Appendix 2: A summary of the evidence supporting the importance of regular physical activity for the prevention of chronic diseases and premature death

Study	Participants	Activity	Results	Main findings/conclusion
All-cause and cardiovascular-related mortality				
Primary prevention				
Paffenbarger et al (Harvard Alumni Health Study), 1986[106]	16 936 men aged 35–74 yr; follow-up 12–16 yr	Leisure-time physical activity assessed with questionnaire on walking, stair climbing, and sports or recreational activity	RR for all-cause mortality: *Walking* • < 5 km/wk = 1.00* • 5–14 km/wk = 0.78 • > 14 km/wk = 0.67 *Stair climbing* • < 20 floors/wk = 1.00* • 20–54 floors/wk = 0.79 • > 54 floors/wk = 0.75 *Sport or recreation* • None = 1.00* • Light (< 4.5 METs) = 1.10 • Moderate (> 4.5 METs) = 0.63	Regular physical activity (> 2000 kcal [> 8400 kJ] per wk) associated with average increase in life expectancy of 1–2 yr by age 80
Blair et al, 1989[7]	10 224 men, 3120 women; 8-yr follow-up	Physical fitness measured with maximal treadmill exercise test. Fitness categorized into quintiles (Q1 = least fit, Q5 = most fit)	Adjusted RR (95% CI) for all-cause mortality among men: • Q1 = 3.44 (2.05–5.77) • Q2 = 1.37 (0.76–2.50) • Q3 = 1.46 (0.81–2.63) • Q4 = 1.17 (0.63–2.17) • Q5 = 1.00* Adjusted RR (95% CI) for all-cause mortality among women: • Q1 = 4.65 (2.22–9.75) • Q2 = 2.42 (1.09–5.37) • Q3 = 1.43 (0.60–3.44) • Q4 = 0.76 (0.27–2.11) • Q5 = 1.00*	Low levels of physical fitness associated with increased all-cause mortality
Lee et al (Harvard Alumni Health Study), 1995[23]	17 321 men; 22-yr and 26-yr follow-up	Physical activity assessed with questionnaires; Q1 = lowest level of activity	RR (95% CI) for all-cause mortality associated with increasing quintiles of energy expenditure: • Q1 = 1.00* • Q2 = 0.94 (0.86–1.04) • Q3 = 0.95 (0.86–1.05) • Q4 = 0.91 (0.83–1.01) • Q5 = 0.91 (0.82–1.00) RR (95% CI) for all-cause mortality associated with energy expenditure (vigorous activities): • < 630 kJ/wk = 1.00* • 630–< 1680 kJ/wk = 0.88 (0.82–0.96) • 1680–< 3150 kJ/wk = 0.92 (0.82–1.02) • 3150–< 6300 kJ/wk = 0.87 (0.77–0.99) • > 6300 kJ/wk = 0.87 (0.78–0.97)	There was a graded inverse relation between physical activity and mortality. Vigorous, but not nonvigorous, activities were associated with longevity

continued

Appendix 2 continued				
Study	Participants	Activity	Results	Main findings/conclusion
Blair et al, 1995[36]	9777 men; mean follow-up 4.9 yr	Physical fitness assessed with maximal exercise test at baseline and follow-up	RR (95% CI) for all-cause mortality: • Unfit to unfit = 1.00* • Unfit to fit = 0.56 (0.41–0.75) • Fit to unfit = 0.52 (0.38–0.70) • Fit to fit = 0.33 (0.23–0.47) RR (95% CI) for CVD-related mortality: • Unfit to unfit = 1.00* • Unfit to fit = 0.48 (0.31–0.74) • Fit to unfit = 0.43 (0.28–0.67) • Fit to fit = 0.22 (0.12–0.39)	Reduction in all-cause and CVD-related mortality was greater among men who maintained or increased adequate physical fitness than among those who were consistently unfit
Wannamethee et al, 1998[24]	4311 men; follow-up 12–14 yr	Self-reported physical activity assessed with questionnaire on regular walking or cycling, vigorous sports or recreational activity	RR (95% CI) for all-cause mortality: • Inactive or occasionally active = 1.00* • Light = 0.61 (0.43-0.86) • Moderate = 0.50 (0.31–0.79) • Moderately vigorous/vigorous = 0.65 (0.45–0.94) RR (95% CI) for CVD-related mortality: • Inactive or occasionally active = 1.00* • Light = 0.61 (0.36–1.04) • Moderate = 0.50 (0.16–0.80) • Moderately vigorous/vigorous = 0.65 (0.37-1.14)	Maintaining an active lifestyle or taking up light or moderate physical activity was associated with a reduction in all-cause and CVD-related mortality
Lee and Paffenbarger (Harvard Alumni Health Study), 2000[25]	13 485 men; 15-yr follow-up	Leisure-time physical activity assessed with questionnaire on walking, stair climbing, and sports or recreational activity	RR (95% CI) for all-cause mortality: • < 4200 kJ/wk = 1.00* • 4200–8399 kJ/wk = 0.80 (0.72–0.88) • 8400–12 599 kJ/wk = 0.74 (0.65–0.83) • 12 600–16 799 kJ/wk = 0.80 (0.69-0.93) • ≥ 16 800 kJ/wk = 0.73 (0.64–0.84)	Vigorous physical activity was associated with a reduction in all-cause mortality. These findings also support the health benefits of moderately intense exercise
Katzmarzyk et al, 2004[33]	19 223 men (15 466 healthy, 3757 with metabolic syndrome); baseline period 1979–1995, follow-up through December 1996	Cardiorespiratory fitness assessed with maximal treadmill exercise test	RR (95% CI) for all-cause mortality: • Men with metabolic syndrome = 1.29 (1.05–1.57) • Unfit v. fit healthy men = 2.18 (1.66-2.87) • Unfit v. fit men with metabolic syndrome = 2.01 (1.38–2.93) RR (95% CI) for CVD-related mortality: • Men with metabolic syndrome = 1.89 (1.36-2.60) • Unfit v. fit healthy men = 3.21 (2.03-5.07) • Unfit v. fit men with metabolic syndrome = 2.25 (1.27–3.97)	Cardiorespiratory fitness provided a strong protective effect against CVD-related and all-cause death

continued

Appendix 2 continued				
Study	Participants	Activity	Results	Main findings/conclusion
Myers et al, 2004[29]	6213 men referred for exercise testing; 842 men (convenience sample) underwent evaluation of current and past activity patterns; 6-yr follow-up	Peak exercise capacity during incremental treadmill stress test; self-report physical activity; Q1 = lowest level, Q4 = highest level	HRR (95% CI) for all-cause mortality by fitness level: • Q1 = 1.00* • Q2 = 0.59 (0.52–0.68) • Q3 = 0.46 (0.39-0.55) • Q4 = 0.28 (0.23-0.34) HRR (95% CI) for all-cause mortality by activity level: • Q1 = 1.00* • Q2 = 0.63 (0.36–1.10) • Q3 = 0.42 (0.23-0.78) • Q4 = 0.38 (0.19-0.73)	Being fit or active was associated with > 50% reduction in mortality. Physical fitness was a stronger predictor of death than physical activity was. An increase of 1000 kcal (4200 kJ) per wk in physical activity or an increase of 1 MET in fitness conferred a mortality benefit of 20%
Oguma et al, 2004[39]	Systematic review and meta-analysis of 30 papers published between January 1966 and March 2003; women only	Dose–response relation between physical activity and CVD-related morbidity and mortality	RR (95% CI) for CVD-related morbidity and mortality RR: • Least active = 1.00* • Second least active = 0.84 (0.75-0.94) • Third most active = 0.77 (0.69–0.87) • Second most active = 0.69 (0.57–0.83) • Most active = 0.67 (0.52–0.85)	Increasing levels of physical activity were associated with a graded reduction in the risk of CVD among women. As little as 1 h/wk of walking was associated with a reduction in CVD-related mortality
All-cause and cardiovascular-related mortality continued				
Secondary prevention				
Wannamethee et al, 2000[40]	772 men with CAD; 5-yr follow-up	Physical activity questionnaire	RR (95% CI) for all-cause mortality by activity level: • Inactive/occasional = 1.00* • Light = 0.42 (0.25–0.71) • Moderate = 0.47 (0.24-0.92) • Moderate/vigorous = 0.63 (0.39–1.03) RR (95% CI) for CVD-related mortality by activity level: • Inactive/occasional = 1.00* • Light = 0.38 (0.20-0.72) • Moderate = 0.50 (0.23–1.06) • Moderate/vigorous = 0.61 (0.34–1.08)	Light or moderate activity was associated with a reduced risk of all-cause mortality among men with established CAD. Regular walking, or moderate or heavy gardening was sufficient to lead to health benefits
Jolliffe et al, 2001[41]	Cochrane database systematic review to December, 1998; 8440 patients with CAD	Cardiac rehabilitation with exercise only or comprehensive program	Pooled-effects OR (95% CI) for all-cause mortality • Exercise only = 0.73 (0.54–0.98) • Comprehensive program = 0.87 (0.71–1.05) Pooled-effects OR (95% CI) for CVD-related mortality • Exercise only = 0.69 (0.51–0.94) • Comprehensive program = 0.74 (0.57–0.96)	Exercise-based rehabilitation was effective in reducing CVD-related and all-cause mortality among men and women with CAD
Oguma et al, 2002[26]	Review of papers published between January 1966 and December 2000; women only	Association between physical activity or fitness and all-cause mortality	RR (95% CI not reported) for all-cause mortality by type of physical activity Median = 0.66 • Total physical activity = 0.75 • Leisure physical activity = 0.66 • Occupational physical activity = 0.54 • Physical fitness = 0.55	Adherence to current physical activity guidelines (energy expenditure 4200 kJ/wk) was associated a reduction in all-cause mortality among women

continued

Appendix 2 continued

Study	Participants	Activity	Results	Main findings/conclusion
Taylor et al, 2004[5]	Systematic review and meta-analysis of 48 RCTs published to March 2003; 8940 patients with CAD	Cardiac rehabilitation v. usual care	OR (95% CI) for reduced all-cause mortality = 0.80 (0.68–0.93) OR (95% CI) for reduced cardiac mortality = 0.74 (0.61–0.96)	Exercise-based cardiac rehabilitation was associated with reductions in cardiac and all-cause mortality among patients with CAD
Diabetes mellitus				
Primary prevention				
Manson et al, 1992[47]	Prospective cohort of 21 271 men; 5-yr follow-up	Physical activity survey. Participants grouped according to no. of days per wk they performed vigorous exercise	HRR (95% CI) for type 2 diabetes by frequency of exercise (adjusted for age and BMI): • 0 times/wk = 1.00* • 1 time/wk = 0.78 (0.56-1.09) • 2–4 times/wk = 0.68 (0.51–0.90) • ≥ 5 times/wk = 0.71 (0.49-1.03)	Regular exercise was associated with a reduction in incidence of type 2 diabetes
Tuomilehto et al, 2001[50]	RCT; 522 middle-aged overweight men and women with impaired glucose tolerance; mean follow-up 3.2 yr	Intervention: detailed advice about moderate activity of 30 min/d, detailed dietary control Control: general oral and written diet and exercise information	Risk reduction of diabetes • Women = 54% (95% CI 26%–81%); $p = 0.008$) • Men = 63% (95% CI 18%–79%); $p = 0.001$) Cumulative diabetes incidence • Intervention: 11% (95% CI 6%–15%) • Control: 23% (95% CI 17%–29%)	Lifestyle changes resulted in reduced incidence of type 2 diabetes by about 58%
Knowler et al, 2002[53]	RCT (placebo, metformin or lifestyle modification program); 3234 nondiabetic people with elevated fasting and post-load plasma glucose levels; mean follow-up 2.8 yr	16-lesson curriculum on diet, exercise and behaviour modification; goal of 7% weight reduction; moderate physical activity for at least 150 min/wk	Diabetes incidence (cases per 100 person-years): • Placebo = 11.0 • Metformin = 7.8 • Lifestyle modification = 4.8 Reduction in diabetes incidence compared with placebo group: • Metformin = 31% (95% CI 17%–43%) • Lifestyle modification = 58% (95% CI 48%–66%)	Lifestyle modification program was more effective than metformin in reducing the incidence of type 2 diabetes
Hsia et al, 2005[63]	Prospective cohort of 87 907 postmenopausal women in Women's Health Initiative observational study; mean follow-up 5.1 yr	Questionnaire on physical activity frequency, duration (scale of strenuous, moderate, or light); self-reported diabetes. Activity divided into quintiles of highest to lowest activity	Adjusted HRR (95% CI) for type 2 diabetes among white women, walking: • Q1 = 1.00* • Q2 = 0.85 (0.74–0.87) • Q3 = 0.87 (0.75-1.01) • Q4 = 0.75 (0.64-0.89) • Q5 = 0.74 (0.62–0.89) $p < 0.001$ for trend across quintiles Adjusted HRR (95% CI) for type 2 diabetes among white women, total physical activity: • Q1 = 1.00* • Q2 = 0.88 (0.76–1.01) • Q3 = 0.74 (0.64–0.87) • Q4 = 0.80 (0.68–0.94) • Q5 = 0.67 (0.56–0.81) ($p = 0.002$) showed strong inverse relation with diabetes risk	Strong inverse relation between physical activity and type 2 diabetes. The relation between physical activity and diabetes was stronger among white women than among women in minority groups (black, Hispanic, Asian); this may be explained by less precise risk estimates in the minority groups

continued

Appendix 2 continued

Study	Participants	Activity	Results	Main findings/conclusion
Laaksonen et al, 2005[51]	RCT (part of Finnish Diabetes Prevention Study); 487 men and women with impaired glucose tolerance; post-hoc analyses of subjects who had completed 12-month leisure-time physical activity questionnaire; 4.1-yr follow-up	Lifestyle changes, including diet, weight loss and leisure-time physical activity	63%–65% reduction in incidence of diabetes among subjects who engaged in moderate to vigorous or strenuous, structured physical activity	Increasing physical activity levels was associated with a reduced incidence of diabetes among people at high risk for diabetes
Diabetes mellitus				
Secondary prevention				
Boulé et al, 2001[64]	Meta-analysis of 14 controlled (11 RCT) clinical trials of type 2 diabetes and glycemic control; none of the studies included drug cointerventions	Predetermined exercise activity of ≥ 8 wk; 12 aerobic training studies and 2 resistance training studies	Glycosylated hemoglobin (HbA_{1c}) lower in exercise than in control groups (0.66%, $p < 0.001$)	Exercise training reduced HbA_{1c} concentration to an extent that was of clinical benefit to people with type 2 diabetes
Gregg et al, 2003[49]	Prospective cohort of 2896 adults examining walking activity and risk of all-cause and CVD-related mortality among people with diabetes; 8-yr follow-up	Interviewer-administered survey in US communities; walking, heart rate and breathing rate assessed in previous 2 weeks	Compared with inactive adults: • Those who walked 2 h/wk had a 39% lower all-cause mortality (HRR 0.61, 95% CI 0.48–0.78) and a 34% lower CVD-related mortality (HRR 0.66, 95% CI 0.4–0.96) • Those who walked 3–4 h/wk had the lowest risk of all-cause mortality (HRR 0.46, 95% CI 0.29–0.71) and of CVD-related mortality (HRR 0.47, 95% CI 0.24–0.91) • Those who moderately increased heart and breathing rate had a 43% lower all-cause mortality (HRR 0.57, 95% CI 0.41–0.80) and a 31% lower CVD-related mortality (HRR 0.69, 95% CI 0.43–1.09)	Walking was associated with a reduction in the incidence of premature death among adults with diabetes
Cancer				
Primary prevention				
Paffenbarger et al (Harvard Alumni Health Study), 1992[68]	17 148 men	Self-reported activity, classified to a physical activity index of kcal/wk	RR (95% CI) for colon cancer: • Inactive = 1.00* • Moderately active = 0.52 (0.28–0.94) • Highly active = 0.50 (0.27–0.93) • Increased activity = 0.87 (0.56–1.35) • Decreased activity = 1.02 (0.65–1.60) RR (95% CI) for prostate cancer: • Inactive = 1.00* • Moderately active = 0.97 (0.77–1.21) • Highly active = 0.99 (0.78–1.26)	Increased levels of physical activity were associated with a reduction in the risk of colon cancer

continued

Appendix 2 continued

Study	Participants	Activity	Results	Main findings/conclusion
Wannamethee et al, 1993[69]	7735 men	Resting heart rate	RR (95% CI): • < 60 beats/min = 1.00* • 60–69 beats/min = 1.50 (0.93–2.43) • 70–79 beats/min = 1.71 (1.05–2.75) • 80–89 beats/min 2.25 (1.34–2.78) • > 90 beats/min 1.68 (0.92–3.10) • > 90 v. < 60 beats/min = 2.33 (1.42–3.74)	Resting heart rate and physical activity were independent predictors of risk of cancer-related death
Kampert et al, 1996[70]	25 341 men, 7080 women; 8-yr follow-up	Questionnaire of physical activity and treadmill test	RR (95% CI), questionnaire: *Men* • Very active = 0.36 (0.05–2.69) • Moderately active = 1.00* • Low active = 1.73 (1.19–2.50) • Sedentary = 2.41 (1.03–5.56) *Women* • Very active = 3.00 (0.65–13.81) • Moderately active = 1.00* • Low active = 0.88 (0.45–2.26) • Sedentary = 1.05 (0.22–4.59) RR (95% CI), treadmill test: • Most fit men and women = 1.00* • Least fit men = 2.78 (1.62–4.71) • Least fit women = 2.13 (0.82–5.53)	Physically active men were at lower risk of death from cancer than sedentary men. Self-reported physical activity was not predictive of cancer-related death among women The risk of cancer-related death declined markedly with increasing fitness levels among men. Among women, there was less of a gradient between fitness and cancer
Shephard et al, 1997[66]	Meta-analyses of all cancers, colon cancer and other tumours; values expressed as geometric means		All cancers (95% CI): • Low intensity, men = 1.66 (1.35-2.04) • Moderate intensity, men = 1.23 (1.00-1.51) Colon cancer (95% CI): • Low intensity, men = 1.37 (1.22-1.53) • Moderate intensity, men = 1.09 (0.97-1.22) • Low intensity, women = 1.36 (1.06-1.74) • Moderate intensity, women = 1.21 (0.97-1.50)	Physical activity was associated with reduced risk of all-cause cancer and of colon, breast, prostate and uterine tumours. A lot of the cancer protection came from moderate rather than vigorous physical activity
Sesso et al, 1998[71]	1566 women aged 45.5 yr free of breast cancer; 31-yr follow-up	Physical activity at baseline assessed with questionnaire; participanats categorized according to energy expenditure (< 500, 500–999, ≥ 1000 kcal/wk)	RR (95% CI) for breast cancer: • < 500 kcal/wk = 1.00* • 500-999 kcal/wk = 0.92 (0.58-1.45) • ≥ 1000 kcal/wk = 0.73 (0.46-1.14) *p* for trend = 0.17 RR (95% CI) for breast cancer, postmenopausal women: • < 500 kcal/wk = 1.00* • 500-999 kcal/wk = 0.95 (0.58-1.57) • ≥ 1000 kcal/wk = 0.49 (0.28-0.86) *p* for trend = 0.015	Inverse relation between physical activity and breast cancer among postmenopausal women

continued

Appendix 2 continued				
Study	Participants	Activity	Results	Main findings/conclusion
Rockhill et al (Nurses Health Study), 1999[110]	121 701 women aged 30–55 yr; 16-yr follow-up	Physical activity at baseline evaluated with questionnaire	RR (95% CI) for breast cancer: • < 1 hr/wk = 1.00* • 01.0-1.9 h/wk = 0.88 (0.79-0.98) • 2.0-3.9 h/wk = 0.89 (0.81-0.99) • 4.0-6.9 h/wk = 0.85 (0.77-0.94) • ≥ 7 h/wk = 0.82 (0.70-0.97) *p* for trend = 0.004	Women who engaged in ≥ 7 hours per week of moderate to vigorous exercise had a 20% lower risk of breast cancer than less active women. An inverse dose–response relation existed between physical activity and cancer incidence
Cancer				
Secondary prevention				
Haydon et al (Melbourne Collaborative Cohort Study), 2005[75]	Prospective cohort of 41 528 men and women (17 049 men) aged 27–75 yr. Cases of colorectal cancer (*n* = 526) were diagnosed in the follow-up (in 2002; average follow-up 5.3 yr)	Non-occupational physical activity assessed at baseline (1990–1994)	RR (95% CI) for overall death: • No exercise = 1.00* • Regular exercise = 0.77 (0.58-1.03) RR (95% CI) for disease-specific death: • No exercise = 1.00* • Regular exercise = 0.73 (0.54-1.00)	A lack of physical activity before diagnosis of colorectal cancer was associated with increased risk of overall and disease-specific premature death
Holmes et al, 2005[74]	2987 nurses aged 30–55 yr with stage I, II or III breast cancer	Physical activity assessed through self-report in 1986 and every 2 yr until 2000 3 MET-h/wk was considered equal to walking 2–2.9 mph for 1 h	RR (95% CI) for breast cancer recurrence: • < 3 MET-h/wk = 1.00* • 3-8.9 MET-h/wk = 0.83 (0.64-1.08) • 9-14.9 MET-h/wk = 0.57 (0.38-0.85) • 15-23.9 MET-h/wk = 0.66 (0.47-0.93) • ≥ 24 MET-h/wk = 0.74 (0.53-1.04) RR of breast cancer death (95% CI): • < 3 MET-h/wk = 1.00* • 3-8.9 MET-h/wk = 0.80 (0.60-1.06) • 9-14.9 MET-h/wk = 0.50 (0.31-0.82) • 15-23.9 MET-h/wk = 0.56 (0.38-0.84) • ≥ 24 MET-h/wk = 0.60 (0.40-0.89)	Physical activity after breast cancer diagnosis may reduce the rate of recurrence from the disease and the risk of death from the disease. The largest benefits were seen among people who performed exercise equivalent to 3-5 hours per week at an average pace
Osteoporosis				
Primary prevention				
Berard et al, 1997[83]	Meta-analysis of 18 prospective intervention trials evaluating healthy postmenopausal women between 1966–1996	Moderate-intensity programs of primarily walking, running, physical conditioning and aerobics	• Large effect size on BMD in vertebral column (L2–4) (0.8745, $p < 0.05$) • No effect seen on BMD in forearm and femoral bone mass	Exercise programs in postmenopausal women (> 50 yr) were effective in preventing BMD loss in vertebral column
Kelley 1998[84]	Meta-analysis of 11 RCTs; 719 postmenopausal women (370 exercise, 349 no exercise); Jan 1975 to Dec 1995	Exercise (aerobic, strength training) v. no exercise	Regional BMD • Aerobic training = +1.62% (95% CI 1.12%-2.12%) • Strength training = +0.65% (95% CI 0.48%-0.83%)	Exercise may slow the rate of bone loss in postmenopausal women

continued

Appendix 2 continued

Study	Participants	Activity	Results	Main findings/conclusion
Kelley 1998[85]	Meta-analysis of 10 prospective studies; 330 postmenopausal women (192 exercise, 138 no exercise); Jan 1975 to Dec 1994	Aerobic activity v. no exercise; change in BMD in lumbar spine	Difference of 2.8% ± 0.77% (95% CI 1.33%–4.35%) in lumbar spine BMD between groups • Exercise = +0.32% ± 2.46% (95% CI –0.94 to 1.58) • Non-exercise = -2.5 ± 2.69% (95% CI –4.60 to 0.96)	Exercise helped to maintain lumbar spine BMD in postmenopausal women
Wolff et al, 1999[87]	Meta-analysis of 25 RCTs and controlled trials; pre- and postmenopausal women; 2 or more interventions compared with each other; 1966 to Dec 1996	Endurance and strength training; change in BMD or bone mineral content of lumbar spine and femoral neck	Overall treatment effect (inverse variance weighting) at lumbar spine: *Premenopausal women* • Endurance + strength training = 0.91 (95% CI 0.44–1.37); $p < 0.05$ *Post-menopausal women* • Endurance training = 0.96 (95% CI 0.43–1.49); $p < 0.05$ • Strength training = 0.44 (95% CI –0.32 to 1.21) • Combined exercise = 0.79 (95% CI 0.35–1.22); $p < 0.05$ Overall treatment effect (inverse variance weighting) at femoral neck: *Pre-menopausal women* • Endurance training = 0.90 (95% CI 0.29–1.50); $p < 0.05$ *Post-menopausal women* • Endurance training = 0.90 (95% CI 0.29–1.51); $p < 0.05$ • Strength training = 0.86 (95% CI –0.18 to 1.91) • Combined exercise = 0.89 (95% CI 0.36–1.42); $p < 0.05$	RCTs revealed consistently that exercise training prevented or reversed the approximate 1% bone loss per year in both the lumbar spine and femoral neck among pre- and postmenopausal women
Bonaiuti et al, 2002[86]	Cochrane database of systematic reviews of 18 RCTs; 289 healthy postmenopausal women	Effect of aerobic, weight-bearing and resistance exercise on BMD of spine (13 studies) or hip (8 studies) v. usual activity or placebo with or without drug consumption 9 aerobic studies, 4 resistance studies, 3 walking studies, 1 repetitive back extension study and 1 weighted leg flexion study	Weighted mean difference in BMD: • Combined aerobic + weight bearing = +1.79% (95% CI 0.58%–3.01%) • Walking = spine +1.31% (95%CI –0.03% to 2.65%); hip +0.92% (95% CI 0.21%–1.64%) • Aerobic = wrist 1.22% (95% CI 0.71%–1.74%)	Aerobic, resistance, and weight-bearing exercise were all effective in increasing BMD in spine in postmenopausal women. Walking was also of benefit for BMD in the hip

continued

Appendix 2 continued

Study	Participants	Activity	Results	Main findings/conclusion
Osteoporosis				
Secondary prevention				
Kemmler et al, 2004[99]	50 early postmenopausal osteopenic women (age 56) in exercise condition group and 33 matched controls (age 56); nonrandomized design	Exercise training: 2 supervised group training sessions/wk (each 60–70 min) and 2 unsupervised home training sessions/wk (each 25 min) over 26 wk; training involved endurance, jumping, strength and flexibility activities	Mean change in lumbar spine BMD (DXA): • Exercise group = 0.7% • Control = –2.3% (significant difference between groups) Mean change in lumbar spine cortical BMD (via QCT): • Exercise group = 3.1% • Control = –1.7% (significant difference between groups) Mean change in lumbar spine trabecular BMD (via QCT): • Exercise group = 0.4% • Control = –6.6% (significant difference between exercise and control)	Exercise program was effective in preventing and attenuating bone loss in early postmenopausal osteopenic women
Liu-Ambrose et al, 2004[98]	98 women living in the community aged 75–85 yr with low bone mass (e.g., diagnosed with osteoporosis or osteopenia)	25-wk RCT consisting of three experimental conditions: resistance training, agility training or stretching (sham). All training took place twice weekly in 50-min group-based sessions	Mean change (± SEM) in cortical bone density: • Resistance training = 1.4% (0.6%) at radial shaft • Agility training = 0.5% (0.2%) at tibial shaft • Sham exercise = –0.4% (0.3%) at tibial shaft and –0.4% (0.5%) at radial shaft	Resistance or agility exercise training programs may elicit significant increase in cortical bone density in appendicular skeleton

Note: This appendix contains highly cited and recent influential investigations. BMD = bone mineral density, CAD = coronary artery disease, CVD = cardiovascular disease, DXA = dual-energy x-ray absorptiometry, HRR = hazard rate ratio, OR = odds ratio, Q = quintile, QCT = quantitative computed tomography, RCT = randomized controlled trial, RR = relative risk ratio, SEM = standard error of the mean.
*Reference group.