Table G3.A12. Summary of Physical Activity Studies Evaluating Primary Prevention of Microvascular Complications of Diabetic Neuropathy (N=3 studies), Diabetic Nephropathy (N=4 studies), Diabetic Retinopathy (N=7 studies)

Author, Journal, Year (Microvascular Complication Evaluated)	N	Random/Control	Intervention/Measures	Finding
LaPorte RE Pediatrics 1986 (1) (retinopathy)	n=696 T1D subjects diagnosed between 1950-1964	Retrospective cohort	Intervention: None Measures: Retinopathy, Physical activity (PA) (history of team sports in high school or college)	No difference in retinopathy and PA (defined as history of team sports in high school or college) Note: ↓mortality and ↓cardiovascular events were significantly associated with this rough PA measure.
Orchard TJ Diabetes Care 1990 (2) (neuropathy, nephropathy, and retinopathy)	175 T1D subjects with duration T1D ≥ 25 years	Retrospective cohort analysis in EDIC I. cohort	No intervention PA and outcome measures: History of PA in youth by standard survey	No association between PA in youth and neuropathy, nephropathy, or retinopathy. Note: PA estimation by subject recall 25+ years after T1D diagnosis may be inaccurate, but any recall bias would have been more likely to cause a Type I error.
Samanta A Diabetes Res Clin Pract 1991 (3) (nephropathy & retinopathy)	n=907 consecutive patients (456 from Asian sub-continent) with adult-onset DM (presumably T2D, but no formal testing to discriminate; attending United Kingdom diabetic center x1+ years)	Cross-sectional United Kingdom hospital clinic representative study	Intervention: None Measurements: PA defined as sedentary, moderately active, or active but methods of determination not disclosed. Retinopathy: dilated funduscope photo Nephropathy: three sequential positive measurements of urine protein including one 24-hour protein >500 mg	No difference in nephropathy or retinopathy with multivariate logistic regression analysis including adjustment for tertile of PA as well as age, sex, duration of diabetes, age at DM diagnosis, hypertension, smoking, treatment with or without insulin, BMI, or HbA1 (Note: No significant contribution found by any of the other covariates included along with PA in this regression analysis.)
Kriska AM J Clin Epidemiol 1991 (4) (neuropathy, nephropathy, and retinopathy)	x=628 male and female subjects with T1D	Cross-sectional design	Intervention: None Measures: Neuropathy by physical exam, nephropathy by urine microalbumin, retinopathy by fundus photographs Current and historical (ages 14-17) PA measured with validated questionnaire.	In males: Neuropathy and nephropathy were inversely associated with historical leisure PA, but no association found for retinopathy. In females: No association found for neuropathy, nephropathy, or retinopathy with historical leisure PA. Note: Lower general PA levels in females may have reduced the power to detect a difference in complications due to insufficient PA levels achieved.

Table G3.A12. Summary of Physical Activity Studies Evaluating Primary Prevention of Microvascular Complications of Diabetic Neuropathy (N=3 studies), Diabetic Nephropathy (N=4 studies), Diabetic Retinopathy (N=7 studies) (continued)

Author, Journal, Year (Microvascular Complication Evaluated)	N	Random/Control	Intervention/Measures	Finding
Cruickshanks KJ Diabetes Care 1992 (5) (retinopathy)	818 individuals diagnosed with T1D, <30 years old	Cross-sectional analysis (between 1984-1986) of Wisconsin Epidemiologic Study of Diabetic Retinopathy registry cohort	Blinded opthalmalogist-defined retinopathy from fundus photo Interviewer-standardized PA survey Incomplete weekly energy expenditure calculation did not consider all potentially contributing activities.	↓ retinopathy prevalence in women (9th grade or older) who reported playing high school or college team sports either currently or in past (OR 0.46, $P< 0.05$) ↓ retinopathy prevalence in women reporting current strenuous PA (OR 0.34, $P< 0.05$) No difference in retinopathy prevalence between men with respect to current/past PA No difference in retinopathy in either sex with respect to current energy expenditure.
Cruickshanks KJ Ophthalmology 1995 (6) (retinopathy)	606 with T1D diagnosed < 30 and without proliferative retinopathy at 1984-1986 exam. (NL and non-proliferative retinopathy in1984-86 included)	Prospective cohort analysis of Wisconsin Epidemiologic Study of Diabetic Retinopathy from entry (1984-1986) to 6-year follow-up (1990-1992)	Intervention: None Measures: Presence and severity of retinopathy (standardized 4-tier scale) Current PA by interviewer-standardized questionnaire, historical PA as defined by high school/college team sports	No difference in retinopathy incidence in either sex with respect to any of the following PA measures: Self-rated activity (strenuous vs. sedentary) Blocks walked daily Stairs climbed daily Sweat activity Sports participation in either past week or past year Calculated current energy expenditure Historical participation in team sports Disparate results from 1992 cross-sectional study possibly due to socio-economic or other bias in the cross-sectional study No risk for increased incidence or progression of retinopathy in 32 weight lifters (vitreous hemorrhage incidence was not assessed)

Table G3.A12. Summary of Physical Activity Studies Evaluating Primary Prevention of Microvascular Complications of Diabetic Neuropathy (N=3 studies), Diabetic Nephropathy (N=4 studies), Diabetic Retinopathy (N=7 studies) (continued)

Author, Journal, Year (Microvascular Complication Evaluated)	N	Random/Control	Intervention/Measures	Finding
Balducci S J Diabetes Complications 2006 (7) (neuropathy)	78 men and women with either T1D or T2D and no neuropathy at entry	+Randomized +Control Intervention group: n=31 (15 Women, 24 T2D) Control group: n=47 (24 Women, 33 T2D)	Intervention: 4 years of supervised exercise * 1 hour 4x/week at 50-85% estimated HR reserve, no formal dietary intervention Measures: Neuropathy electrophysiologic measures (e.g., nerve conduction velocity)	↓ neuropathy incidence in intervention group. 14 times more likely to develop motor neuropathy and 6 times more likely to develop sensory neuropathy in control group vs. intervention (P< 0.05) Twice as likely to develop prolonged vibration perception threshold in control group vs. intervention (P< 0.05)
Waden J Diabetes Care 2008 (epub 10/27/2007) (8) (nephropathy and retinopathy)	1,945 Finnish subjects with T1D	Cross-sectional analysis Finnish population represented	Measures: PA in MET-hour/week by validated modified Minnesota leisure time activity questionnaire Sedentary: <10 MET hours/week, Moderately Active 10-40 MET hours/week, Active > 40 MET hours/week Microalbuminuria and macroalbuminuria definition: urinary albumin excretion rate (UAER) 30-300 mg/24 hour (microalbuminuria) or > 300 mg/24 hour (macroalbuminuria) in ≥ 2/3 consecutive 24-hour urine collections Retinopathy definition: Abstracted from chart review of each patient's medical record	In logistic regression model controlling for duration of diabetes, sex, and BMI: Total LTPA was non-significantly associated with lower rates of diabetic nephropathy (OR 0.88, 95% CI 0.76-1.02). Greater risk of nephropathy with low frequency LTPA (< 1 session/week vs. ≥1 session/week, OR 1.90, 1.39-2.60), and low intensity LTPA vs. higher intensity LTPA (OR 2.31, 1.72-3.10). Subjects with normal UAER (n=1,108) had lower percentage of low intensity activity as compared with those with microalbuminuria (n=223) or macroalbuminuria (n=187), (21.4% low intensity in normal UAER, 30.5% microalbuminuria, 43.7% macroalbuminuria, P <0.05 for both microalbuminuria and macroalbuminuria vs. normal UAER).

↓, decrease; BMI, body mass index; DM, diabetes mellitus; EDIC I, Epidemiology of Diabetes Interventions and Complications 1; HR, heart rate; LTPA, leisure-time physical activity; MET, metabolic equivalent task; OR, odds ratio; PE, physical exam; T1D, type 1 diabetes; T2D, type 2 diabetes; UAER, urinary albumin excretion rate

Reference List

1. LaPorte RE, Dorman JS, Tajima N, Cruickshanks KJ, Orchard TJ, Cavender DE, Becker DJ, Drash AL. Pittsburgh Insulin-Dependent Diabetes Mellitus Morbidity and Mortality Study: physical activity and diabetic complications. Pediatrics 1986 Dec;78(6):1027-33.

2. Orchard TJ, Dorman JS, Maser RE, Becker DJ, Ellis D, LaPorte RE, Kuller LH, Wolfson SK, Jr., Drash AL. Factors associated with avoidance of severe complications after 25 yr of IDDM. Pittsburgh Epidemiology of Diabetes Complications Study I. Diabetes Care 1990 Jul;13(7):741-7.

3. Samanta A, Burden AC, Jagger C. A comparison of the clinical features and vascular complications of diabetes between migrant Asians and Caucasians in Leicester, U.K. Diabetes Res.Clin.Pract. 1991 Dec;14(3):205-13.

4. Kriska AM, LaPorte RE, Patrick SL, Kuller LH, Orchard TJ. The association of physical activity and diabetic complications in individuals with insulin-dependent diabetes mellitus: the Epidemiology of Diabetes Complications Study--VII. J.Clin.Epidemiol. 1991;44(11):1207-14.

5. Cruickshanks KJ, Moss SE, Klein R, Klein BE. Physical activity and proliferative retinopathy in people diagnosed with diabetes before age 30 yr. Diabetes Care 1992 Oct;15(10):1267-72.

6. Cruickshanks KJ, Moss SE, Klein R, Klein BE. Physical activity and the risk of progression of retinopathy or the development of proliferative retinopathy. Ophthalmology 1995 Aug;102(8):1177-82.

7. Balducci S, Iacobellis G, Parisi L, Di BN, Calandriello E, Leonetti F, Fallucca F. Exercise training can modify the natural history of diabetic peripheral neuropathy. J.Diabetes Complications 2006 Jul;20(4):216-23.

8. Waden J, Forsblom C, Thorn LM, Saraheimo M, Rosengard-Barlund M, Heikkila O, Lakka TA, Tikkanen H, Groop PH. Physical activity and diabetes complications in patients with type 1 diabetes: the Finnish Diabetic Nephropathy (FinnDiane) Study. Diabetes Care 2008 Feb;31(2):230-2.