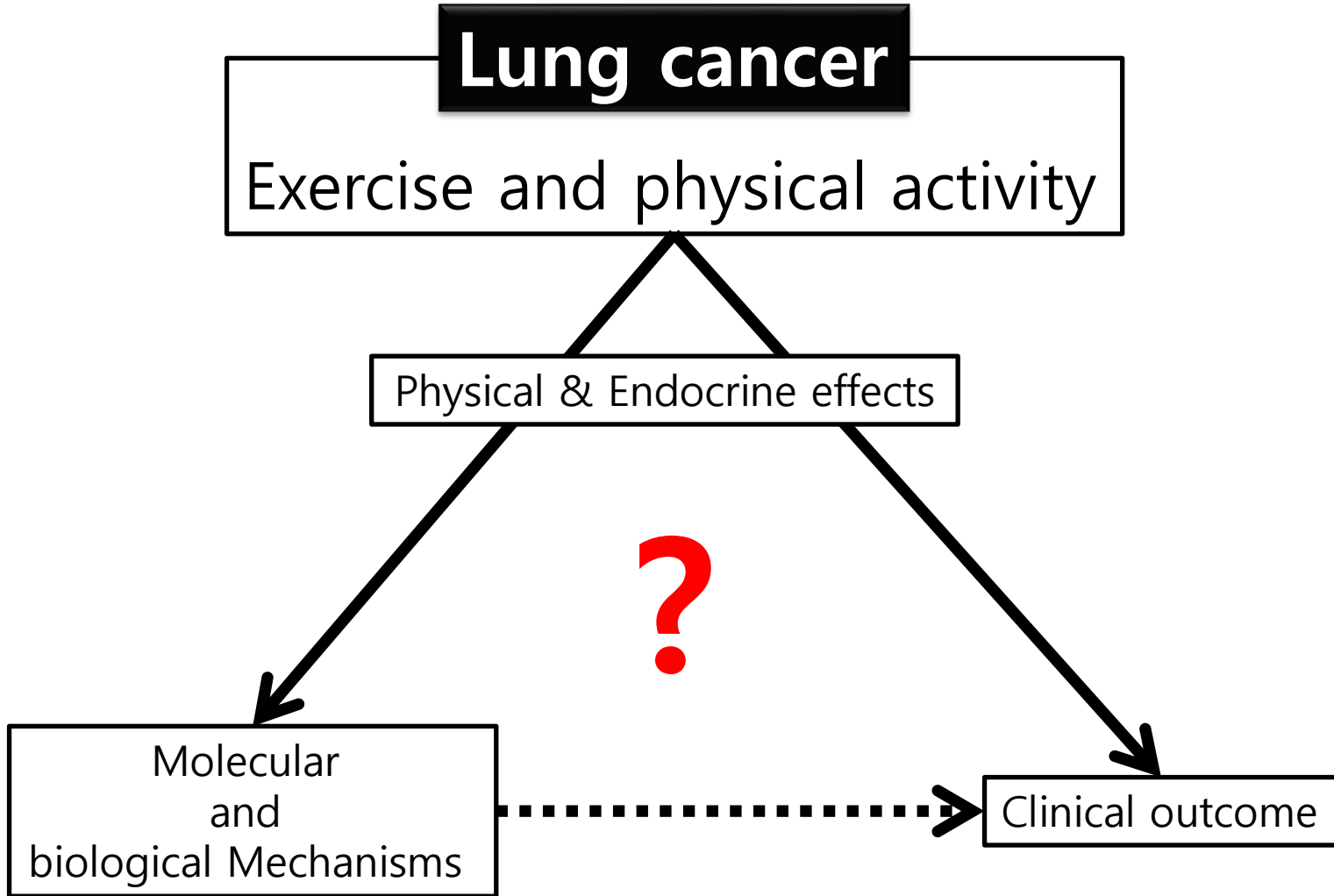
Exercise and physical activity

Physical & Endocrine effects



Molecular
and
biological Mechanisms

Clinical outcome



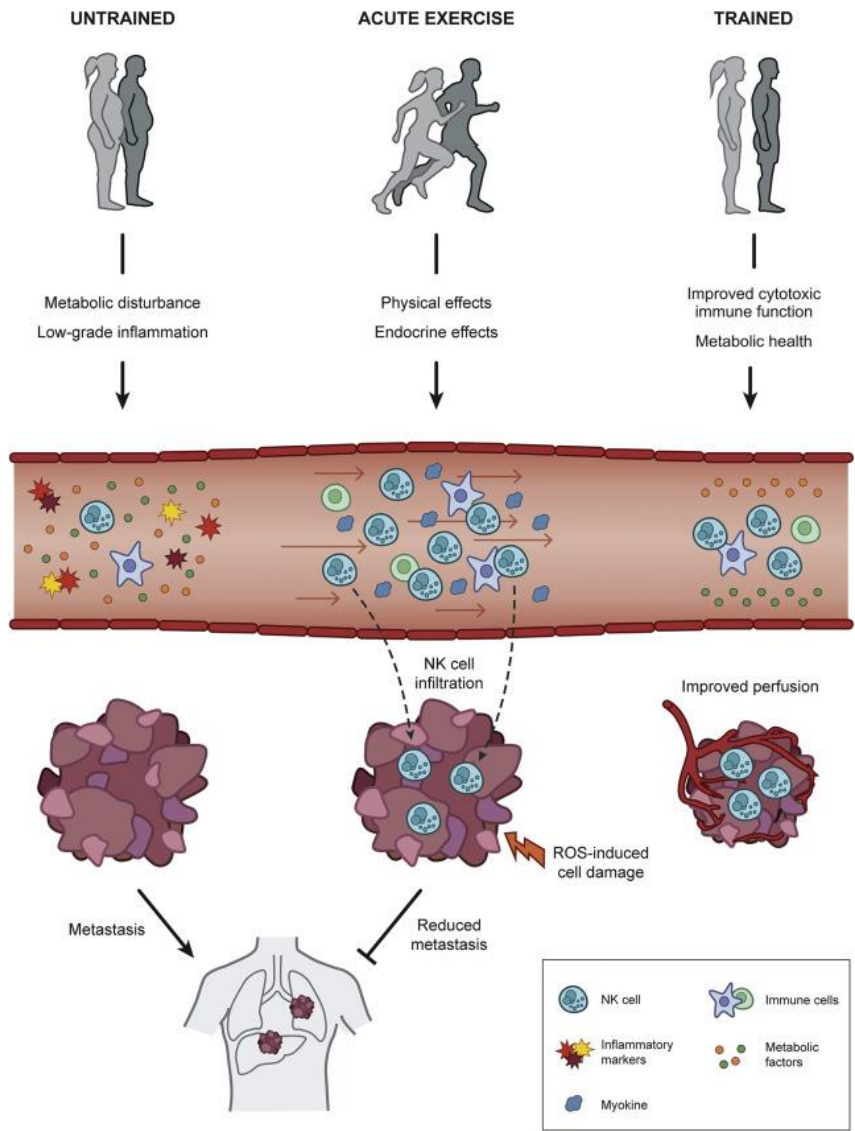


Exercise

Effect on cancer Immune

MOLECULAR AND BIOLOGICAL MECHANISMS

Molecular Mechanisms Linking Exercise to Cancer Protection



Physical
 Sympathetic activation
 Blood flow ↑
 Shear stress ↑
 Temperature ↑

Endocrine
 Catecholamines
 myokines, etc.

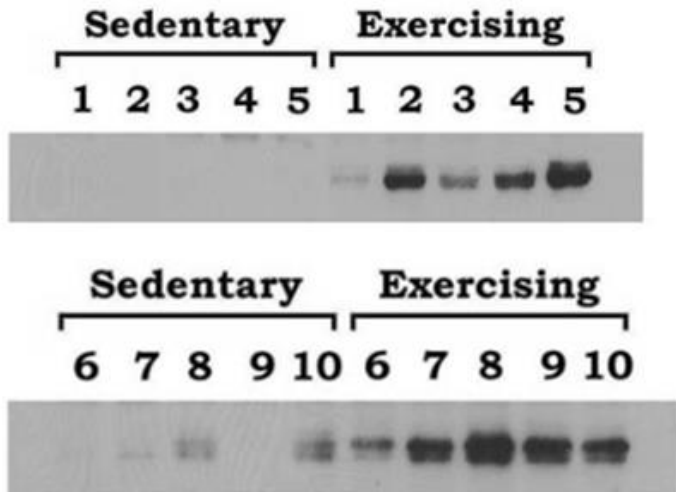


Immediate stress on tumor metabolism

**Immune function ↑
systemic inflammation ↓
Blood perfusion ↑
immunogenic profile ↑
immune cell infiltration ↑**

p53, Apoptosis

- P53, tumor suppressor protein
- Murine model of lung ADC
- Daily **wheel running** 4 weeks



Western blots, p53

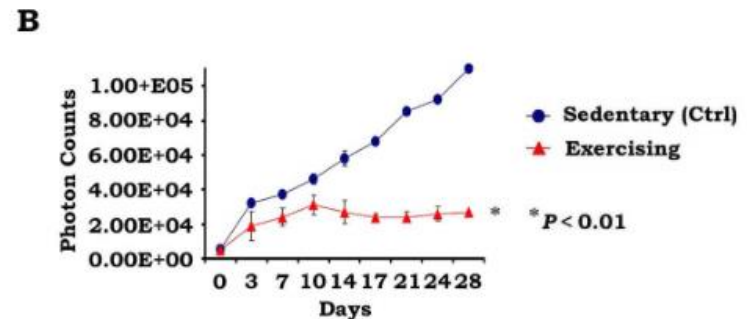
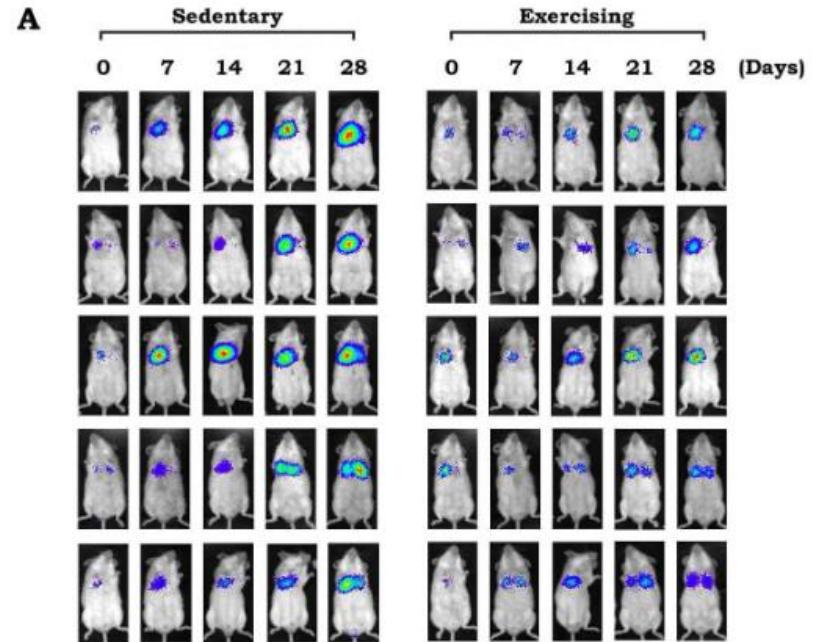


Figure 2. Exercise repressed lung tumor growth in vivo. (A) Whole-body images were taken weekly of 5 representative mice in each cohort (individual pictures of all mice are not shown because of space limitations). Each row depicts lung tumor growth of an individual mouse tumor over 4 weeks. (B) Changes in mean photon counts in lung tumors over time are compared between sedentary (control [Ctrl]) mice versus exercising mice (all mice; there were 10 mice in each group), with sedentary mice exhibiting a significantly more rapid increase in mean photon counts.

Phosphoinositide 3-kinase(PI3K)/AKT pathway, Cell proliferation

- NSCLC cells
 - A549, H460, H1299
- Normal lung fibroblasts
 - MRC5
- High intensity interval exercise
- Post exercise serum (5min, 1hr, 24hr) → cells

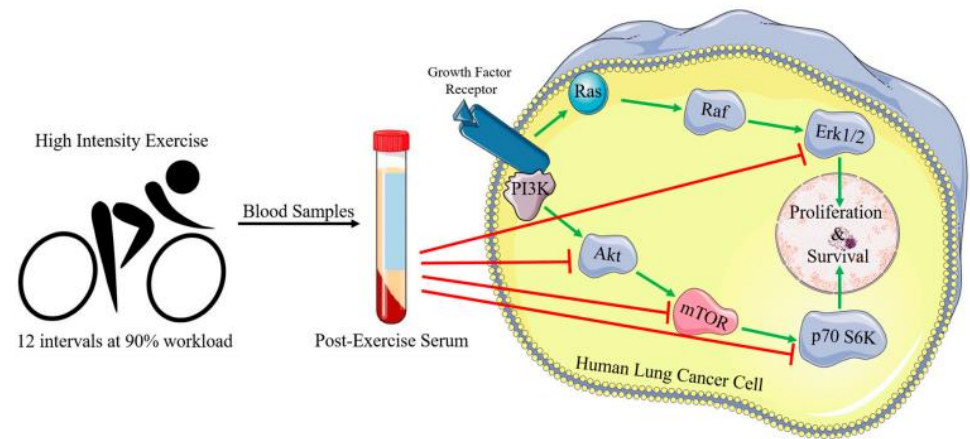
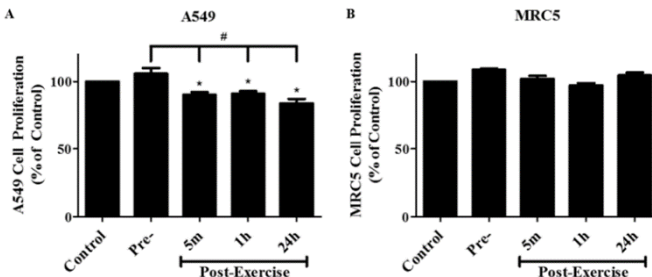
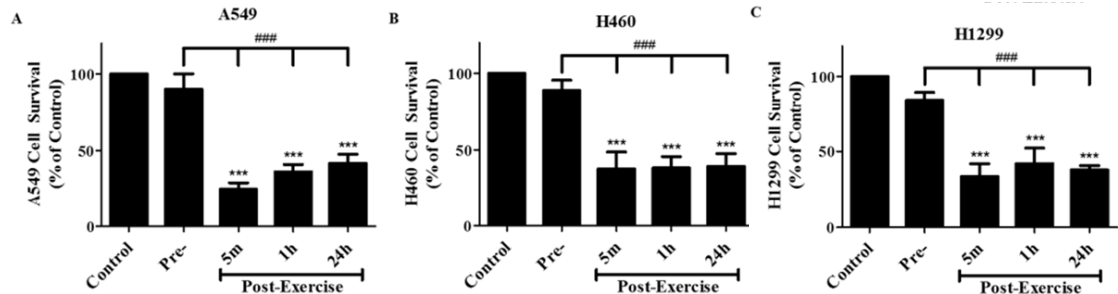


Figure 8. Potential mechanism of the inhibition of lung cancer cell proliferation and survival by post-exercise serum. Post-exercise serum inhibited Akt, mTOR, p70 S6K, and Erk1/2 phosphorylation/activation and resulted in significant inhibition of cell proliferation and survival.

Cell proliferation

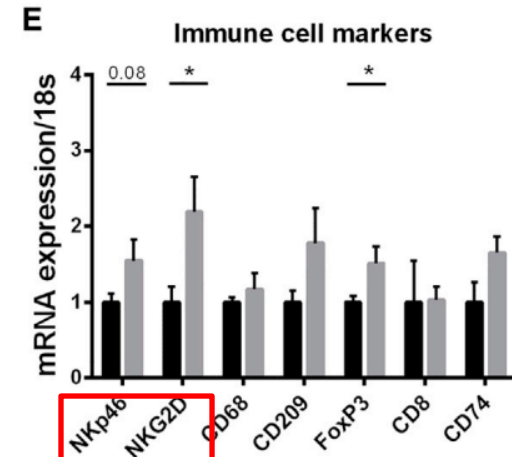
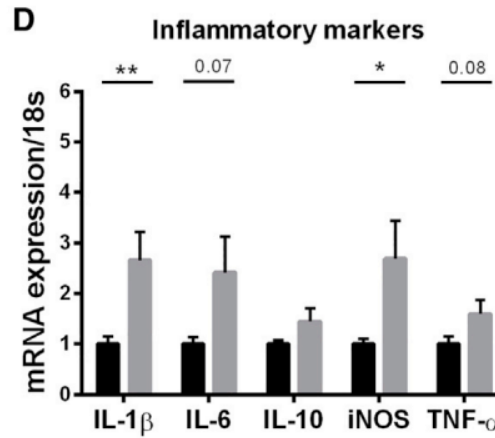
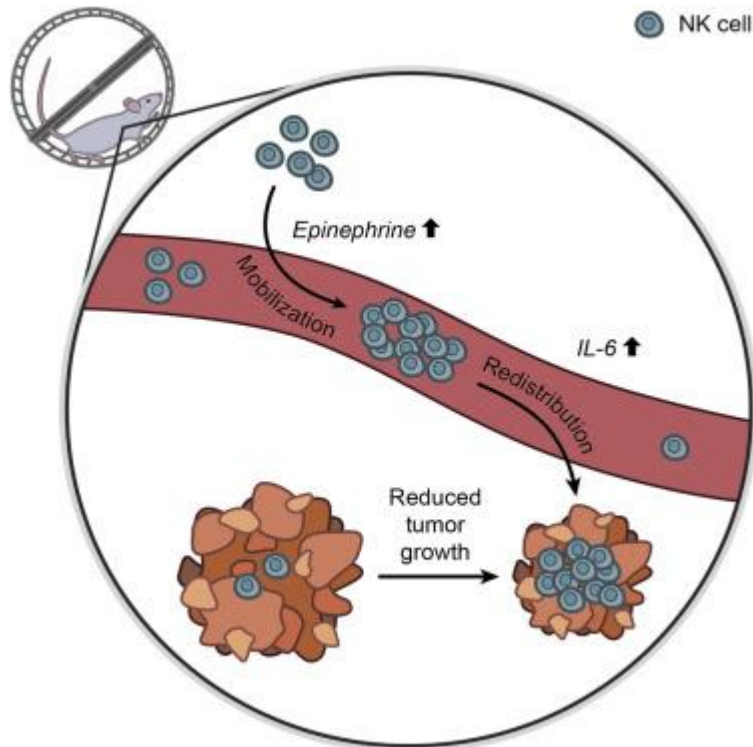


Cell survival



Immunomodulation on TME

- 6 weeks of wheel running in Lewis lung cancer (LLC) mice
- Reduced tumor volume
- Upregulation of proinflammatory cytokines



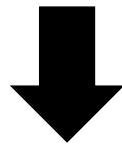
(D) inflammatory cytokines and
(E) immune cell markers in Lewis Lung tumors

Frequency of immune cells

Number of tumors per lung

Molecular Mechanisms

- Emerging evidence indicates that **EXERCISE** is also directly linked to control of **TUMOR BIOLOGY**
- Not direct significance to lung cancer patients



May ultimately improve the clinical outcome



Exercise

Clinical outcome

PERIOPERATIVE IMPACT



Pre-operative exercise

Maximize exercise capacity

Peak Oxygen Consumption

Functional capacity

Minimize the post-operative burden

Post-operative pulmonary complications

Intensive care admissions

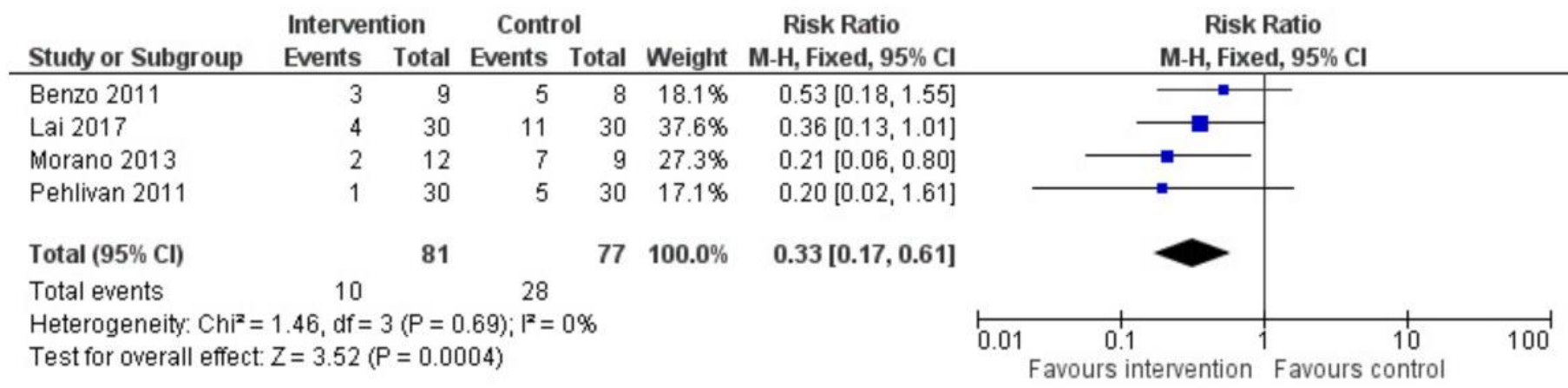
Length of hospital stay
Readmissions

Early and late mortality

Pre-operative exercise (NSCLC)

- RCT 2~4, total patients < 200
- Type, frequency, and intensity varied
 - 3 times/day for one week to 5 times/week for four weeks
 - Aerobic exercise training
 - Inspiratory muscle training and education or breathing exercises
 - Resistance training (1 study)
 - Stretches (1 study)

Postoperative pulmonary Complication

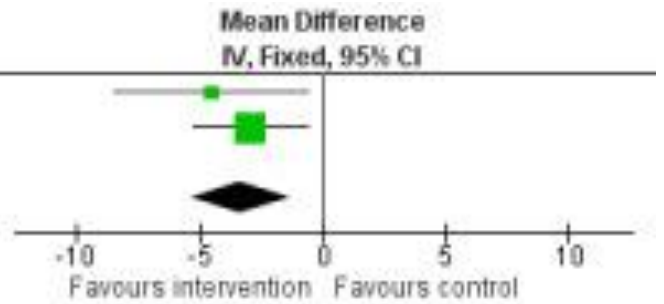


Pre-operative exercise (NSCLC)

Number of days patients needed an intercostal catheter

| Study or Subgroup | Intervention | | | Control | | | Weight | Mean Difference IV, Fixed, 95% CI |
|-----------------------|--------------|-----|-----------|---------|-----|-----------|---------------|--------------------------------------|
| | Mean | SD | Total | Mean | SD | Total | | |
| Benzo 2011 | 4.3 | 2.1 | 9 | 8.8 | 5.3 | 8 | 26.6% | -4.50 [-8.42, -0.58] |
| Morano 2013 | 4.5 | 2.8 | 12 | 7.4 | 2.6 | 9 | 73.4% | -2.90 [-5.26, -0.54] |
| Total (95% CI) | | | 21 | | | 17 | 100.0% | -3.33 [-5.35, -1.30] |

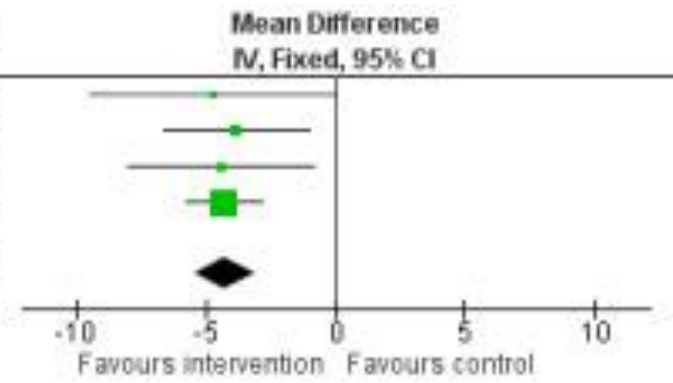
Heterogeneity: Chi² = 0.47, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 3.22 (P = 0.001)



Postoperative length of hospital stay

| Study or Subgroup | Intervention | | | Control | | | Weight | Mean Difference IV, Fixed, 95% CI |
|-----------------------|--------------|-----|-----------|---------|-----|-----------|---------------|--------------------------------------|
| | Mean | SD | Total | Mean | SD | Total | | |
| Benzo 2011 | 6.3 | 3 | 9 | 11 | 6.3 | 8 | 6.1% | -4.70 [-9.49, 0.09] |
| Lai 2017 | 6.9 | 4.4 | 30 | 10.7 | 6.4 | 30 | 18.2% | -3.80 [-6.58, -1.02] |
| Morano 2013 | 7.8 | 4.8 | 12 | 12.2 | 3.6 | 9 | 10.9% | -4.40 [-7.99, -0.81] |
| Pehlivan 2011 | 5.4 | 2.7 | 30 | 9.7 | 3.1 | 30 | 64.8% | -4.30 [-5.77, -2.83] |
| Total (95% CI) | | | 81 | | | 77 | 100.0% | -4.24 [-5.43, -3.06] |

Heterogeneity: Chi² = 0.15, df = 3 (P = 0.99); I² = 0%
Test for overall effect: Z = 7.02 (P < 0.00001)



Pre-operative exercise

- Type, frequency, and intensity varied
 - **Supervised training**
 - one ~ 4 weeks, 20 ~ 60 min/session
 - 2 /day ~ 3~7 sessions/week
 - Aerobic training
 - Increases the HR ≥ 5 min
 - 60–80% peak work capacity
 - Inspiratory muscle, strength, stretching training

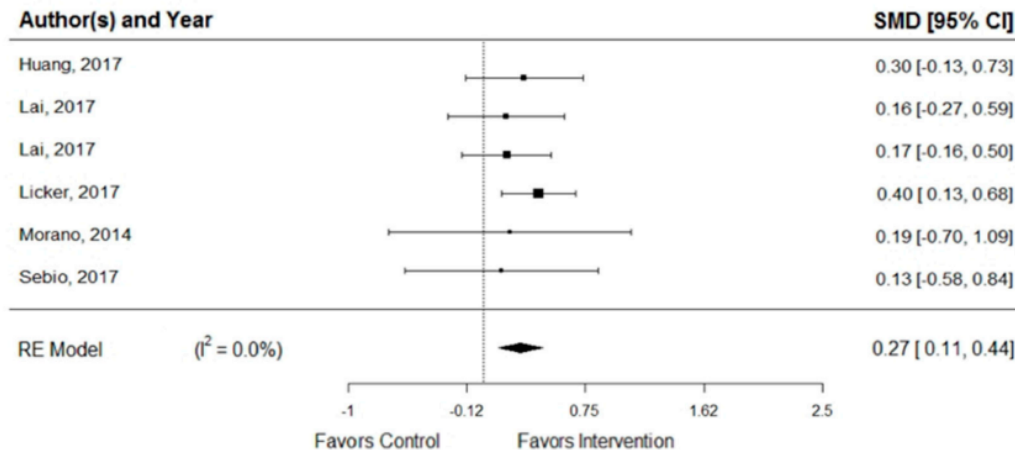


Review

Systematic Review and Meta-Analysis of Randomized, Controlled Trials on Preoperative Physical Exercise Interventions in Patients with Non-Small-Cell Lung Cancer

Ilem D. Rosero¹, Robinson Ramírez-Vélez¹, Alejandro Lucia^{2,3,4}, Nicolas Martínez-Velilla^{1,4}, Alejandro Santos-Lozano^{2,5}, Pedro L. Valenzuela⁶, Idoia Morilla¹ and Mikel Izquierdo^{1,4,*}

Functional capacity, 6MWD



Pre-operative exercise

Maximize exercise capacity

Peak Oxygen Consumption

Functional capacity

Minimize the post-operative burden

Post-operative pulmonary complications

Intensive care admissions

Length of hospital stay
Readmissions

Early and late mortality

Lack of
Large RCTs
Mortality data
Long term benefits data
Cost-effectiveness data

Acute post-operative exercise (in-hospital)

Bed rest

Physical deconditioning
Diminished muscle mass
Increased pulmonary complications
 (atelectasis and pneumonia)
Increased risk of VTE

'early mobilization'

| Recommendations | Evidence level | Recommendation grade |
|--|---|----------------------|
| Intercostal muscle- and nerve-sparing techniques are recommended | Moderate | Strong |
| Reapproximation of the ribs during thoracotomy closure should spare the inferior intercostal nerve | Moderate | Strong |
| Surgical technique A VATS approach | Enhanced recovery after surgery (ERAS) protocols | |
| Postoperative phase | | Strong |
| Chest drain management | | |
| The routine application of external suction should be avoided | Low | Strong |
| Digital drainage systems reduce variability in decision-making and should be used | Low | Strong |
| Chest tubes should be removed even if the daily serous effusion is of high volume (up to 450 ml/24 h) | Moderate | Strong |
| A single tube should be used instead of 2 after anatomical lung resection | Moderate | Strong |
| Urinary drainage | | |
| In patients with normal preoperative renal function, a transurethral catheter should not be routinely placed for the sole purpose of monitoring urine output | Moderate | Strong |
| It is reasonable to place a transurethral catheter in patients with thoracic epidural anaesthesia | Low | Strong |
| Early mobilization and adjuncts to physiotherapy | | |
| Patients should be mobilized within 24 h of surgery | Low | Strong |
| Prophylactic minitracheostomy use may be considered in certain high-risk patients | Low | Weak |

Post-operative exercise

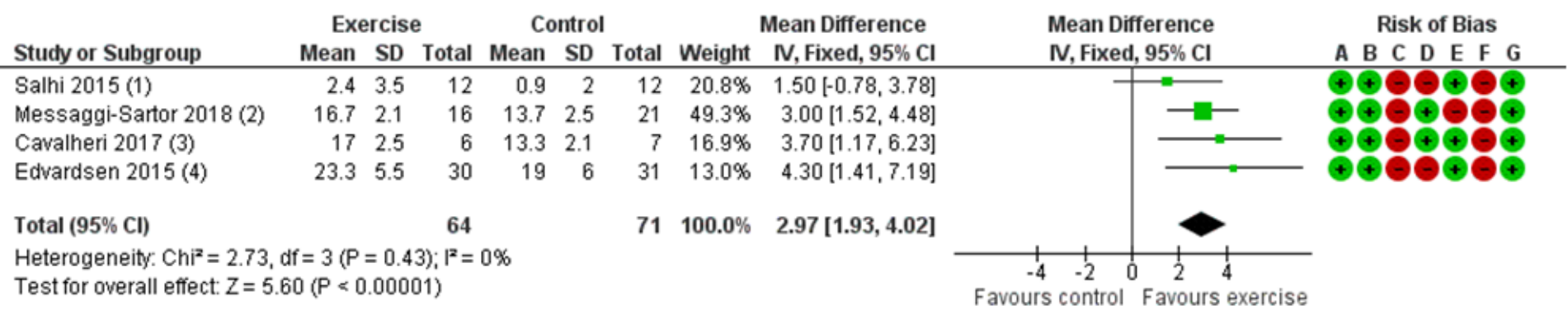
Recovery

Rehabilitation

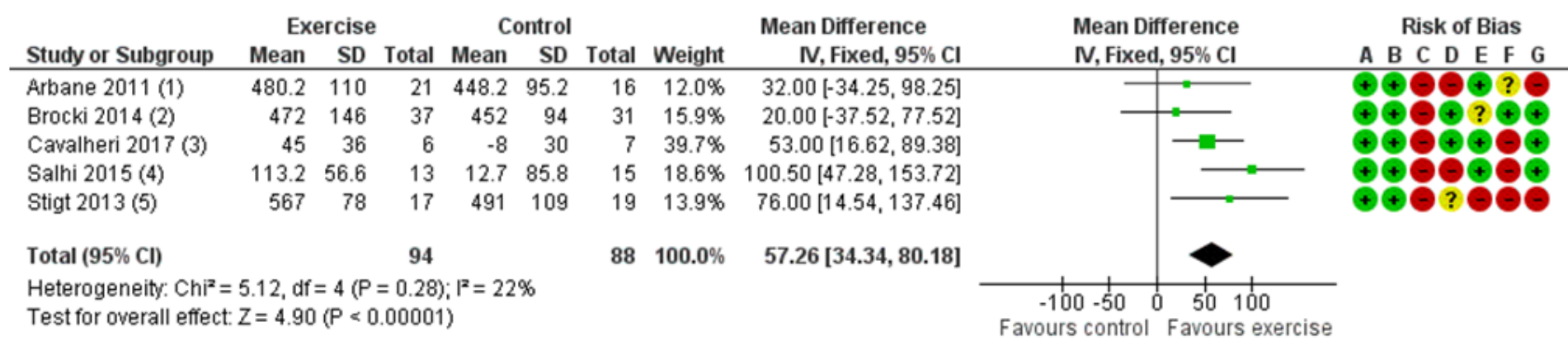
- Published RCTs commenced Frequency
 - 5–10 weeks following surgery
 - 6–12 weeks in duration (up to 20 weeks)
 - 2 to 3 times/week with **supervisor**
 - Supplemented with **home-based** exercise to achieve 5 times/week
- Exercise prescription
 - Aerobic exercise (moderate intensity)
 - High-intensity interval training on a stationary bike or a treadmill
 - Whole-body resistance training
 - Inspiratory muscle training
- Similar to **pulmonary rehabilitation with COPD**

Post-operative exercise

Exercise capacity (VO₂peak in mL/kg/min)

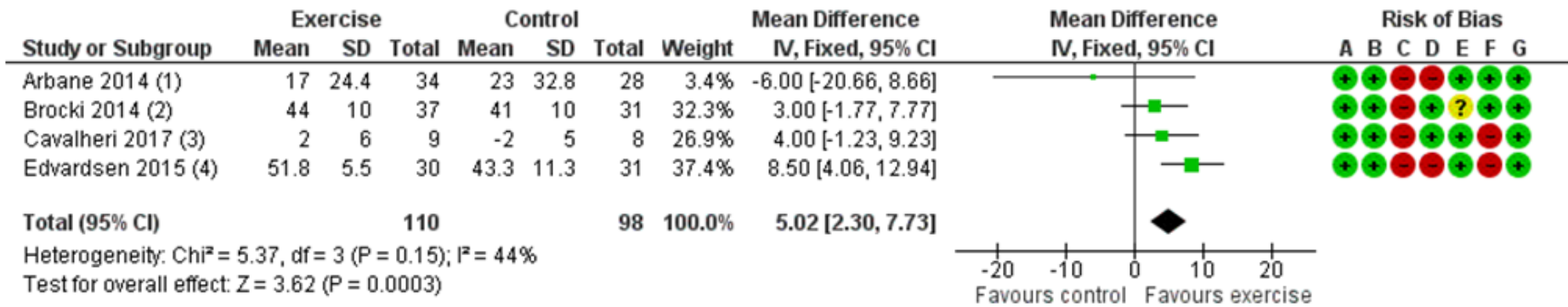


Exercise capacity (6MWD in metres)

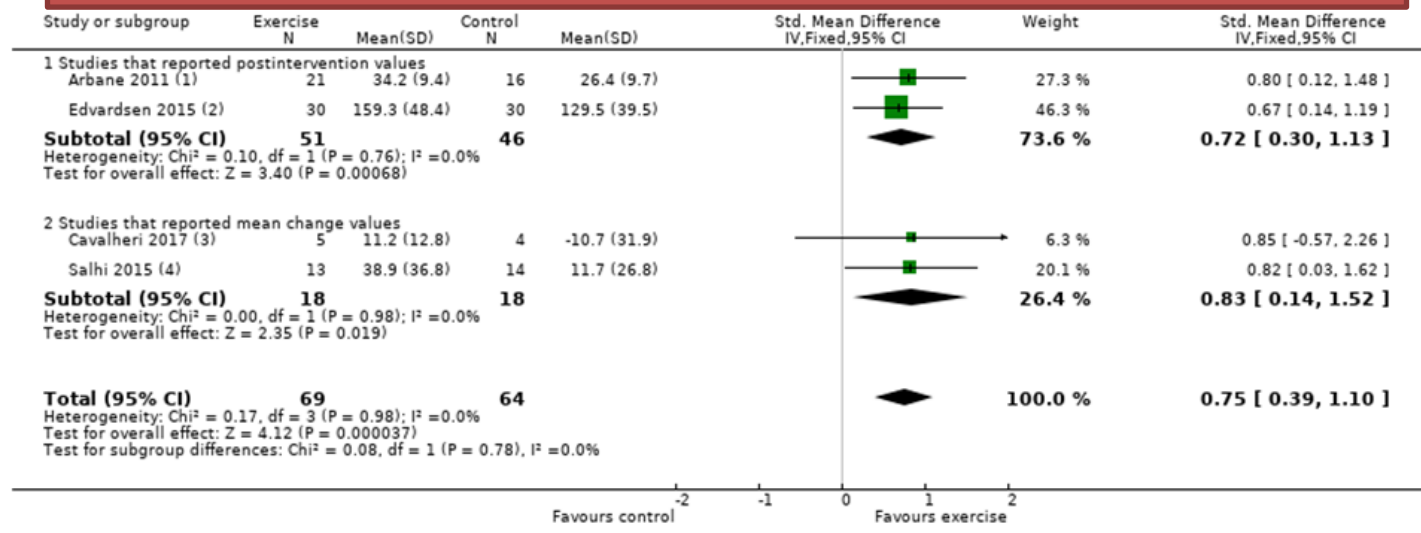


Post-operative exercise

General health-related quality of life (SF-36 - physical component score)



Force-generating capacity of peripheral muscle (quadriceps)



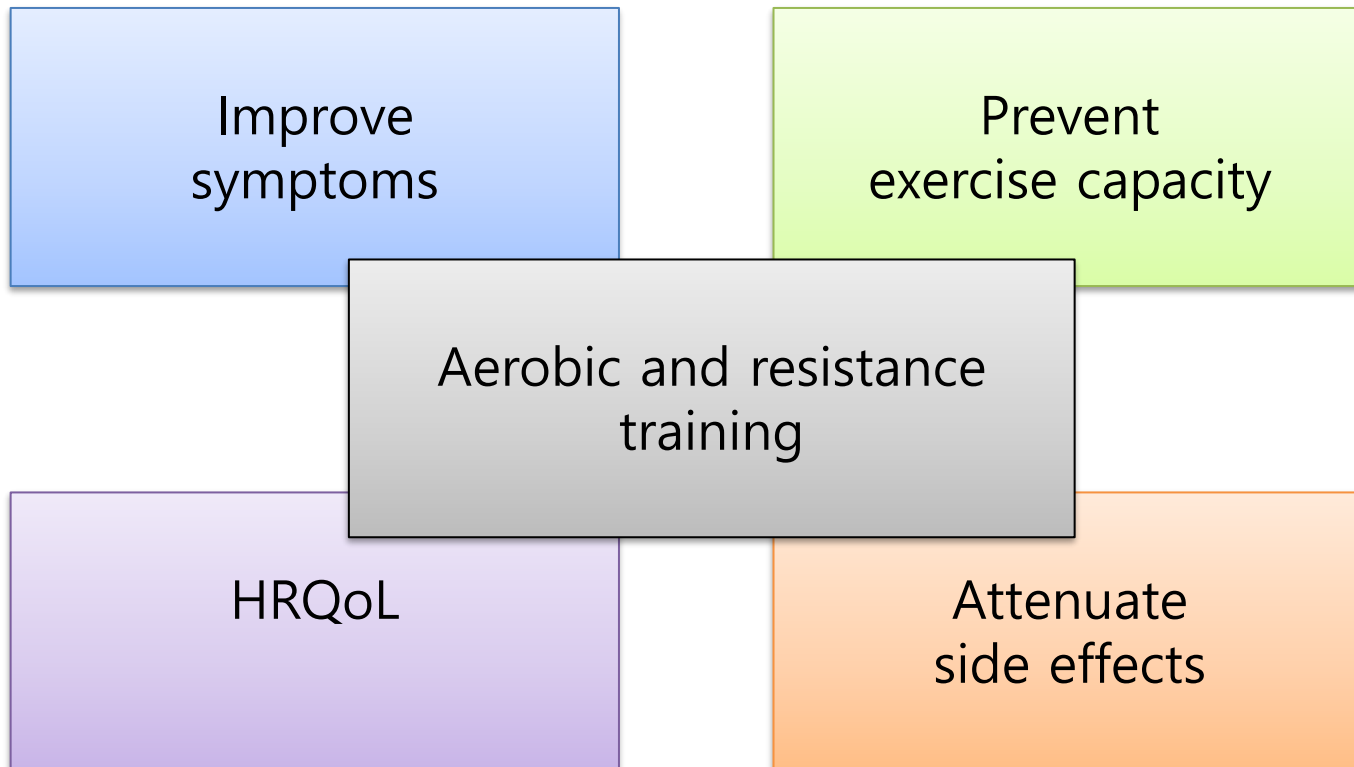


Exercise

Clinical outcome

ADVANCED LUNG CANCER

Exercise training in advanced stage lung cancer

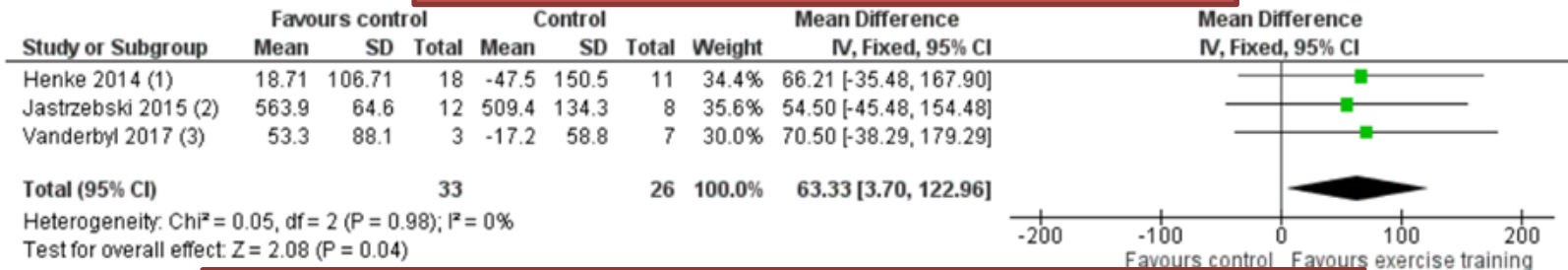


Exercise training in advanced stage lung cancer

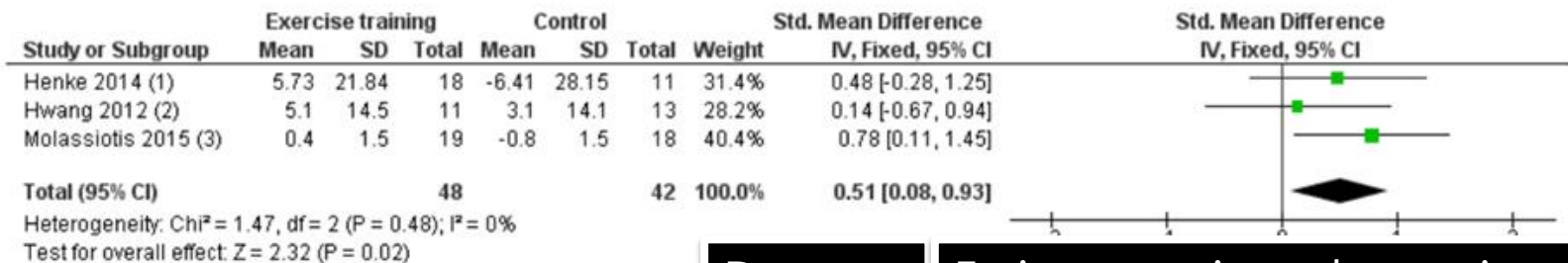
- **Very low to low certainty** for the effectiveness
 - Fewer RCT
 - Small sample sizes
 - Overall high risk of bias
(dyspnea, severe cancer related symptom, various regimen, etc.)
- A Cochrane review 6 RCT (total patients < 150)
 - During medical treatment
 - Length 6 to 12 weeks
 - **Supervised exercise** from 1 to 5 days a week

Exercise training in advanced stage lung cancer

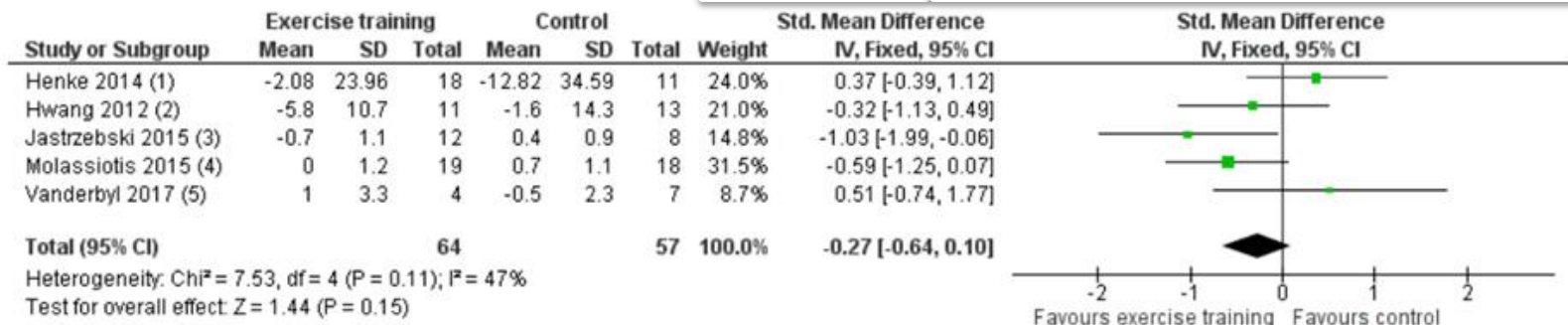
Exercise capacity (6MWD in metres)



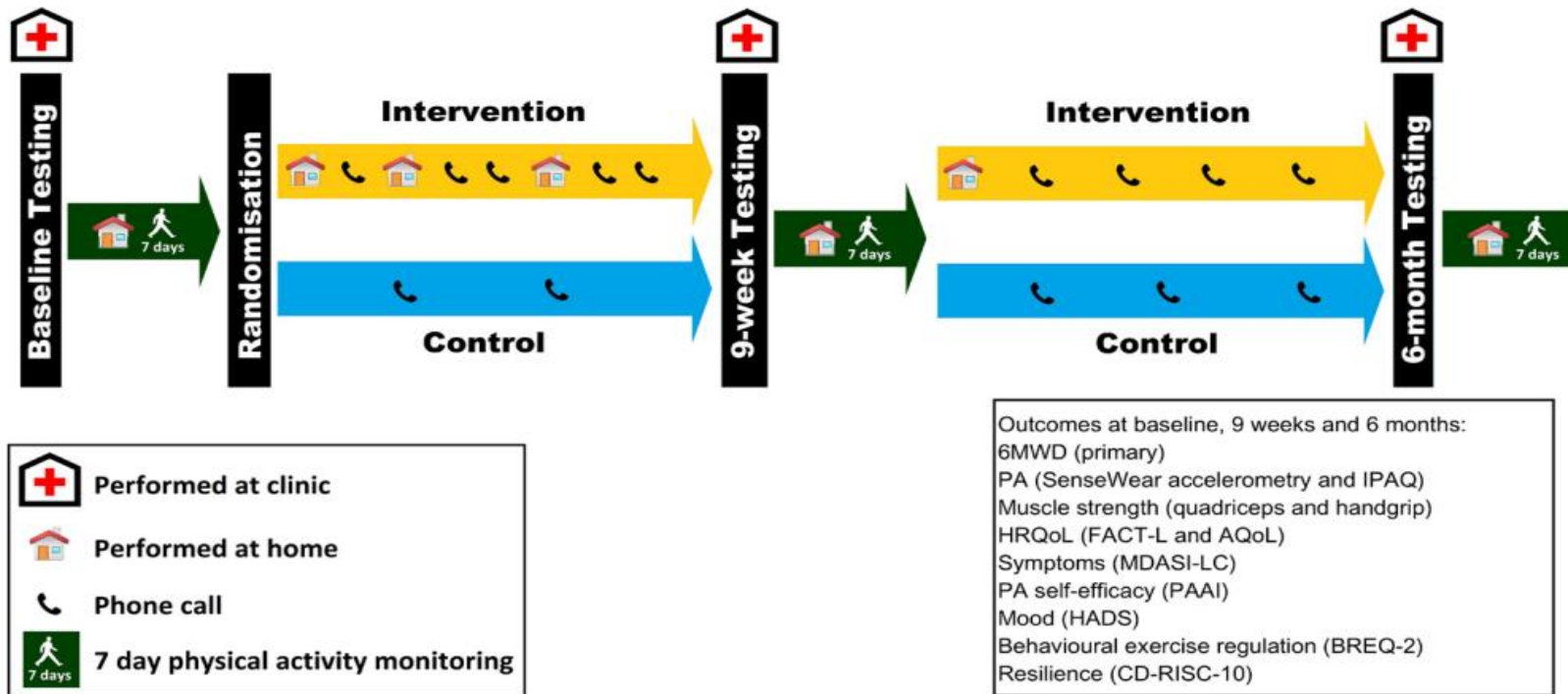
Disease-specific global health-related quality of life



Dyspnea Fatigue, anxiety, depression, FEV1



Efficacy of home-based rehabilitation

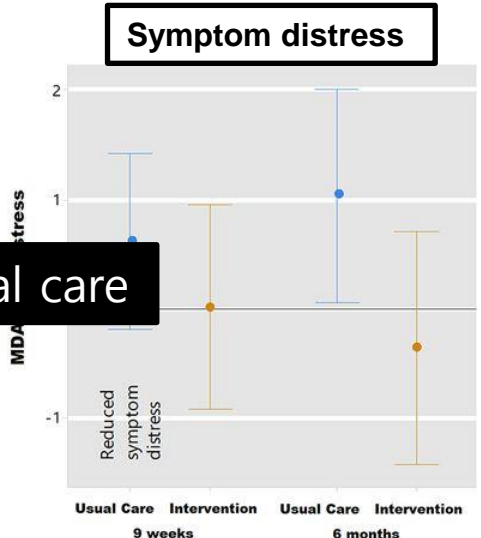
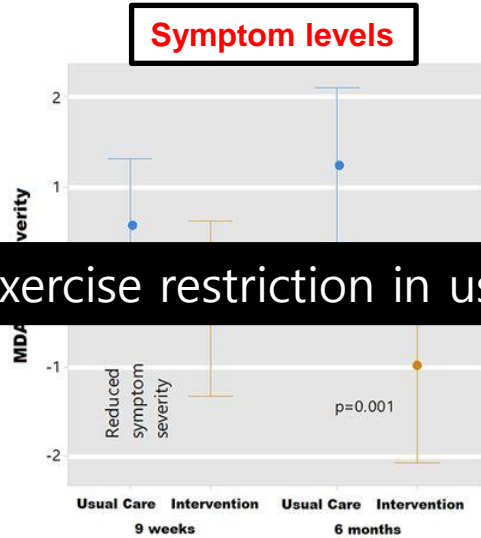
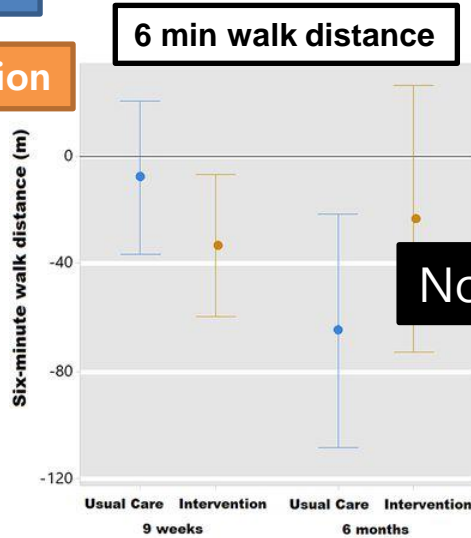


- Inoperable NSCLC (n=90)
- American College of Sports Medicine guidelines
 - Walking (preferred form of aerobic exercise in lung cancer patients)
 - Minimum of 10 min walking twice weekly at a moderate intensity
 - Resistance training

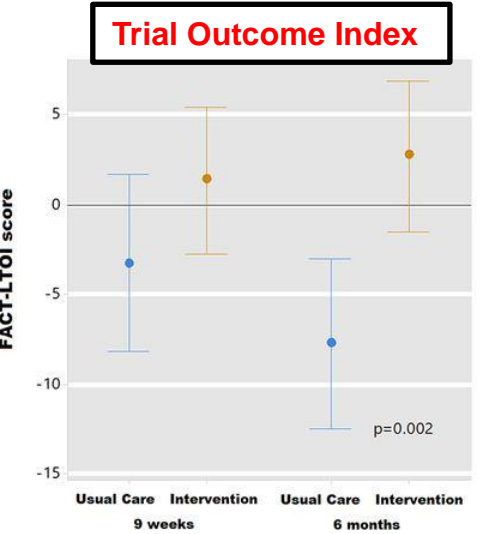
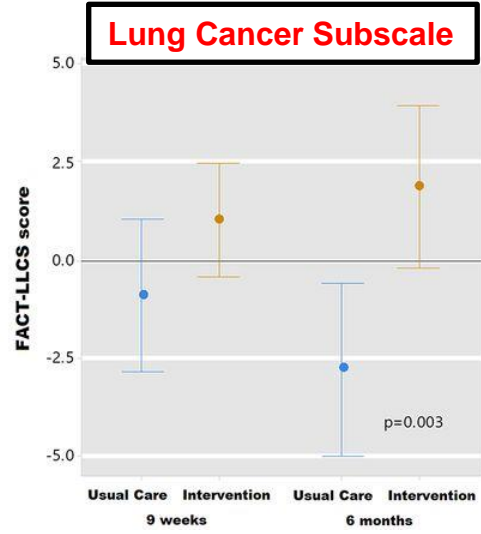
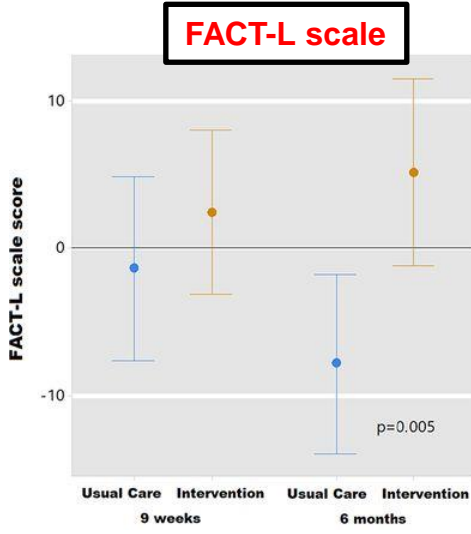
Efficacy of home-based rehabilitation

Usual care

intervention



No exercise restriction in usual care

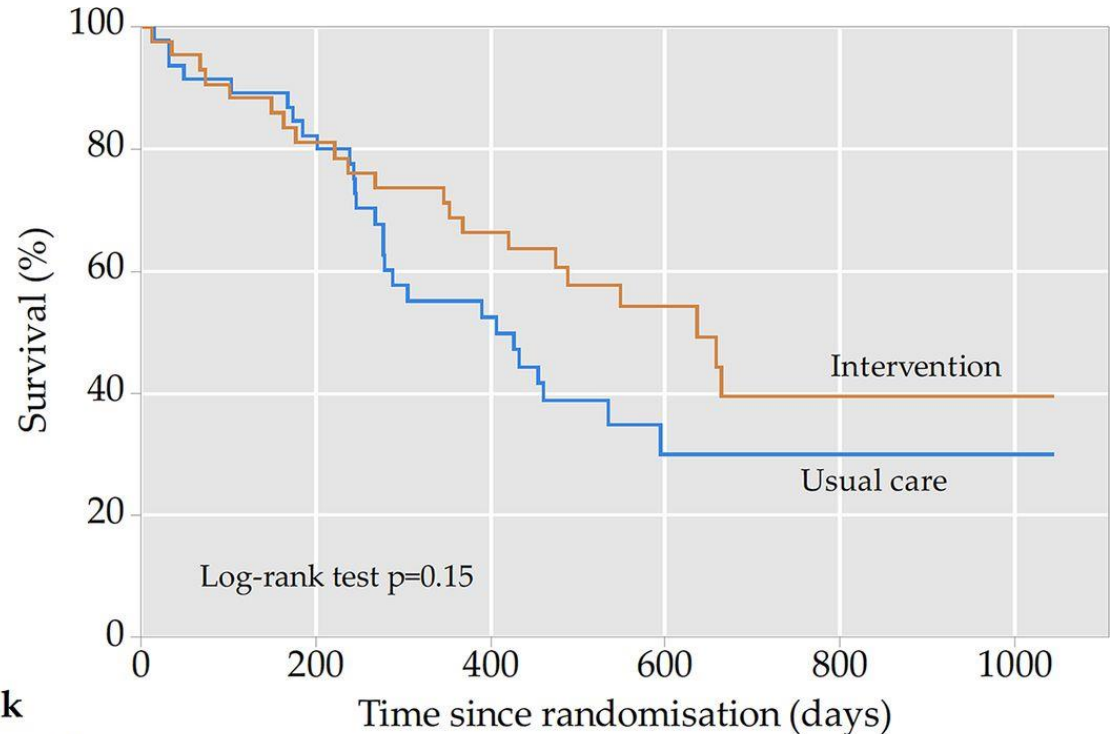


Efficacy of home-based rehabilitation

Baseline AGE

| Intervention group (n=45) | Usual care (n=47) |
|---------------------------|-------------------|
| 64.6 (13.4) | 62.5 (10.9) |

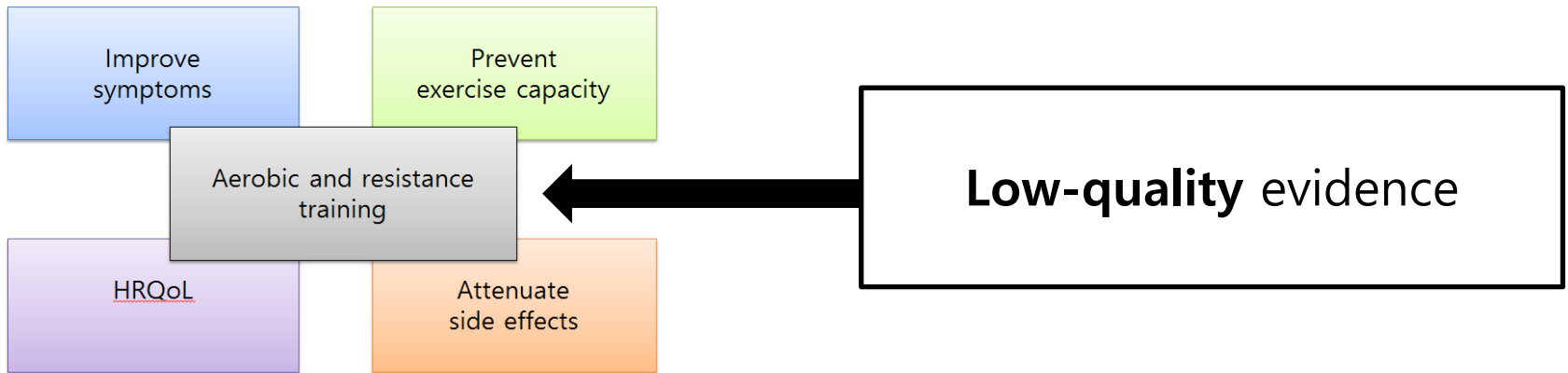
Significantly different (mean (95% CI) **6.4** (2.9 to 9.9) years, $p=0.0004$)



Number at risk (number censored)

| | | | | | | |
|--------------|--------|--------|--------|---------|--------|--------|
| Intervention | 45 (0) | 33 (4) | 26 (5) | 12 (15) | 2 (22) | 0 (24) |
| Usual care | 47 (0) | 35 (4) | 20 (7) | 6 (14) | 3 (17) | 1 (19) |

Exercise training in advanced stage lung cancer



**Low
risk of harm**

**Need for high-quality
RCT**



Exercise

How to exercise

HOW TO EXERCISE



Peri-operative exercise

-호흡재활 지침서 2015-

- 수술 전후 호흡재활은 폐와 관련된 상태를 최적화할 수 있으며, 수술 후 합병증 예방 및 빠른 회복에 도움을 준다.
- 특히 폐절제술, 폐용적축소수술의 경우 적극적인 수술 전후 호흡재활이 필요하다.
- 폐이식 수술 전후의 호흡재활은 모든 폐이식 환자들에게 필수적인 프로그램이다.

표 6-6. 폐암을 포함하여 흉부 또는 상복부 수술 예정인 환자의 호흡재활 프로그램 내용

- Exercise training to increase muscle strength and endurance
- Pulmonary rehabilitation once chemotherapy or radiation therapy is completed
- Self-management strategies
- Assessment of need for assistive equipment and services
- Psychosocial intervention: coping, stress, and anxiety management techniques
- Education
 - Breathing retraining
 - Pacing
 - Energy conservation
 - Nutrition
 - When to seek health care services

Barriers limiting to exercise

- Most patients are **insufficiently active or sedentary**
- **low adherence and high drop-out rate**
 - Cancer-related side effects
 - Lack of interest and motivation
- Specifically related to health status (Age, sarcopenia, comorbidity)
- Lack of access to services
- Lack of interest
- Disease course and therapeutic approach
- Environmental and personal exercise preferences
- Social implications

Role in supporting patients with lung cancer to be physically active

- Doctors discussing physical activity with their patients
'Exercise as part of their cancer management'
 - Encourage increased physical activity, avoid sedentary time
 - Support setting individualized activity goal
 - Involve family and caregivers
 - Assess symptoms and assist
 - Understanding safety criteria
 - Refer to an exercise professional
 - Empower patients to take control their own goal
- Exercise testing and prescription for patients with lung cancer adheres to

GENERAL PRINCIPLES

ACSM (American College of Sports Medicine) Guidelines for Exercise and Cancer

What can exercise do?

What can exercise do?

- **Prevention of 7 common cancers***







Dose: 2018 Physical Activity Guidelines for Americans: 150-300 min/week moderate or 75-150 min/week vigorous aerobic exercise

- **Survival of 3 common cancers****

Dose: Exact dose of physical activity needed to reduce cancer-specific or all-cause mortality is not yet known; Overall more activity appears to lead to better risk reduction

**bladder, breast, colon, endometrial, esophageal, kidney and stomach cancers*

***breast, colon and prostate cancers*

| | | | |
|---|---|---|--|
|  Physical Function | 3x/week for 30-60 min per session of moderate to vigorous | 2-3x/week of 2 sets of 8-12 reps for major muscle groups at moderate to vigorous intensity | 3x/week for 20-40 min per session of moderate to vigorous aerobic exercise, plus 2-3x/week of resistance training 2 sets of 8-12 reps for major muscle group at moderate to vigorous intensity |
|  Anxiety | 3x/week for 30-60 min per session of moderate to vigorous | Insufficient evidence | 2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity |
|  Depression | 3x/week for 30-60 min per session of moderate to vigorous | Insufficient evidence | 2-3x/week for 20-40 min of moderate to vigorous aerobic exercise plus 2x/week of resistance training of 2 sets, 8-12 reps for major muscle groups at moderate to vigorous intensity |
|  Lymphedema | Insufficient evidence | 2-3x/week of progressive, supervised, program for major muscle groups does not exacerbate lymphedema | Insufficient evidence |
| Moderate Evidence | | | |
|  Bone health | Insufficient evidence | 2-3x/week of moderate to vigorous resistance training plus high impact training (sufficient to generate ground reaction force of 3-4 time body weight) for at least 12 months | Insufficient evidence |
|  Sleep | 3-4x/week for 30-40 min per session of moderate intensity | Insufficient evidence | Insufficient evidence |

Citation: bit.ly/cancer_exercise_guidelines

Moderate intensity (40%-59% heart rate reserve or VO₂R) to vigorous intensity (60%-89% heart rate reserve or VO₂R) is recommended.

Exercise
is Medicine®

AMERICAN COLLEGE
of SPORTS MEDICINE



AMERICAN COLLEGE
of SPORTS MEDICINE
LEADING THE WAY

GENERAL PRINCIPLES OF PHYSICAL ACTIVITY

- Physical activity and exercise recommendations should be tailored to individual survivors' **Survivor's abilities and preference**
- Physical activity for cancer survivors:^a
 - ▶ Survivors should engage in **At least 150 min of weekly activity** activity or 75 minutes of vigorous intensity activity or equivalent combination spread out over the course of the week. **Ultimate goal of 300 min** minutes or more **Moderate intensity**
 - ▶ Two to three sessions per week of strength/resistance training that include major muscle groups ([See SPA-A](#))
 - ▶ **Stretch major muscle at least 2 days/wk** week on days that other exercises are performed
- Engage in general physical activity daily (eg, take the stairs, park in the back of parking lot)
 - ▶ Physical activity includes exercise, daily routine activities, and recreational activities
- Avoid prolonged sedentary behavior (eg, sitting for long periods)
 - ▶ Schedule movement/activity breaks regularly
 - ▶ **Stand or move while** on the phone, using the computer, or watching television

GUIDANCE FOR RESISTANCE TRAINING RECOMMENDATIONS

- Health benefits of resistance training include improvement in **Muscle strength, endurance, functional status, bone density** maintenance/improvement in bone density
- Core and strength training is important to **Maintain balance, minimize fall risk**
- All **Major muscle groups** (ie, neck, shoulders, arms, back, core, and legs) should be incorporated into a resistance training program.
- Resistance training
 - ▶ Frequency: **2~3 times/wk** adequate rest between sessions
 - ▶ Intensity: **2~3 sets of 10~15 repetitions** repetitions per set; consider increasing weight amount as tolerated with **2~3 sets of 10~15 repetitions** es
 - ▶ Rest: 2- to 3-minute rest period between sets and exercises
 - ▶ For survivors who wish to start resistance training, refer to trained personnel or **Exercise specialist if available**
- Utilize weight amount that would allow for performance of 10–15 repetitions.
- For survivors at risk for or with lymphedema, [See SLYMPH-B](#).

| EXAMPLES OF PHYSICAL ACTIVITY | | |
|--|---|---|
| <p>Light Exercise^a (No noticeable change in breathing pattern)</p> <ul style="list-style-type: none"> • Leisurely biking at 5 miles/hour or less • Activity-promoting video game • Light housework (light sweeping, dusting) • Bowling • Playing catch • Slow walking • Child care • Restorative yoga • Tai chi | <p>Moderate Exercise^b (Can talk, but not sing)</p> <ul style="list-style-type: none"> • Ballroom/line dancing • Biking on level ground or with few hills • General gardening • Baseball, softball, volleyball • Doubles tennis • Using a manual wheelchair • Brisk walking • Water aerobics • Moderate-intensity yoga (ie, Vinyasa) • Pilates <p style="text-align: center; color: red; font-size: 1.2em;">Brisk walking</p> | <p>Vigorous Exercise^b (Can say a few words without stopping to catch a breath)</p> <ul style="list-style-type: none"> • Aerobic/Fast dancing • Biking faster than 10 miles/hour • Heavy gardening • Hiking uphill • Jumping rope • Martial arts • Race walking, jogging, running • Running sports (basketball, hockey, soccer) • Swimming (fast pace or laps) • Singles tennis • Stair climbing • High-intensity yoga |

| STRATEGIES TO INCREASE PHYSICAL ACTIVITY |
|--|
| <ul style="list-style-type: none"> • Physician recommendation • Referral to trained personnel or exercise specialist if available • Supervised exercise program or classes • Telephone counseling • Motivational interviewing^c • Evaluate readiness to change, importance of change, self-efficacy • Cancer survivor-specific print materials (See SURV-B 2 of 2) • Set short- and long-term goals • Consider use of pedometer or wearable fitness tracker to monitor activity goals (eg, obtain 10,000 steps per day) • Encourage social support (exercise buddy, group) |

^aFrom the National Heart, Lung, and Blood Institute (http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/phy_act.htm) and the Compendium of Physical Activities (<https://sites.google.com/site/compendiumofphysicalactivities>).

^bReproduced and adapted from U.S. Department of Health and Human Services. Move Your Way. Washington, DC: U.S. Department of Health and Human Services. <https://health.gov/moveyourway>. Accessed March 16, 2020.

^cConsider referral to trained personnel.

ACS, ACSM and NCCN guideline

Avoiding inactivity
Engage in regular physical activity

>150 min/wk of moderate aerobic activity
or
>75 min/wk of vigorous aerobic activity

Flexibility and strength exercise
2~3 times/wk

Stretch major muscle group
2 times/wk

Physically deconditioned patients

Individual survivor's abilities and preference

Flexible
Start easily
Progress slowly

Cancer specific consideration

- ACSM guidelines-

| Issue | Advice |
|-------------------------------|--|
| Comorbid disease | Complete screening in line with general guidelines and choose exercises that avoid exacerbation of symptoms , for example hydrotherapy . |
| Bony metastases | Avoid strength assessment of muscles that attach to or act on a bony lesion site . Sites without metastases can be tested. Advise patients to avoid weights involving the affected bones and try swimming . Do not avoid resistance training . |
| Peripheral neuropathy | Assess balance, mobility and falls risk and modify exercise prescription as required (eg use a Stationary cycle or water rather than a treadmill for aerobic exercise). |
| Infection and Immunity | Advise patients that exercising with a fever is contraindicated . Precautions exist for patients with impaired hematological parameters; for example, patients with low neutrophil counts ($\leq 0.5 \times 10.9$ cells/ μ L) should avoid public gyms. |
| Cancer cachexia | Commence with prescription for resistance training only to increase muscle mass |

Contents



Exercise

1. Effect on cancer Immune
 - Molecular and biological mechanism
2. Clinical outcome
 - Perioperative impact
 - Advanced lung cancer
3. How to exercise

Nutrition

1. Lung cancer prevention
2. Sarcopenia
3. Clinical outcome
4. How to support nutrition

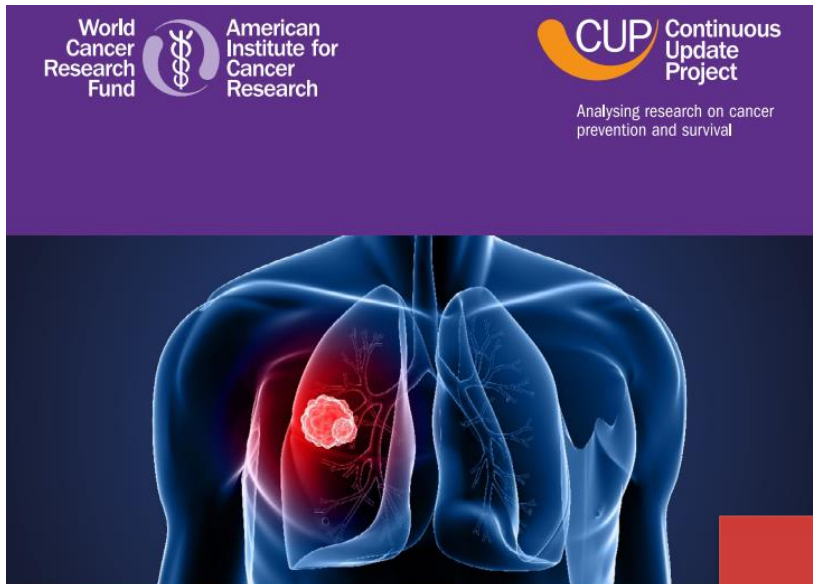




Nutrition

LUNG CANCER PREVENTION

Impact of nutrition on the lung cancer Prevention



Diet, nutrition, physical activity and **lung cancer**

Revised 2018

- 1 The International Agency for Research on Cancer (IARC) has graded arsenic and arsenic compounds as Class 1 carcinogens. The grading for this entry applies specifically to inorganic arsenic in drinking water.
- 2 The evidence is derived from studies using high-dose supplements (20 mg/day for beta-carotene; 25,000 IU/day for retinol) in current and former smokers.
- 3 The evidence applies to current and former smokers only.
- 4 The evidence applies to current smokers only.
- 5 The evidence applies only to individuals who have never smoked.

| 2017 | DIET, NUTRITION, PHYSICAL ACTIVITY AND LUNG CANCER | | |
|-----------------|--|---|--|
| | | DECREASES RISK | INCREASES RISK |
| STRONG EVIDENCE | Convincing | | Arsenic in drinking water ¹ High-dose beta-carotene supplements ² |
| | Probable | | |
| | Limited – suggestive | Vegetables ³ Fruit ³ Foods containing carotenoids Foods containing beta carotene Foods containing retinol | Red meat Processed meat Alcoholic drinks |

ARSENIC in drinking water

Beta-CAROTENE supplements in current and former smokers

Impact of nutrition on the lung cancer Prevention –limited evidence

Decreases risk

- Vegetables, and Fruits
in current and former smokers
- **Foods** containing carotenoids
- **Foods** containing beta-carotene
- **Foods** containing retinol
- **Foods** containing Vitamin C
in current smoker
- **Foods** containing isoflavones
in never smoker
- Physical activity

Increases risk

- Red meat
- Processed meat
- Alcoholic drinks



Nutrition

SARCOPENIA

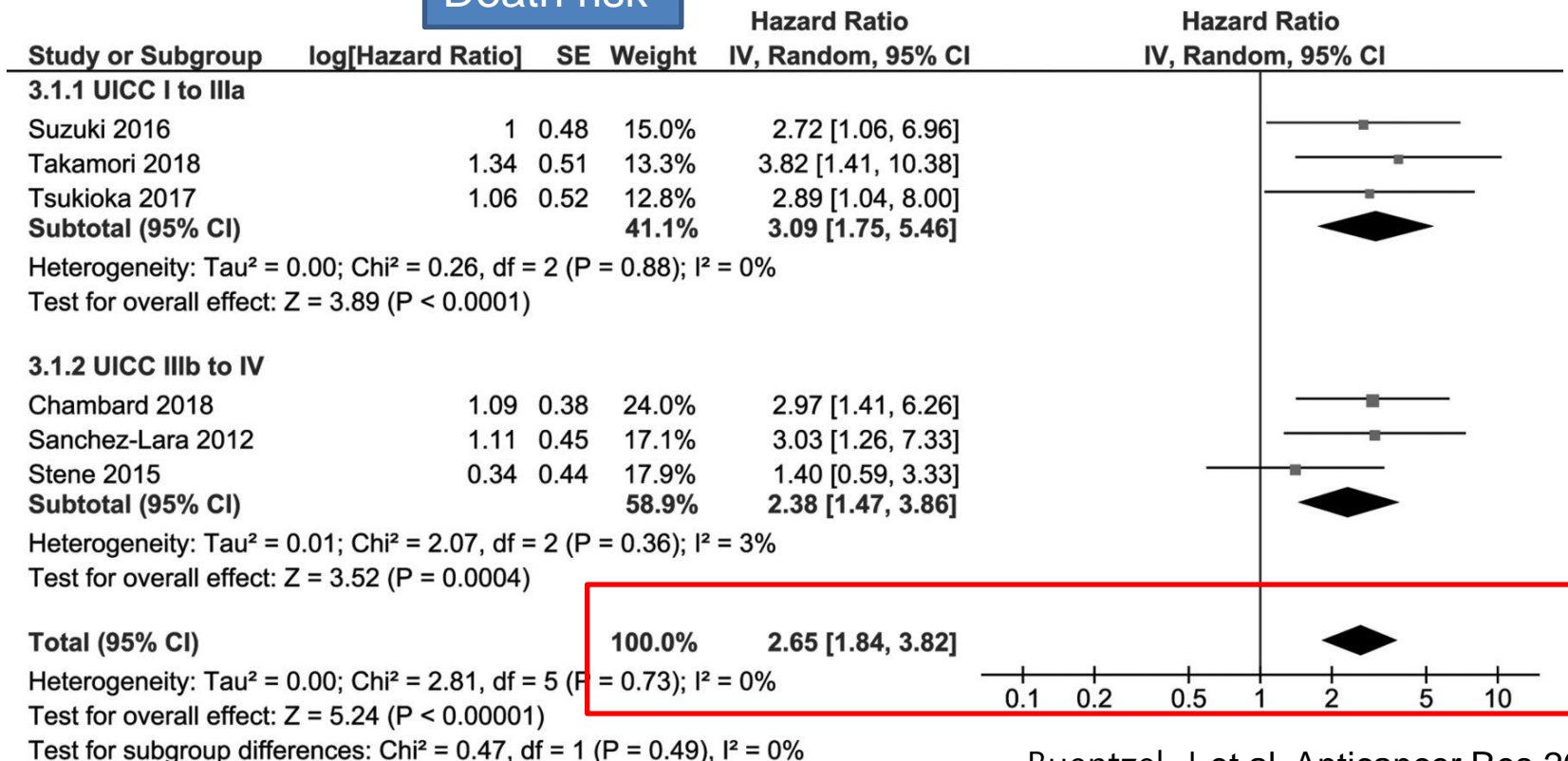


Risk factor for death

Sarcopenia is independent risk factor

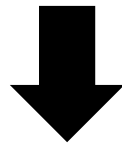
→ Worse prognosis and increased death risk

Death risk



Nutritional approaches

- Nutritional approaches to prevent and treat cancer **Sarcopenia**
 - Adequate energy intake
 - Adequate supply of protein for maintenance or gain of muscle
 - Use of supplements



Nutritional counselling, planning

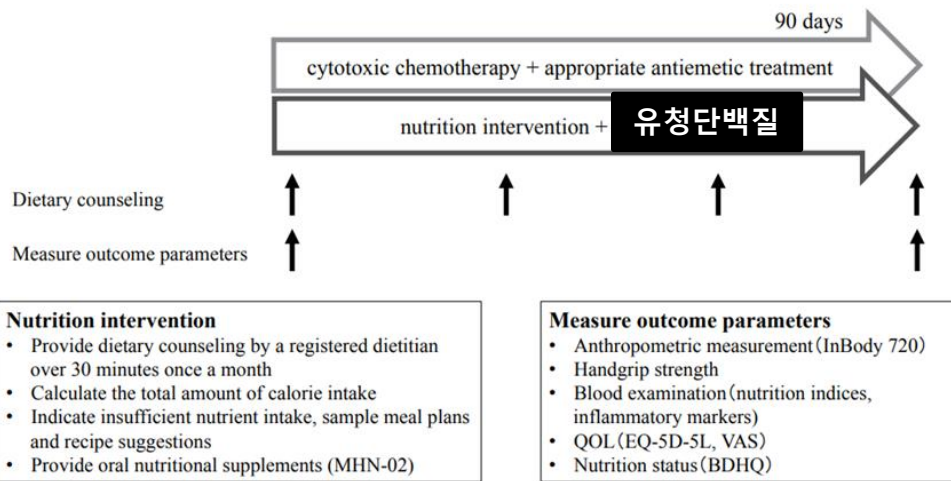


Nutrition

CLINICAL OUTCOME



Early nutritional intervention with a dietary counselling



- Dietary counseling 30min/month
- Calculated the total calorie intake
- Indicate insufficient intake, sample meal plans and recipe suggestions
- Oral nutritional supplements (유청단백)

Table 4. Body weight change in the study patients and retrospective controls

| | | Patients | Retrospective controls | Unadjusted analysis* | | | IPTW analysis† | | |
|--------------------|------|----------|------------------------|----------------------|--------|---------|----------------|--------|---------|
| | | | | OR | 95% CI | P value | OR | 95% CI | P value |
| <i>n</i> | | 10 | 38 | | | | | | |
| Body weight change | Gain | 6 (60%) | 8 (21%) | 5.6 | 1.2–25 | 0.044 | 8.4 | 1.6–42 | 0.01 |
| | Loss | 4 (40%) | 30 (79%) | | | | | | |

IPTW analysis for the study patients versus retrospective controls was estimated using a logistic regression model based on age, sex, chemotherapy (platinum-based doublet chemotherapy or non-platinum chemotherapy), body height, and body weight.

*chi-square test; †generalized estimating equations.
 CI, confidence interval; IPTW, inverse probability of treatment weight; OR, odds ratio.

Eicosapentaenoic Acid (EPA)

Table 4

Global, functional and symptom scales of Health-Related Quality of Life, differences within (Friedman test) and between ONS-EPA and C groups (*t*-student).

| | | Control | Δ | ONS-epa | Δ | <i>p</i> ** |
|-----------------------------|------------|--------------|------------|--------------|-----------|-------------|
| Global health status | T0 | 62.3 ± 23 | -6.0 ± 2 | 54.3 ± 28 | 11.1 ± 4 | 0.136 |
| | T1 | 56.1 ± 23 | | 61.8 ± 18 | | |
| | T2 | 56.5 ± 26 | | 65.4 ± 23 | | |
| | <i>p</i> * | 0.209 | | 0.021 | | |
| Functional Scales | | | | | | |
| Physical functioning | T0 | 74.0 ± 23 | -1.8 ± 0.3 | 64.5 ± 31 | 8 ± 3 | 0.419 |
| | T1 | 67.6 ± 29 | | 66.9 ± 25 | | |
| | T2 | 72.3 ± 27 | | 72.5 ± 22 | | |
| | <i>p</i> * | 0.802 | | 0.507 | | |
| Symptom scales | | | | | | |
| Fatigue | T0 | 35.9 ± 21 | -1.2 ± 0.7 | 42.7 ± 24 | -10.4 ± 6 | 0.04 |
| | T1 | 38.5 ± 27 | | 39.9 ± 20 | | |
| | T2 | 34.7 ± 20 | | 32.3 ± 24 | | |
| | <i>p</i> * | 0.772 | | 0.05 | | |
| Appetite | T0 | 36.8 ± 34 | -8.6 ± 4 | 41.5 ± 34 | -6.6 ± 2 | 0.05 |
| | T1 | 39.3 ± 34 | | 27.3 ± 25 | | |
| | T2 | 28.2 ± 30 | | 34.9 ± 31 | | |
| | <i>p</i> * | 0.454 | | 0.05 | | |
| N/V | T0 | 8.2 ± 14 | 11.4 ± 7 | 19.5 ± 23 | 8.4 ± 3 | 0.830 |
| | T1 | 28.0 ± 69 | | 33.0 ± 24 | | |
| | T2 | 19.6 ± 21 | | 27.9 ± 30 | | |
| | <i>p</i> * | 0.02 | | 0.10 | | |
| Neuropathy | T0 | 11.7 ± 22 | 20.1 ± 13 | 19.9 ± 29 | 1 ± 0.4 | 0.05 |
| | T1 | 20.5 ± 16 | | 22.0 ± 27 | | |
| | T2 | 31.8 ± 30 | | 20.9 ± 25 | | |
| | <i>p</i> * | 0.004 | | 0.951 | | |
| Diarrhoea | T0 | 6.1 ± 13 | 2.4 ± 1 | 20.0 ± 27 | -8 ± 6 | 0.19 |
| | T1 | 14.7 ± 24 | | 19.2 ± 26 | | |
| | T2 | 8.6 ± 14 | | 12.0 ± 12 | | |
| | <i>p</i> * | 0.320 | | 0.438 | | |

ONS-EPA = Oral nutritional supplement containing eicosapentaenoic acid.

Δ = differences between T0 and T2 within groups.

**p* within groups. Friedman Test.

***p* between groups. *T*-Student.

- NSCLC 92 pts
- Paclitaxel + platinum 2cycle
- No difference in OS

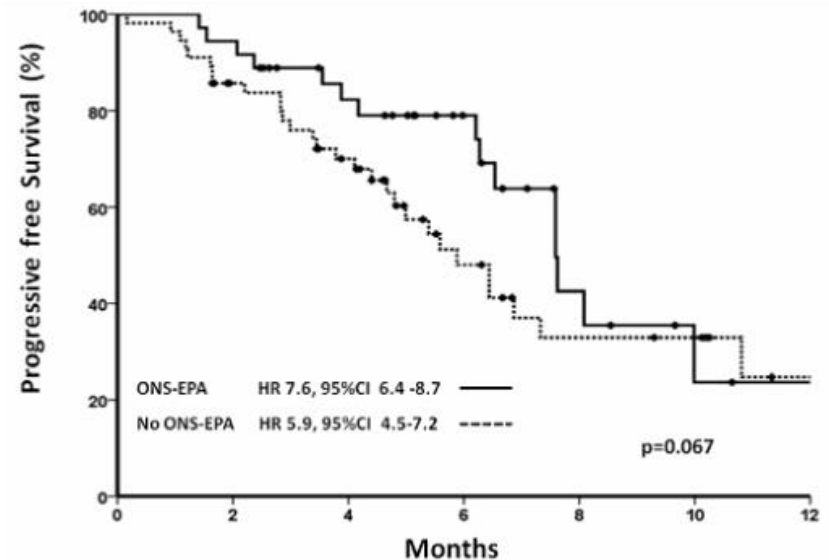


Fig. 2. Progression free survival Kaplan Meyer curves of ONS-EPA and C groups.

ProSure

- Nutritional supplement with eicosapentaenoic acid (ProSure) as a **Donation**, with no interference in the trial design and results analysis.



Fish oil supplementation

-Fish oil EPA-

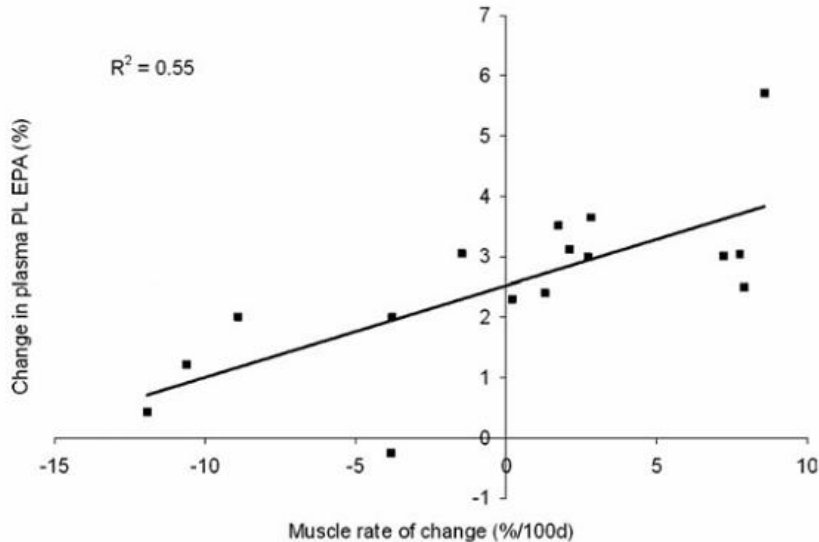


Figure 1. Relation between change in plasma phospholipid (PL) eicosapentaenoic acid (EPA) and change in muscle from baseline to end of fish oil supplementation is shown (n = 16).

- N=16(fish oil, 2.2gEPA/day)/40
- NSCLC Receiving 1st line CTx.
- Gain or maintain muscle mass

| Changes | Standard of Care Group | Fish Oil Group | Reference Group |
|--------------------------------|------------------------|---------------------------|-----------------|
| Weight change, kg | -2.3 ± 0.9 | 0.5 ± 1.0 ^b | 1.9 ± 0.3 |
| Muscle rate of change, %/100 d | -6.8 ± 2.6 | 0.1 ± 1.6 ^b | -6.0 ± 0.9 |
| IMAT rate of change, %/100 d | 9.5 ± 5.2 | -16.4 ± 13.9 ^b | 11.1 ± 3.5 |
| TAT rate of change, %/100 d | -3.9 ± 5.0 | -5.0 ± 6.5 | -6.0 ± 4.6 |

CT indicates computed tomography; IMAT, intermuscular adipose tissue; TAT, total adipose tissue.

^aThe number of patients varies because of images outside the viewing field. Results are shown as the mean ± standard error.

^bSignificantly different from standard of care ($P < .05$, using the two-sample Student *t* test).

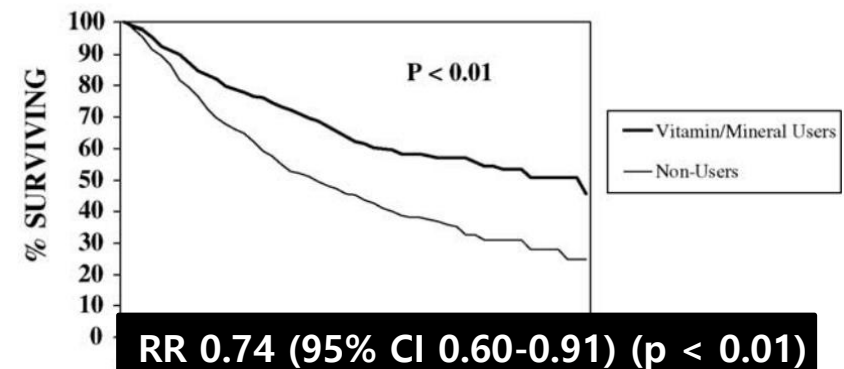
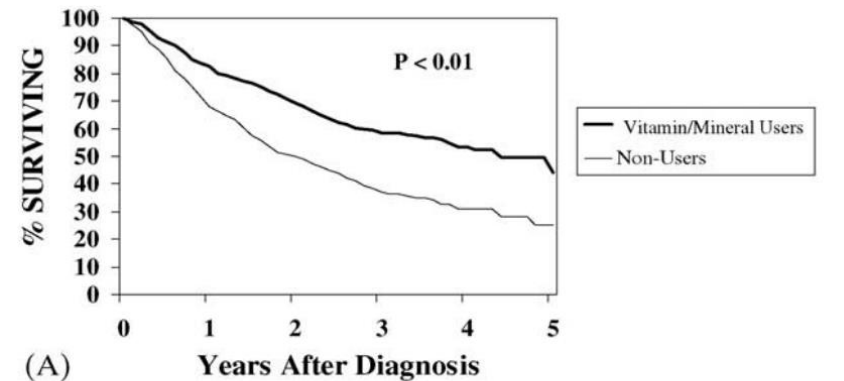
Pathologic type 구분 X
Chemo regimen 구분 X

Vitamin/mineral supplements

- ACS states that taking a **daily multi-vitamin/mineral** during treatment in **amounts not exceeding** the Recommended Daily Value could benefit those having **difficulty consuming a healthy diet**

Table 1 Baseline characteristics

| | Vitamin/mineral users (n = 714) | Non-users (n = 415) | p-Value |
|---|---------------------------------|---------------------|---------|
| Median age (25th, 75th percentile) | 67 (59, 73) | 67 (59, 74) | 0.50 |
| Male (%) | 55 | 65 | < 0.01 |
| Pack-years of smoking (%) | | | < 0.01 |
| 0 | 17 | 12 | |
| 1–20 | 16 | 10 | |
| 21–40 | 22 | 24 | |
| 41–60 | 21 | 25 | |
| Over 60 | 24 | 29 | |
| Co-morbid conditions (at diagnosis) (%) | | | |
| Chronic obstructive pulmonary disease | 36 | 40 | 0.17 |
| Asthma | 12 | 9 | 0.2 |
| Other lung disease | 19 | 17 | 0.59 |
| Other cancer (not gender-related) | 22 | 20 | 0.5 |
| Diabetes | 3 | 4 | 0.45 |
| Heart disease | 7 | 7 | 0.94 |
| Cerebral vascular accident | 0.4 | 2 | 0.06 |
| Hypertension | 6 | 5 | 0.66 |
| Tumor histology (%) | | | < 0.01 |
| Adenocarcinoma | 62 | 53 | |
| Squamous | 26 | 30 | |
| Other | 12 | 17 | |
| Stage (%) | | | 0.02 |
| IA | 26 | 19 | |
| IB | 16 | 18 | |
| IIA | 4 | 3 | |
| IIB | 9 | 8 | |
| IIIA | 15 | 17 | |
| IIIB | 10 | 11 | |
| IV | 20 | 23 | |
| Treatment 6 months after diagnosis (%) | | | |
| Chemotherapy | 33 | 37 | 0.17 |
| Radiation | 25 | 36 | < 0.01 |
| Surgery | 72 | 65 | 0.02 |



Adjustment for multiple prognostic factors



Nutrition

HOW TO SUPPORT NUTRITION



Management of Cancer Cachexia: ASCO Guideline

Eric J. Roeland, MD¹; Kari Bohlke, ScD²; Vickie E. Baracos, PhD³; Eduardo Bruera, MD⁴; Egidio del Fabbro, MD⁵; Suzanne Dixon, MPH, MS, RD⁶; Marie Fallon, MD⁷; Jørn Herrstedt, MD, DMSci⁸; Harold Lau, MD⁹; Mary Platek, PhD, MS, RD¹⁰; Hope S. Rugo, MD¹¹; Hester H. Schnipper, LICSW, BCD, OSW-C¹²; Thomas J. Smith, MD¹³; Winston Tan, MD¹⁴; and Charles L. Loprinzi, MD¹⁵

Recommendations

Nutritional Interventions

Recommendation 1.1. Clinicians may refer patients with advanced cancer and loss of appetite and/or body weight to a registered dietitian for assessment and counseling, with the goals of providing patients and caregivers with practical and safe advice for feeding; education regarding high-protein, high-calorie, nutrient-dense food; and advice against fad diets and other unproven or extreme diets (Type of recommendation: informal consensus; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 1.2. Outside the context of a clinical trial, clinicians should not routinely offer enteral tube feeding or parenteral nutrition to manage cachexia in patients with advanced cancer. A short-term trial of parenteral nutrition may be offered to a very select group of patients, such as patients who have a reversible bowel obstruction, short bowel syndrome, or other issues contributing to malabsorption, but otherwise are reasonably fit. Discontinuation of previously initiated enteral or parenteral nutrition near the end of life is appropriate (Type of recommendation: informal consensus; Evidence quality: low; Strength of recommendation: moderate).

Information about additional nutritional interventions considered by the Expert Panel is provided in [Table 1](#).

Pharmacologic Interventions

Recommendation 2.1. Evidence remains insufficient to strongly endorse any pharmacologic agent to improve cancer cachexia outcomes; clinicians may choose not to offer medications for the treatment of cancer cachexia. There are currently no FDA-approved medications for the indication of cancer cachexia (Type of recommendation: evidence based; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 2.2. Clinicians may offer a short-term trial of a progesterone analog or a corticosteroid to patients experiencing loss of appetite and/or body weight. The choice of agent and duration of treatment depends on treatment goals and assessment of risk versus benefit (Type of recommendation: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).

Information about additional pharmacologic interventions considered by the Expert Panel is provided in [Table 1](#).

Other Interventions

Recommendation 3. Outside the context of a clinical trial, no recommendation can be made for other interventions, such as exercise, for the management of cancer cachexia.

Management of Cancer Cachexia: ASCO Guideline

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TABLE 1. Summary of recommendations for the treatment of cancer cachexia in patients with advanced cancer

| Intervention | Strength of Recommendation | Strength of the Evidence | Benefits ^a | Harms ^a |
|---|---|--------------------------|-----------------------|--------------------|
| Nutritional interventions | | | | |
| Dietary counseling ^{25,26,37} | Moderate in favor | Low | Moderate | Low |
| Parenteral or enteral nutrition (routine use) ^{31,42} | Moderate against | Low | Low | Moderate to high |
| Omega-3 fatty acids ^{26,29,40} | No recommendation | Low | Low | Low |
| Vitamins, minerals, and other dietary supplements ³⁸ | No recommendation | Low | Low | Low |
| Pharmacologic interventions | | | | |
| Progesterone analogs ^{30,33,35,36,43} | Moderate in favor | Intermediate | Moderate | Moderate |
| Corticosteroids ⁴³ | Moderate in favor | Intermediate | Moderate | Moderate |
| Anamorelin ^{24,32,68} | No recommendation (not commercially available) | Intermediate | Moderate | Low |
| Olanzapine ⁵⁶ | No recommendation | Low | Moderate | Low |
| Androgens ^{36,43,59} | Moderate in favor | Intermediate | Moderate | Low |
| Thalidomide ^{34,36} | No recommendation | Low | Low | Low |
| NSAIDs ^{39,41} | No recommendation | Low | Low | Low |
| Cyproheptadine ⁴³ | No recommendation | Low | None | Low |
| Cannabinoids ^{36,43} | Weak against | Low | None | Low |
| Melatonin ^{36,43} | Weak against | Low | None | Low |
| TNF inhibitors ^{36,43} | Moderate against | Intermediate | None | Moderate |
| Hydrazine sulfate ⁴³ | Strong against | Intermediate | None | Moderate |
| Other interventions | | | | |
| Exercise ²⁷ | No recommendation | Low | Unknown | Unknown |

GENERAL PRINCIPLES

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; TNF, tumor necrosis factor.

^aCategorization of benefits and harms was based on use of the intervention for cancer cachexia in the populations that were enrolled in randomized controlled trials.

GENERAL PRINCIPLES OF NUTRITION

- Assess dietary pattern for daily intake of **Added fats and/or sugar**, **Fruits, vegetables and unrefined grains**, and **Red meats, processed meats and food, alcohol**.
- Assess timing of meals and snacks. **Dietary pattern** in size, frequency of eating out, and use of added fats and/or sugars to foods or beverages.
- All survivors should be encouraged to:
 - ▶ Make informed choices about food to ensure variety and adequate nutrient intake.
 - ▶ Limit **Red meat < 0.5kg/week** per week and avoid processed meat.
 - ▶ Limit refined sugars and **Added fats and/or sugar** in foods.
 - ▶ Eat a diet that is at least **At least 50% plant-based** majority of food being vegetables, fruit, and whole grains.^{a,b}
 - ▶ Track calorie intake.
 - ◊ Self-monitoring of caloric density and intake has been shown to be an effective strategy for weight management.
 - ◊ **Prolonged fasting X** **Intermittent fasting** may maximize caloric and nutrient intake.
 - ▶ Consume alcohol sparingly if at all. **Consume alcohol sparingly if at all**
- For patients desiring further recommendations for dietary guidelines
 - ▶ Consider referral to a dietitian or nutritionist.
 - ▶ The USDA approximate food plate volumes (www.choosemyplate.gov) are:
 - ◊ Vegetables and fruits should comprise half the volume of food on the plate
 - ◊ Vegetables: 30% of plate; fruits 20% of plate
 - ◊ Whole grains: 30% of plate
 - ◊ Protein: 20% of plate
- Recommended sources of dietary components:
 - ▶ Fat: plant sources such as olive or canola oil, avocados, seeds and nuts, and fish
 - ▶ Carbohydrates: fruits, vegetables, whole grains, and legumes
 - ▶ Protein: poultry, fish, legumes, low-fat dairy foods, and nuts
- Currently there is no consensus either refuting or supporting the role of soy food (3 or fewer servings per day) of soy foods is considered prudent.



ption

Summary -Exercise-



- Exercise is directly linked to control of tumor biology
- Perioperative exercise is recommended
- Exercise in advanced lung cancer has low certainty, but a low risk of harm
- Exercise is part of lung cancer management
- Encourage increased physical activity and avoid sedentary time



Summary

-Nutrition-



- Arsenic in drinking water and high dose β - carotene are risk factors of lung cancer
- Sarcopenia is an independent risk factor of lung cancer mortality
- Nutritional approach is needed for the prevent and treat of cancer sarcopenia (nutritional counselling and planning)



감사합니다.



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