

1 - 2:15 pm

One Size Fits All: Benefits of Exercise

SPEAKER Neil Skolnik, MD

primed

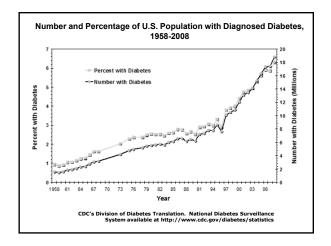
Presenter Disclosure Information

The following relationships exist related to this presentation:

▶ Neil Skolnik, MD: Consultant for AstraZeneca. Medical Advisory Board for AstraZeneca. Speaking and teaching for AstraZeneca.

Off-Label/Investigational Discussion

▶ In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.



Benefits of Exercise

- Cancer
- Diabetes
- Depression
- Miscellaneous Effects
- Cardiovascular Disease
- All-cause Mortality
- Dose and Response
- The Exercise Prescription

Cancer

Breast Cancer and Exercise

- Retrospective Case-Control Trial (55-64 y.o):
 - 1123 women with Breast Ca
 - 904 women without
- Exercise vs. non-exercise Odds Ratio 0.55

British J Ca 1999;80:1852

Breast Cancer and Exercise

- Prospective cohort study: 72,608 postmenopausal women followed x 5 yrs.
- High vs low physical activity
- High physical activity: 29% lower incidence of breast cancer

Cancer Causes & Control 2003;14:519-529

Moderate-Intensity Physical Activity Ameliorates the Breast Cancer Risk in Diabetic Women

- Case-Control study: 1000 cases and 1074 controls
- For the group with diabetes as a whole, postmenopausal women had a 2.7 x risk of breast cancer.

Diabetes Care 35:2500-2502,

Colon Cancer and Physical Activity

- Prospective Cohort Studies 19 studies
 - Males High levels vs low levels of
 - Occupational activity RR- o. 79
 - Recreational activity RR 0.78
 - Women
 - Occupational activity no significant difference
 - Recreational activity RR 0.71

Colorectal Dis 2005;7:204-21

Colon Adenoma and Physical Activity

- Meta-analysis of 20 studies
- High Physical Activity vs. Low Phys Act
 - RR o.84 for all adenomas
 - RR 0.70 for large/advanced polyps

British J Ca 2011;104:882-885

Midlife Cardiorespiratory Fitness, Incident Cancer, and Survival After Cancer in Men

- Prospective, observational cohort study of 13,949 community-dwelling men who had a baseline fitness examination.
- Cardiorespiratory fitness levels were assessed between 1971 and 2009, and incident lung, prostate, and colorectal cancer using Medicare claims data from 1999 to 2009

JAMA Oncol. doi:10.1001/jamaoncol.2015.0226 Published online March 26, 2015.

Midlife Cardiorespiratory Fitness, Incident Cancer, and Survival After Cancer in Men

■ Outcomes: (1)incident prostate, lung, and colorectal cancer and (2) all-cause mortality and cause-specific mortality among men who developed cancer at age ≥65 years.

JAMA Oncol. doi:10.1001/jamaoncol.2015.0226 Published online March 26, 2015

American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention

- One-third of the more than 572,000 cancer deaths that occur in the United States each year can be attributed to diet and physical activity habits.
- Physical activity may reduce the risk of cancers of the breast, colon, endometrium, advanced prostate cancer, and possibly, pancreatic cancer.

CA Cancer J Clin 2012;62:30-67

Diabetes

Case

- 43 year-old woman presents for follow up of routine blood work after annual physical exam.
- PMH- none
- PE WNL except BMI 32.5
- Labs Total Chol 235, Triglycerides 225, HDL Chol 45, LDL-chol 135; A1c 6.1
- Approach ?

Diabetes Prevention Program Research Group (DPPT)

- 3234 persons with "Pre-diabetes" (elevated fasting and post-load plasma glucose) randomized to:
 - Placebo
 - Metformin (850 mg twice daily)
 - Lifestyle-modification program

N Engl J Med 2002;346:393-403.

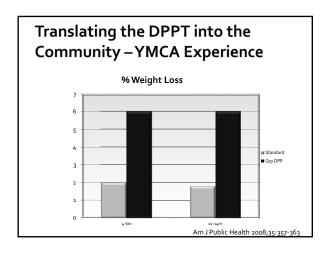
The Look AHEAD (Action for Health in Diabetes) Trial

- A randomized trial comparing the effects of intensive lifestyle intervention (ILI) vs. diabetes support and education (DSE; the control group)
- Population 5145 overweight or obese individuals with type 2 diabetes
- Endpoint Incidence of major CVD events in
- Average Age 59
- Mean BMI 36
- Duration: 4 year results reported

Arch Intern Med. 2010;170(17):1566-1575

Translating the DPPT into the Community – YMCA Experience

- Group-based DPP intervention delivered by YMCA staff vs brief counseling alone
- 92 adults
 - Average age 58 years old
 - BMI-31
 - A1c 5.6



Diet and Exercise Programs Work

- 53 studies
- Compared with usual care, diet and physical activity promotion programs
 - reduced type 2 diabetes incidence (RR, 0.59)
 - decreased body weight (net change, -2.2%)
 - fasting blood glucose level and improved other cardiometabolic risk factors
- More intensive programs were more effective.

Ann Intern Med. Published online 14 July 2015 doi:10.7326/M15-0452

Meta-analysis of studies of exercise, diabetes and All-cause Mortality

- Meta-analysis of 17 studies of the effect of exercise on All-cause Mortality (ACM) and CV disease in patients with diabetes.
- Highest Physical Activity compared to lowest Physical activity group, Relative Risk of:
 - ACM 0.61 (0.52-0.70)
 - CVD 0.71 (0.60-0.84)

Diabetes Care 36:471-479, 2013

Does Exercise offset the Increased CV Risk of Diabetes?

- Observational trial of 53,587 Norwegian men and women
- Compared to physically inactive people without diabetes, hazard ratio of CV Mortality:
 - Inactive people with diabetes 2.81
 - Physically active (>3hrs light activity per week) with diabetes – 0.89
 - Physically active (>3hrs light activity per week) without diabetes – 0.78

Diabetes Care 36:690-695, 2013

Exercise and Diabetes Conclusion

Depression

Depression

- Epidemiology- depression is more common in those with low levels of physical activity.
- Physiology
 - Physical activity may change endorphin and monoamine levels and reduce cortisol levels, which may improve mood.
 - Exercise stimulates growth of new nerve cells and release of brain-derived neurotrophic factors.

Exercise for Depression. Cochrane Database of Sytematic Reviews 2009, Issue 3, Art. No.: CD004366.DOI:10.1002/14651858.CD004366.pub4

Depression

 Meta-Analysis of 13 studies lasting from 4-16 weeks: Exercise leads to a 31% better odds of depression remission by end of study

J Clin Psychiatry 2011; 72:529

Depression – Cochrane Review

- Twenty-three trials comparing exercise with no treatment or control intervention.
- Pooled data indicated a <u>large clinical effect</u>.
 - In the three trials with "adequate allocation concealment" the pooled result was -0.42 indicating a moderate effect.
- Effect apparent for both aerobic and resistance exercise
- Cognitive therapy and exercise performed about the same.

Exercise for Depression. Cochrane Database of Sytematic Reviews 2009, Issue 3, Art. No.: CD004366.DOI:10.1002/14651858.CD004366.pub4

Chronic Disease, Depression and Exercise

- Ninety articles involving 10,534 sedentary patients with a chronic illness – primarily CV disease, chronic pain, fibromyalgia, obesity, cancer, Alzheimer's Disease, and COPD
- Exercise training significantly reduced depressive symptoms
- Similar to the effect of pharmacotherapy on depressive symptoms among patients with stroke and fibromyalgia.

Arch Intern Med. 2012;172(2):101-111

Anxiety and Exercise

 Anxiety related disorders have a prevalence of approximately 25-35% lower among those reporting physical activity than those who do not.

> Prev Med 2003;36:698-703 Depression and Anxiety 2013; 30: 362

Miscellaneous Effects

Erectile Function

- Exercise is Associated with Better Erectile Function in Men Under 40. Prevalence of ED:
 - Sedentary lifestyle 44%
 - Active lifestyle 22% (*P* = 0.04)

J Sex Med 2012;9:524-530

Osteoporosis

 Exercise decreases the risk of osteoporosis and falls

Bull World Health Organ vol.81 no.11 Genebra Nov. 2003; Sports Medicine 1998; 6:359-368

Asthma

- Randomized trial of aerobic exercise (n=43)
- In patients with moderate to severe asthma aerobic training:
 - Decreases bronchial hyperresponsiveness
 - Decreases frequency of exacerbations (0.6 vs 1.5 exacerbations/patient; p=0.021)
 - Improved quality of life (ACQ-6)

Thorax 2015;70:732-739

Exercise and Weight Management for Atrial Fibrillation

- Of 1415 consecutive patients with AF, 825 had BMI≥27 kg/m2 and were offered weight management.
- After screening for exclusion criteria, 355 were included in this analysis.

(LEGACY Study), Journal of the American College of Cardiology (2015), doi: 10.1016/j.jacc.2015.03.002.

Exercise and Weight Management for Atrial Fibrillation

- Structured motivational and goal-directed program using face-to-face counselling, visits at least every three months, more frequent as needed
- Protocol included intensive diet and exercise program with goal weight loss of 10% and exercise of 200 minutes per week (starting with 20 minutes three times a week).

(LEGACY Study), Journal of the American College of Cardiology (2015), doi: 10.1016/j.jacc.2015.03.002.

Cognitive Function

The Fitness for the Aging Brain Study - FABS

- Population: 138 participants with mild cognitive dysfunction
- Randomized to exercise (150 min/wk) vs. usual care
- Results: intervention group improved 0.26 points vs. usual care deteriorated 1.04 points on the ADAS-Cog (70 point scale) at the end of the intervention (6m)
- At 18 m a non-sig improvement was sustained (0.73 vs 0.04)

JAMA. 2008;300(9):1027-1037

Cognitive Function

- Thirty-three adults (17 women) with mild cognitive impairment ranging in age from 55 to 85 years (mean age,70 years).
- Randomized either to a high-intensity aerobic exercise or stretching control group

Arch Neurol. 2010;67(1):71-79

Cognitive Function

- Results
 - Women aerobic exercise improved performance on multiple tests of executive function
 - Men favorable effect only on Trails B performance

Arch Neurol. 2010;67(1):71-79

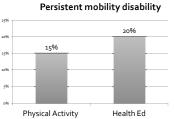
Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults

The LIFE Study Randomized Clinical Trial

- Background:
 - Reduced mobility is common in older adults
 - It is an independent risk factor for morbidity, hospitalization, disability, and mortality.
- Methods
 - Multicenter, randomized trial x 2.6 years
 - Men and women aged 70 to 89 years who had physical limitations, but were able to walk 400 m.
 - Structured, moderate-intensity physical activity program (n = 818)

JAMA. 2014;311(23):2387-2396

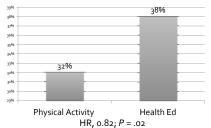
Persistent Mobility Disability



HR, 0.72; P = .006

Major Mobility, disability or death

Major mobility disability or death



Taking up physical activity in later life and healthy ageing

- 3454 initially disease-free men and women (aged 63.7±8.9 years at baseline) from the English Longitudinal Study of Ageing, a prospective study of community dwelling older adults.
- Self-reported physical activity was assessed at baseline (2002–2003) and through follow-up.
- Healthy ageing, assessed at 8 years of follow-up (2010-2011), was defined as those participants who survived without developing major chronic disease, depressive symptoms, physical or cognitive impairment.

Br J Sports Med 2014;48:239-243

Taking up physical activity in later life and healthy ageing

- At follow-up, 19.3% of the sample was defined as healthy ageing.
- In comparison with inactive participants, moderate (OR, 2.67), or vigorous activity (3.53) at least once a week was associated with healthy ageing, after adjustment for age, sex, smoking, alcohol, marital status and wealth.
- Becoming active (multivariate adjusted, 3.37) or remaining active (7.68) was associated with healthy ageing in comparison with remaining inactive over follow-up.

Br J Sports Med 2014;48:239-243

Lifestyle-related Risk Factors and Risk of Future (20 yr)
Nursing Home Admissions; 6462 Adults

Risk Factor	45-64 years Hazard Ratio (95% CI)	
Smoking	1.56 (1.23-1.99)	
Physical Inactivity	1.40 (1.05-1.87)	
BMI ≥30.0	1.35 (0.96-1.89)	
High BP	1.35 (1.06-1.73)	
High Cholesterol	1.14 (0.89-1.44)	
Diabetes	3.25 (2.04-5.19)	

Valiyeva E et al. Arch Int Med 2006; 166:985

Physical Activity, Cardiovascular Disease and Mortality

Primordial Prevention - Aerobic Center Longitudinal Study (ACLS)

- 13,344 study participants 10,224 men and 3120 women
- Received a preventive medical examination at the Cooper Clinic in Dallas, Tex, 1970-1981.
- At baseline, all patients had no personal history of MI, HTN, CVA, or diabetes; no resting EKG abnormalities; and no abnormal responses on the exercise EKG.
- Average follow-up 8 years, for total of 110,482 person-years of observation.

JAMA. 1989;262:2395-2401)

Physical Activity and Mortality

- Observational study of 16,936 harvard alumni, age 35-74.
- 12-16 years follow-up
- Physical activity and relation to mortality

Fitness and BMI as Predictors of CV Disease Mortality In Diabetes

- 2316 men with diabetes and no history of stroke or myocardial infarction (mean age, 50 [10] years)
- Maximal exercise test during 1970 to 1997 with mortality surveillance to December 31, 1998

N Engl J Med 1986;314:605-13

Arch Intern Med. 2005;165:2114-2120

Cardiorespiratory Fitness as a Quantitative Predictor of All-Cause Mortality

- Looked at studies where 1) CRF was assessed by an exercise stress test; (2) the association of CRF with all-cause mortality and with CVD was evaluated
- Thirty-three studies (102,980 participants) included in meta-analysis.

JAMA. 2009;301(19):2024-2035

Cardiorespiratory Fitness as a Quantitative Predictor of All-Cause Mortality

"It is possible that consideration of low CRF as a major coronary risk factor could be put into practical use.....through identification of low exercise tolerance by exercise stress testing"

JAMA. 2009;301(19):2024-2035

EXERCISE CAPACITY AND MORTALITY AMONG MEN REFERRED FOR EXERCISE TESTING

- 6213 consecutive men referred for treadmill exercise testing for clinical reasons during a mean (±SD) of 6.2±3.7 years of follow-up.
 - 3679 had an abnormal exercise-test result or a history of cardiovascular disease, or both,
 - 2534 had a *normal* exercise-test result and no history of cardiovascular disease.

N Engl J Med 2002;346:793-801.

Fitness as a CV Risk Factor

- Cohort study follow-up of 11,049 men who had clinical exam at the Cooper Institute in Dallas, Texas, before 1990 and followed until:
 - CVD death,
 - Non-CVD death,
 - Attainment of age 90 years
- 281,469 person-years of follow-up, median follow-up 25.3 years, 1,106 CVD deaths

Journal of the American College of Cardiology. 2011;57: 1604

Fitness as a CV Risk Factor

- Differences in fitness levels (low fitness vs. high fitness) were associated with marked differences in the lifetime risks for CVD death at each index age:
 - 45 years: 13% versus 3%;55 years: 34% versus 15%65 years: 35% versus 17%.

Journal of the American College of Cardiology. 2011;57: 1604

Lifetime risks for CVD death by risk factor burden and fitness

 Among persons with elevated cholesterol, hypertension, diabetes, or current smoking status, the presence of a higher fitness level in mid-life attenuated substantially the risk from traditional risk factors.

Journal of the American College of Cardiology. 2011;57: 1604

Reclassification of mortality risk by assessment of physical activity

- 6,962 patients
- A simple question about do you exercise three times a week enough to experience a fast heart beat, sweat or shortness of breath predicts mortality over 10 years
- Age-adjusted 36% higher risk of mortality amount those who do not exercise.

Myers. The American Journal of Medicine (2015) 128, 396-402

Could it Just be that Healthier People Exercise More?

Finnish Twin Study

- 1975 baseline: 7925 healthy men and 7977 healthy women of the Finnish Twin Cohort aged 25 to 64 years
- Questionnaire on physical activity habits and known predictors of mortality.
- Category:
 - Conditioning Exercisers Exercise at least 6 times per month with an intensity corresponding to at least vigorous walking for a mean duration of 30 minutes
 - Senentary no leisure physical activity were classified as sedentary
 - Occasional Exercisers others

JAMA. 1998;279:440-444

<u>Changes</u> in Physical Fitness and All-Cause Mortality

- Prospective study of 9777 men, with two clinical examinations (mean interval between examinations, 4.9 years) to assess change or lack of change in physical fitness
- Risk of mortality during follow-up after the subsequent examination (mean follow-up from subsequent examination, 5.1 years).
- Main Outcome Measures All-cause(n=223) and cardiovascular disease (n=87) mortality.

JAMA. 1995;273:1093-1098

Changes in Fitness and Fatness on the Development of Cardiovascular Disease Risk Factors Hypertension, Metabolic Syndrome, and Hypercholesterolemia

Lee DC, et al. J Am Coll Cardiol. 2012;59(7):665-72.

Changes in Fitness and Fatness on the Development Cardiovascular Disease Risk Factors

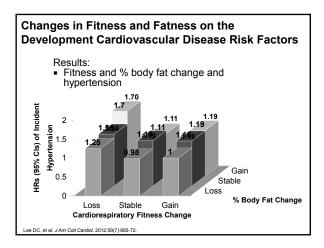
Study Question:

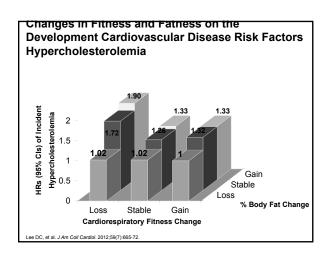
 Does a change in fitness and fatness in middle age, not just baseline fitness and fatness, affect the development of cardiovascular risk factors?

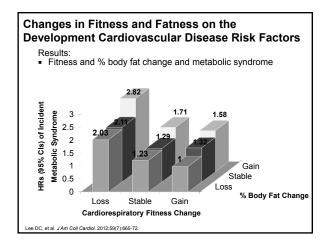
Study Design:

- Prospective cohort study of 3,148 healthy adults
 - Fitness determined by treadmill test
- Fatness expressed by % body fat and body mass index (BMI)
- Changes between 1st and 2nd exam categorized as: Loss, Stable, or Gain

Lee DC, et al. J Am Coll Cardiol. 2012;59(7):665-72.







Changes in Fitness and Fatness on the Development CV Disease Risk Factors

Conclusion:

 Both maintaining or improving fitness and preventing fat gain are important to reduce the risk of developing cardiovascular disease risk factors in healthy adults.

Lee DC, et al. J Am Coll Cardiol. 2012;59(7):665-72.

Exercise Dose and Quality of Life

- Randomized trial of the effect of 50%, 100%, and 150% of the physical activity recommendation on QOL over 6 months.
- 430 sedentary postmenopausal women (body mass index range, 25.0- with elevated systolic blood pressure randomized to
 - a nonexercise control group (n=92)
 - or 1 of 3 exercise groups: exercise energy expenditure of 4 (n=147), 8 (n=96), or 12 (n=95) kilocalories per kilogram of body weight per week.

Arch Int Med 2009; 169:269

Comparative effectiveness of exercise and drug interventions

Efficacy of Statins for Primary Prevention

- Background: Statins have been shown to reduce the risk of all-cause mortality among individuals with a history of coronary heart disease. It is unclear whether statins have similar mortality benefit in a high-risk primary prevention setting.
- Method Meta-analysis of trials of statintherapy in individuals without CVD, though with risk factors.

Efficacy of Statins for Primary Prevention

- 11 studies, 65,229 participants followed for approximately 244,000 person-years, during which 2793 deaths occurred.
- The use of statins in this high-risk primary prevention setting was not associated with a statistically significant reduction (RR, o.91; 95% confidence interval, o.83-1.01) in the risk of all-cause mortality.

Arch Intern Med. 2010;170(12):1024-1031

Comparative effectiveness of exercise and drug interventions on mortality

- Meta-analyses of randomized controlled trials with mortality outcomes comparing the effectiveness of exercise and drug interventions with each other or with control (placebo or usual care).
- 305 randomized controlled trials with 339 274 participants.

Comparative effectiveness of exercise and drug interventions on mortality

- No statistically detectable differences were evident between exercise and drug interventions in the secondary prevention of coronary heart disease and pre-diabetes.
- Physical activity interventions were more effective than drug treatment among patients with stroke.
- Diuretics were more effective than exercise in heart failure.

BMJ 2013;347:f5577

Exercise and Dose

If we could give every individual the right amount of nourishment and exercise, not too much and not too little, we could find the safest way to health

— Hippocrates, Father of Western Medicine.

Guideline Statements

AHA – Science Advisory: Better Population Health Through Behavior Change in Adults

- Addressing health behaviors leads to 3 novel emphases:
- (1) Preserving positive "cardiovascular health" by promoting healthy lifestyle behaviors;
- (2) treating unhealthful behaviors (poor-quality diet, excess energy intake, physical inactivity, smoking), in addition to risk biomarkers (adverse blood lipids, high blood pressure, hyperqlycemia, obesity); and
- (3) a combination of individual level and populationbased health promotion strategies

Circulation. 2013;128:2169

 "Health is being lost from childhood through young adulthood and that the major reasons are adverse health behaviors related to diet, physical activity, healthy weight maintenance, and smoking."

"The elimination of these health risk behaviors would make it possible to prevent at least 80% of heart disease, stroke, and type 2 diabetes mellitus, and even 40% of cancers."

USPSTF: Behavioral Counseling to Promote Healthy Diet and Physical Activity

 Comprehensive review of the evidence on whether primary care counseling for healthful diet and physical activity modify outcomes in patients with CV risk factors.

Ann Intern Med. 2014;161:587-593

Benefits of Behavioral Counseling Interventions

- USPSTF found moderate evidence that intensive behavioral counseling interventions have moderate benefits for CVD risk in overweight or obese adults who are at increased risk for CVD:
 - increases in levels of physical activity.
 - decreases in blood pressure, lipid and fasting glucose levels, and body mass index (BMI) The reduction in glucose levels was large enough to decrease the incidence of diabetes.

Ann Intern Med. 2014;161:587-593

USPSTF

 Interventions involved an average of 5 to 16 contacts over 9 to 12 months depending on their intensity

Ann Intern Med. 2014;161:587-593

The Exercise Prescription

Current (Traditional) Approach

- Give Half-hearted Advice
- Do Not Describe a Clear Plan
- Do Not Arrange for Follow-up
- Assume Failure

Why don't we?

- Time
- Lack of Training
- Reimbursement
- No Measure of Success
- Previous failures
- Guilt

Activity Guidelines

- Children (6-17 y/o)
 - 60 minutes a day of moderate or vigorous aerobic physical activity
 - Vigorous activity at least 3 days a week
 - Muscle and bone strengthening at least 3 days per week.

Activity Guidelines

- Adults (18-64)
 - 150 minutes of moderate aerobic activity weekly or;
 - 75 minutes of vigorous aerobic activity weekly
 - Muscle strengthening activities of all major muscle groups 2 or more days per week

Activity Guidelines

- Older adults (65+)
 - Same as adult except
 - Addition of balance exercises if at risk for falls

How?

- Preventative Medicine section of the Physical Exam
- Exercise as a Vital Sign
- Every well patient, every time
- Quality Measures
- Exercise Rx

How?

- Assess the risk behavior,
- Advise change,
- Agree on goals and an action plan via shared decision making,
- Assist with treatment, and
- Arrange follow-up

Circulation. 2013;128:2169

How?

- A majority of providers perform the first 2 A's: Assess the risk behavior and advise behavior change.
- In contrast, only a small minority continue on to <u>agree</u> on goals, <u>assist</u> with treatment, and arrange follow-up
- It is these latter, less frequently performed 3 A's that have the greatest impact on healthful behavior change

Circulation. 2013;128:2169

Stages of Change

Stage of Change	<u>Description</u>	Action	
		Independent	Supervision Necessary
Pre-contemplation	Patient not ready to exercise	Encourage patient to consider exercising; tell patient about health benefits of exercise	
Contemplation	Patient interested in or thinking about exercising	Give handout; refer to non- clinical exercise professional	Refer to clinical exercise professional
Preparation	Patient exercising less than recommended amount	Give handout; refer to non- clinical exercise professional	Refer to clinical exercise professional
Action & Maintenance	Patient exercising recommended amount	Encourage continued exercise	Encourage continued supervised exercise

Adapted from:

Marcus, B.H. & Forsyth, L.A. Motivating People to Be Physically Active. 2009, Human Kinetics.

Prochaska, J.O., DiClemente, C.C., & Norcross, J.C. (1993). In search of how people change: Applications to addictive behaviors. American Psychologist, 47, 1102-1114.

How?

- Primary Goal Develop Exercise Habit
- Next set Concrete Steps
 - Short-Term Goals
 - Long-term Goals
 - Team Approach Personal Trainers
- Anticipatory Guidance Anticipate Hurdles
- Follow-up

Summary

- Exercise has a vast amount of beneficial effects on the body
- 150 minutes of moderate intensity exercise
- Add strength and balance exercises if over 65
- Get out and Get Healthy