# Exercise

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## Learning objectives | Understand and apply:

- Primary care interventions improve uptake of moderate-to-vigorous activity
- MVPA associated with improved mortality
- More daily steps assoc with more lifespan & ~ 7000 seems to be the "sweet spot" between benefit and no benefit
- Adopting more "low risk lifestyle factors" including exercise in midlife is assoc with longer life
- Sub-symptom threshold aerobic exercise hastens concussion recovery
- Return-to-play (RTP) is safe among athletes recovering from COVID

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MVPA = Moderate-to-vigorous-intensity physical activity

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## Background

- "…*chronic disease is not an inevitable consequence of aging.*"
- Most chronic diseases are partly *attributable to decreasing levels of physical activity and increasing levels of sedentarism*, along with increased consumption of highly processed foods and other environmental changes.
- Physical inactivity is a potent risk factor for disease.
- Total physical activity in the United States declined by 32% from 1965 to 2009.

Future articles in this series will include key terminology, basic exercise physiology, exercise dosing, etc

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The Evidence for Exercise in Medicine — A New Review Series. NEJM Evid 2022; 1 (1).

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## Background

METS = a common way to quantify exercise.

- 1 MET = 3.5 milliliters of oxygen/kg body weight/minute
- 1 MET = the average amount of oxygen consumption at rest
- 1 MET = 1.2 KCAL/minute

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## Background

**Examples of moderate- and vigorous-intensity exercises**

| Moderate-intensity aerobic exercise 3 – 6 METS | Vigorous-intensity aerobic exercise > 7 METS |
|---|---|
| Stationary cycling – moderate effort | Stationary cycling – vigorous effort |
| Hiking | Jogging/running |
| Water aerobics | Step aerobics |
| Yoga | Stair climber at a fast pace |
| Tennis – doubles | Tennis –singles |
| Golf - walking | Handball/racquetball/squash |

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## Background

The US Department of Health and Human Services recommends for all US adults:

- 150 minutes/week of moderate-intensity (~ **22/minutes per day**) exercise, or
- 75 minutes per weeks of vigorous-intensity exercise.

The talk test is a simple way to measure relative intensity.

Moderate Intensity
- In general, if you're doing moderate-intensity activity, you can talk but not sing during the activity.

Vigorous Intensity
- In general, if you're doing vigorous-intensity activity, you will not be able to say more than a few words without pausing for a breath.

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Centers for Disease Control and Prevention | Measuring Physical Activity Intensity

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## #1: PCP Interventions ↑ uptake of MVPA

**Objective:** To examine the effectiveness of physical activity interventions delivered or prompted by primary care health professionals
**Design**: Systematic review & meta-analysis of 46 RCTS (16,198 participants) with 3 – 60 mo follow-up

**Results:**
- Physical activity interventions (vs controls) increased:
  - MVPA by 14 minutes a week
  - The odds of patients meeting guidelines for MVPA ↑ by 33%
- Only seen in trials using self-reported measures and not in trials that used devices to measure PA
- Interventions with at least five contacts had a larger effect on self-reported minutes of MVPA than those with fewer contacts.

**Conclusion:** Physical activity interventions delivered by health professionals in primary care settings appear effective in increasing participation in physical activity as measured by self-report

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Effectiveness of physical activity interventions delivered or prompted by health professionals in primary care settings: systematic review and meta-analysis of randomised controlled trials. BMJ 2022;376:e068465

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## #2: MVPA & Mortality

**Objective:** Determine whether a low dose of MVPA (< 150 min/week) is effective in reducing mortality, in participants older than 60 years.

**Design:** Systematic review and meta-analysis of 9 cohort studies (122 K participants) with ~10 years of follow up & 18 K deaths

**Primary outcome:** Risk ratio for death: Inactive | Low MVPA (1 – 499 METS/wk) | Moderate MVPA (500 – 999 METS/wk | High MVPA (> 1000 METS/wk)

**Results:**
- Mortality risk (compared to inactive participants):
  - 0.78 with low dose MVPA
  - 0.72 with moderate dose MVPA
  - 0.65 for high dose MVPA

**Conclusion:** "A dose of MVPA below current recommendations reduced mortality by 22% in older adults"

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MPVA based upon MET-minutes

Even a low-dose of moderate-to-vigorous physical activity reduces mortality by 22% in adults aged ≥60 years: a systematic review and meta-analysis. Br J Sports Med. 2019 Oct;49(19):1262-7

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## #3: Exercise more, sit less

**Objective:** To examine the associations between total physical activity (including different intensities) and sedentary time and all-cause mortality.

**Design:** Systematic review and meta-analysis of 8 studies (35 K participants, ($\bar{x}$ age 62.6 | 73% female) ) with ~6 years of follow up & 2149 deaths. Physical activity & sedentary time measured by accelerometer

**Primary outcome:** All-cause mortality

**Results:**
- Mortality risk | Physical Activity RR for mortality:
  - Least activity RR = 1.0
  - Moderate activity RR = 0.34 – 0.44
  - Most activity RR = 0.22
- Mortality risk | Sedentary time RR for mortality:
  - Least sedentary RR for mortality 1.0.
  - Moderately sedentary RR = 1.28 – 1.71
  - Most sedentary RR = 2.63

**Conclusion:** "Higher levels of total physical activity, at any intensity, and less time spent sedentary, are associated with substantially reduced risk for premature mortality"

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Dose-response associations between accelerometry measured physical activity and sedentary time and all-cause mortality: systematic review and harmonised meta-analysis. BMJ. 2019 Aug 21;366:l4570

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## #4: Live longer, even if you exercise a little bit

**Objective:** To investigate the association of running participation and the dose of running with the risk of all-cause, cardiovascular and cancer mortality.

**Design:** Systematic review and meta-analysis of 14 studies (232 K adult participants) with 5.5 - 35 years of follow up & 26 K deaths.

**Primary outcome:** All-cause, cardiovascular and cancer mortality

**Results:**
- Running vs non-running | Mortality risk:
  - All-cause RR = 0.73
  - CV RR = 0.70
  - Cancer RR = 0.77

No significant dose-response trends for weekly frequency, weekly duration, pace and the total volume of running.

**Conclusion:** "Increased rates of participation in running, regardless of its dose, would probably lead to substantial improvements in population health and longevity. "

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Is running associated with a lower risk of all-cause, cardiovascular and cancer mortality, and is the more the better A systematic review and meta-analysis. Br J Sports Med British Journal of Sports Medicine Published Online First: 04 November 2019

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## Exercise Snacks

The New York Times

PHYS ED

Even a 20-Second Exercise 'Snack' Can Improve Fitness

As little as 20 seconds of brisk stair climbing, done several times a day, might be enough to increase aerobic fitness.

"… people can complete a meaningful series of insta-workouts without leaving their office building or even changing out of their dress shoes…"

"…hurry up 60 steps — three flights of stairs — … quickly … one step at a time. These ascents lasted about 20 seconds twice daily."

At the end of 6 weeks, participants increased aerobic fitness 5%

" … intermittent, quickie stair climbing can be an effective workout…"

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NY Times Jan 23, 2019

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## Exercise Snacks

The New York Times

PHYS ED

Even a 20-Second Exercise 'Snack' Can Improve Fitness

As little as 20 seconds of brisk stair climbing, done several times a day, might be enough to increase aerobic fitness.

"We are not suggesting that this type of exercise can or should" replace all other physical activity, he continues. "But it is one possible way for people who think they are too busy to work out to fit exercise into their lives."

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NY Times Jan 23, 2019

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## #5: ↑ % of time in VPA = more benefit

**Objective:** To examine the association of the proportion of VPA to total physical activity (defined as moderate to vigorous physical activity [MVPA]) with all-cause mortality, cardiovascular disease mortality, and cancer mortality.

**Design**: Cohort of 403,681 adults (51% ♀; $\bar{x}$ age 42.8) providing self-reported physical activity for 10.1 yrs
**Outcome**: Mortality

**Results:**

- MPA (150 – 299 min/wk) vs 0 minutes/wk
  - 17% ↓ all cause mortality
  - 25% ↓ CV mortality
  - 6% ↓ CA mortality
- VPA (> 75 – 149 min/wk) vs 0 minutes/wk
  - 20% ↓ all cause mortality
  - 21% ↓ CV mortality
  - 11 ↓ CA mortality

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Association of Physical Activity Intensity With Mortality A National Cohort Study of 403 681 US Adults. JAMA Intern Med. 2021;181(2):203-211.

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## #5: ↑ % of time in VPA = more benefit

**Objective:** To examine the association of the proportion of VPA to total physical activity (defined as moderate to vigorous physical activity [MVPA]) with all-cause mortality, cardiovascular disease mortality, and cancer mortality.

**Design**: Cohort of 403,681 adults (51% ♀; $\bar{x}$ age 42.8) providing self-reported physical activity for 10.1 yrs
**Outcome**: Mortality

**Results:**

- Among participants performing any MVPA
  - 50-75% VA vs no vigorous activity assoc with a 17% ↓ all cause mortality

**Conclusion:** ".. for the same volume of MVPA, a higher proportion of VPA to total physical activity was associated with lower all-cause mortality. Clinicians and public health interventions should recommend 150 minutes or more per week of MVPA but also advise on the potential benefits associated with VPA to maximize population health."

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Association of Physical Activity Intensity With Mortality A National Cohort Study of 403 681 US Adults. JAMA Intern Med. 2021;181(2):203-211.

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## #6: More steps = lower mortality

**Objective:** Describe the dose-response relationship between step count and intensity and mortality.
**Design**: 4840 participants (54% ♀; $\bar{x}$ age 56.8)
**Methods:** Accelerometer-measured # steps per day and 3 measures of step intensity
**Outcome**: Mortality after 10.1 yrs of follow up
**Results:**

| | < 4000 steps/d | 4000 – 8000 steps/d | 8000 – 12,000 steps/d | > 12,000 steps/d |
|---|---|---|---|---|
| **Mortality** (per 1000 person years) | 76.7 | 21.4 | 6.9 | 4.8 |

Compared to persons with < 4000 steps/d
- 8000 steps/d assoc with 51% ↓ in mortality
- 12000 steps/d assoc with 65% ↓ in mortality

More steps greater benefit

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Association of Daily Step Count and Step Intensity With Mortality Among US Adults. JAMA. 2020;323(12):1151-1160.

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## #6: More steps = lower mortality

**Objective:** Describe the dose-response relationship between step count and intensity and mortality.
**Design**: 4840 participants (54% ♀; $\bar{x}$ age 56.8) providing self-reported physical activity for 10.1 yrs
**Methods:** Accelerometer-measured # steps per day and 3 measures of step intensity
**Outcome**: Mortality after 10.1 yrs of follow up
**Results:**

| | 19 – 56 steps/min | 56 – 70 steps/min | 70 – 83 steps/min | 83 - 150 steps/min |
|---|---|---|---|---|
| **Mortality** (per 1000 person years) | 33 | 13 | 7 | 5.3 |

More steps/minute = greater benefit

**Conclusions:** "…a greater number of daily steps was significantly associated with lower all-cause mortality."

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Numbers rounded up from original data

Association of Daily Step Count and Step Intensity With Mortality Among US Adults. JAMA. 2020;323(12):1151-1160.

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## #7: More steps = lower mortality

**Objective:** To estimate the assoc of steps/day with premature all-cause mortality (age 41-65 years)
**Design**: 2110 participants (57.1% ♀; $\bar{x}$ age 45.2; 42.1% black) wearing an accelerometer
**Outcome**: Mortality after 10.8 yrs.

**Methods:** Accelerometer-measured # steps per day
- Low step volume = mean # steps /d = < 7,000
- Moderate step volume = mean # steps /d 7000 – 10000
- High step volume = mean # steps /d > 10000

**Results:**

| | <7000 steps/d | 7000 - 10000 steps/d | > 10000 steps/d | 83 - 150 steps/min |
|---|---|---|---|---|
| **Mortality** (per 1000 person years) | 33 | 13 | 7 | 5.3 |

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Numbers rounded up from original data

Steps per Day and All-Cause Mortality in Middle-aged Adults in the Coronary Artery Risk Development in Young Adults Study. JAMA Netw Open. 2021;4(9):e2124516.

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## #7: More steps = lower mortality

**Objective:** To estimate the assoc of steps/day with premature all-cause mortality (age 41-65 years)
**Design**: 2110 participants (57.1% ♀; $\bar{x}$ age 45.2; 42.1% black) providing self-reported physical activity
**Outcome**: Mortality after 10.8 yrs.

| | <7000 steps/d | 7000 - 10000 steps/d | > 10000 steps/d |
|---|---|---|---|
| **Mortality difference** (per 1000 person years) | | 53 | 41 |
| Hazard Ratio | 1 | 0.28 | 0.45 |
| Results similar for gender and ethnicity | | | |

**Conclusion:** Adults taking at least 7000 steps/d, compared with those taking fewer than 7000 steps/d, had approximately 50% to 70% lower risk of mortality.

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Numbers rounded up from original data

Steps per Day and All-Cause Mortality in Middle-aged Adults in the Coronary Artery Risk Development in Young Adults Study. JAMA Netw Open. 2021;4(9):e2124516.

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## #8: ↑ exercise by 10 minutes/d assoc with 110,000 fewer deaths/yr

**Objective:** To examine the assoc of MVPA & mortality in a population-based sample of US adults and to estimate the number of deaths prevented annually with modest increases in moderate-to-vigorous physical activity intensity (MVPA).
**Design**: 4840 adults (53% women, 10.4% non-Hispanic black, 5.1% Mexican-American) with accelerometer data.
**Outcome**: Mortality
**Results:**

| | Minutes/Day (accelerometer data) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0-19 | 20 -39 | 40 - 59 | 60 - 79 | 80 - 99 | 100 - 119 | 120 - 139 | > 140 |
| **Mortality Hazard Ratio** | 1 | 0.69 | 0.51 | 0.40 | 0.34 | 0.32 | 0.30 | 0.28 |
| Results similar for gender and ethnicity | | | | | | | | |

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Numbers rounded up from original data

Estimated Number of Deaths Prevented Through Increased Physical Activity Among US Adults. JAMA Intern Med. 2022;182(3):349-352

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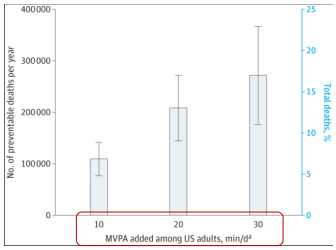
## #8: ↑ exercise by 10 minutes/d assoc with 110,000 fewer deaths/yr




100 – 280 K Deaths prevented by added amount of MVPA among US Adults aged 40 to 85 years or older

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Numbers rounded up from original data

Estimated Number of Deaths Prevented Through Increased Physical Activity Among US Adults. JAMA Intern Med. 2022;182(3):349-352

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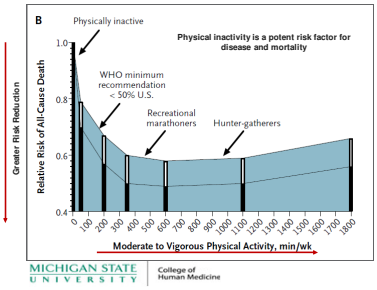
## Review | Evidence for Exercise in Medicine




1. "Small amounts of physical activity garner tremendous mortality benefit when compared with no physical activity (approximately 20% reduction)…"
2. There is no optimal amount of physical activity.
3. There is no convincing evidence for harm at very high levels of physical activity."

"… numerous observational data sets linking health outcomes to habitual physical activity are strongly suggestive of a causal effect."

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The Evidence for Exercise in Medicine — A New Review Series. NEJM Evid 2022; 1 (3)

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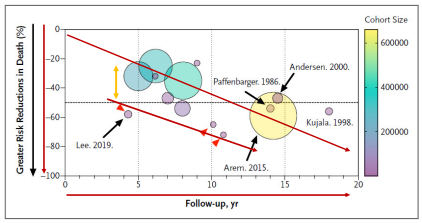
## Physical Activity & Mortality Reduction




Red arrows = accelerometer-based studies | the Δ suggests the historical magnitude of benefit was underestimated

The longer the follow up the greater the risk reduction

Duration of habitual physical activity

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Estimated Number of Deaths Prevented Through Increased Physical Activity Among US Adults. JAMA Intern Med. 2022;182(3):349-352

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## Life's Essential 8 | Checklist for Heart Health

| | |
|---|---|
| Physical Activity | 2 ½ hours of MPA or 75 minutes of VPA/week. |
| Diet | Whole foods, lots of fruits & vegetables, lean protein, nuts, seeds, cooking in non-tropical oils such as olive and canola. |
| Nicotine Exposure | None |
| Sleep | Most adults need 7-9 hours of sleep each |
| Body Weight | Optimal BMI = 25 |
| Cholesterol | Control levels of non-HDL, or "bad," cholesterol |
| Blood Sugar | Manage blood sugar |
| Blood Pressure | < 120 / < 80 = optimal |
| Moderate ETOH | |

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Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory From the American Heart Association. Circulation. 2022;0:10.1161/CIR.0000000000001078

ACC/AHA Site accessed July 2 2022

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## #9: Adopt low risk lifestyle factors & live longer

**Objective:** To examine how a healthy lifestyle is related to life expectancy that is free from major chronic diseases.

**Design:** Prospective cohort study Nurse's health Study (1980-2014; n=73 196) and the Health Professionals Follow-Up Study (1986-2014; n=38 366).

**Primary outcome:** Life expectancy free of diabetes, cardiovascular diseases, and cancer as a function of 5 low risk lifestyle factors. (smoking, BMI, exercise, mod ETOH, diet)

**Results:**

~ 10 yrs additional life
- Life expectancy at age 50 | Women
- 23.7 years | 0 low risk lifestyle factors
- 34.4 years | 4 or 5 low risk lifestyle factors

~ 8 yrs additional life
- Life expectancy at age 50 | Men
- 23.5 years | 0 low risk lifestyle factors
- 31.1 years | 4 or 5 low risk lifestyle factors

**Conclusion:** "Adherence to a healthy lifestyle at mid-life is associated with a longer life expectancy free of major chronic diseases."

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Yanping Li et al. Healthy Lifestyle and Life Expectancy Free of Cancer, Cardiovascular Disease, and Type 2 Diabetes: Prospective Cohort Study. BMJ 2020; 368

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## #10: Adopt low risk lifestyle factors & live longer

**Objective:** To estimate the impact of lifestyle factors on premature mortality and life expectancy in the US population.

**Design:** Prospective cohort study Nurse's health Study (1980-2014; n=78,865) and the Health Professionals Follow-Up Study (1986-2014; n=44,354). 34 years of follow up with 42,167 deaths

**Primary outcome:** Mortality as a function of 5 low risk lifestyle factors. (smoking, BMI, exercise, mod ETOH, diet)

**Results:**

- Life expectancy at age 50
  - 29 years women | 0 low risk lifestyle factors
  - 25.5 years men | 0 low risk lifestyle factors
- Life expectancy at age 50 |
  - 43.1 years women | 5 risk lifestyle factors
  - 37.6 years men | 5 low risk lifestyle factors

Difference 12.2 – 14 years

**Conclusion:** "Adopting a healthy lifestyle could substantially reduce premature mortality and prolong life expectancy in US adults."

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Li Y et al. Impact of Healthy Lifestyle Factors on Life Expectancies in the US Population. Circulation 2018;138:345

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## #11: Aerobic exercise & concussion recovery

**Objective:** To assess the effectiveness of aerobic exercise vs a stretching program among 103 adolescents ($\bar{x}$ age 15.3 | 46% female) within ~ 5 days of SRC

**Intervention:** RCT of: 1) aerobic exercise or, 2) placebo-like stretching program (designed to not elevate heart rate), both for ~ 20 minutes/d.

**Primary outcome:** Days from injury to recovery

**Results:**

- Time to recovery 13 vs 17 days (P=.009)

**Conclusion:** "… individualized subsymptom threshold aerobic exercise treatment …during the first week after SRC speeds recovery and may reduce the incidence of delayed recovery

Sport-related concussion (SRC)

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Leddy JJ et al. Early Subthreshold Aerobic Exercise for Sport-Related Concussion: A Randomized Clinical Trial. JAMA Pediatr. 2019 Apr 1;173(4):319-325

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## #12: Aerobic exercise & concussion recovery

**Objective:** To validate the safety, efficacy, and generalizability of, and objective adherence to, prescribed early targeted heart rate subsymptom threshold aerobic exercise for adolescent recovery from SRC and for reducing the risk of persistent post-concussive symptoms.

**Methods:** RCT of 118 adolescents (13 – 18 years old) presenting within 10 days of SRC

**Intervention:** RCT of: 1) aerobic exercise or, 2) placebo-like stretching program (designed to not elevate heart rate), both for ~ 20 minutes/d

**Primary outcome:** Clinical recovery (return to baseline sx, normal exercise tolerance & PE) at 4 wks

**Results:**

- Exercise assoc with likelihood of recovery at 4 weeks
- Risk of post concussive sx ↓ 48%

**Conclusion:** "… early treatment with subsymptom threshold aerobic exercise safely speeds recovery from sport-related concussion and reduces the risk for persistent post-concussive symptoms.."

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Early targeted heart rate aerobic exercise versus placebo stretching for sport-related concussion in adolescents: a randomised controlled trial. The Lancet Child & Adolescent Health. Volume 5, Issue 11, November 2021, Pages 792-799

Sport-related concussion (SRC)

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## #13: Return-to- Play Post COVID

**Objective:** To assess the prevalence of detectable inflammatory heart disease in professional athletes with prior COVID-19 infection, using current RTP screening recommendations.

**Design:** Cross-sectional study of RTP mandatory cardiac testing performed between May - October 2020 on 789 professional athletes (1.5% ♀ | $\bar{x}$ age 25 | 58.3% had prior sx, 41.7% asx) who had tested (+) for COVID-19 in professional sports leagues (NFL , MLB etc). Testing occurred 19 days after (+) test

**Testing:** Screening = troponins, ECGs & resting ECHO | if screen (+) then further testing (cardiac MRI &/or stress ECHO

**Primary outcome:** % of abnormal screening tests | & results and outcomes of additional testing

**Results:**

- (+) troponins = 3.8% | Abl ECG = 1.3% | Abl ECHO = 2.5%
- 0.6% had cardiac MRI with findings suggestive of myocarditis or pericarditis -> restriction from play
- No adverse events occurred in those who underwent cardiac screening and returned to play

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Prevalence of Inflammatory Heart Disease Among Professional Athletes With Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening. JAMA Cardiol. 2021;6(7):745-752

RTP = return to play

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## #13: Return-to- Play Post COVID

**Objective:** To assess the prevalence of detectable inflammatory heart disease in professional athletes with prior COVID-19 infection, using current RTP screening recommendations.

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**Testing:** Screening = troponins, ECGs & resting ECHO | if screen (+) then further testing (cardiac MRI &/or stress ECHO

**Primary outcome:** % of abnormal screening tests | & results and outcomes of additional testing

**Conclusion:**

"… few cases of inflammatory heart disease have been detected …long term follow up is ongoing"

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Prevalence of Inflammatory Heart Disease Among Professional Athletes With Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening. JAMA Cardiol. 2021;6(7):745-752

RTP = return to play

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## Conclusions

- Primary care interventions improve uptake of moderate-to-vigorous activity
- MVPA associated with improved mortality
- More daily steps assoc with more lifespan & ~ 7000 seems to be the "sweet spot"
- Adopting more "low risk lifestyle factors" midlife is assoc with longer life
- Sub-symptom threshold aerobic exercise hastens concussion recovery
- Return-to-play (RTP) is safe among most athletes recovering from COVID

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MVPA = Moderate-to-vigorous-intensity physical activity

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