2017-10-01

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A dissertation submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

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ABSTRACT

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Physical activity impacts health and disease in multiple body tissues including the intervertebral discs. Fluid flow within the disc is an indicator of disc health that can be observed using diffusion weighted magnetic resonance imaging. We monitored activity levels of 26 participants, age 35 to 55 yrs, using Actigraph accelerometers for four days to evaluate vigorous-intensity activity, moderate to vigorous-intensity activity, and sedentary time. Participants underwent structural and diffusion weighted magnetic resonance imaging to evaluate intervertebral disc health and fluid flow. They also underwent bone density scans, carotid artery ultrasounds, a treadmill test, and a physical exam for pain, range of motion, and instability. These measures were used to correlate MRI indicators of intervertebral disc health with participant activity. Participants with any vigorous-intensity physical activity compared with no vigorous-intensity activity had significantly greater L5/S1 apparent diffusion coefficient values ($p = 0.002$, corresponding to higher freedom of diffusive movement for cellular nutrients and metabolic waste. Sagittal T2 values in the L5/S1 were also higher ($p = 0.004$, corresponding to higher water content in the discs. Higher apparent diffusion coefficients were also found in participants with more than 30 minutes compared with less than 30 minutes of daily moderate to vigorous physical activity ($p = 0.03$, and in participants with less than 67% awake time as sedentary time compared with more than 67% sedentary time ($p = 0.03$. Increased dynamic loading through physical activity and decreased static loading from sedentary time benefit intervertebral disc health. Physical activity, particularly vigorous activity, is beneficial in helping maintain intervertebral disc health.

Keywords: intervertebral disc health, physical activity, sedentary time

ACKNOWLEDGEMENTS

The MRI imaging for this study was funded by a seed grant from the BYU MRI Facility. I appreciate this support in allowing me and my colleagues to complete this study. I appreciate my advisor, Dr. Ulrike Mitchell, for her willingness to take me as a student and for her constant support. I also appreciate the help and support of my committee members. I am especially grateful for the support of my children, Samuel, Emma, Hezekiah, and Anna in allowing me to take the time to complete this degree. Most especially I am eternally grateful for my husband Anton, who not only provided continuous support and love but also his expertise in spine research.

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INTRODUCTION

Physical activity impacts numerous aspects of health and disease, including the health of specific body tissues, particularly as it relates to nutrient delivery to those tissues. For example, physical activity improves cardiovascular health creating a more efficient cardiorespiratory system to transport nutrients and waste throughout the body, increases muscle strength and power through improved muscle cell remodeling and growth, improves insulin sensitivity which decreases the risk of diabetes and its related nutrient transport complications, and increases bone mass and strength.[1] Intervertebral discs are similarly impacted by physical activity, and research in small animals suggests that physical activity potentially alters nutrient delivery.[2]

Intervertebral disc (IVD) health is strongly associated with nutrient flow within the disc, providing cells with adequate nutrition to build and maintain disc matrix.[3] The outer annulus of the disc receives nutrients from the surrounding vasculature, and the inner annulus and nucleus receive nutrients via diffusion through the vertebral endplates.[3,4] While intrinsic factors such as endplate permeability, blood flow, and genetic factors all play an important role in maintaining IVD health,[5,3,6] extrinsic lifestyle factors, specifically physical activity or inactivity, also influence disc nutrient flow and health.[2,7,8] For instance, static mechanical compression of the IVD decreases disc height, reducing diffusion distances from the endplate to the disc center; while simultaneously decreasing fluid content, which both decreases the ability of solutes to diffuse and alters metabolic rates.[3] On the other hand, dynamic mechanical loading due to activity alters localized strain fields and enhances bulk fluid transport, aiding in both nutrient transfer and metabolic waste removal.[9] These effects are more pronounced with large molecular weight solutes (with proportionally lower diffusion rates), as the additional force of vertebral loading allows these solutes to move beyond the disc periphery and aids nutrients in the fluid in

fully traversing the disc tissue.[10] The exchange of fluid within the disc does not directly contribute to diffusion-dominated nutrient transport of smaller molecules, but it does affect the nutrient diffusive gradients that result from cellular metabolism.[3,5,10] These fluid movement effects allow us to examine fluid flow imaging as an indirect measure of nutritional state.

The amount of time chronically spent in one position as well as limited or sporadic vigorous physical activity (VPA) and moderate-to-vigorous physical activity (MVPA) could potentially influence nutrient transport in the disc and therefore disc health. Fluid velocities have been shown to be greatest immediately following load application or removal as occurs with physical activity in opposition to sedentary behavior.[10] These activity-related effects on disc tissues are of interest as current lifestyles tend to limit VPA and MVPA, and include historically disproportionate high amounts of sedentary time, both in occupational and recreational time. Indeed, half to two-thirds of modern adult waking hours are spent sedentary,[11,12] with an average of 8.4 to 14.6 hours of recorded time being sedentary.[13] Disc degeneration, particularly with disc space narrowing,[14] is associated with pain.[15] Thus, it is reasonable to presume that decreased MVPA and increased sedentary time may be causative in the high rates of spine pain that prevail in virtually all industrialized nations.[16-18]

Previous work has evaluated IVD health in the context of fluid flow[10,19] and applied mechanical loading.[8,20] In the EPILIFT study, cumulative workload has been positively associated with degenerative disc disease,[21] however there was a nonsignificant decrease in disc degeneration with resistance exercise.[22] IVD health in the general population has been evaluated through numerous studies using both MRI and tissue extraction in surgical patients.[23] Individuals with muscular weakness (likely due to physical inactivity) are at greater risk of low back pain and injury.[24]

This is the first study of which we are aware to specifically address the effects of VPA, MVPA and sedentary behavior on IVD health in the context of chronic daily activity levels. We hypothesized that both the amount of sedentary time and the amount of time spent in moderate-vigorous activity may influence IVD health in affecting the fluid flow enhanced by vertebral loading patterns. Specifically, we evaluated three hypotheses: 1) Participants with any amount of daily vigorous physical activity have better disc health than those without vigorous activity, 2) Participants with greater than 30 minutes of daily MVPA have better disc health when compared to participants with less than 30 minutes of daily MVPA, and 3) Participants with high levels of daily sedentary time (greater than 67% of daily awake time) have diminished disc health compared to individuals with lower sedentary time. Rationale for these groupings is included in the methods section. We evaluated IVD disc health using MRI measurements of both IVD fluid content and disc fluid flow (i.e., apparent diffusion coefficient and fractional anisotropy). Simultaneous with these measurements, we also evaluated relationships between MVPA and sedentary time and other metrics of overall wellness including bone density and cardiovascular health.

METHODS

This was a case-control study, level of evidence 3, where 26 healthy men and women aged 35 to 55 were recruited by word of mouth and social media based on self-described "high" and "low" sedentary time, no back injury, and ability to safely participate in an MRI scan. Power analysis[25] was performed (alpha = 0.05, desired statistical power = 0.90) using a minimum expected effect size and standard deviation based on the differences in fractional anisotropy peaks seen in previously published diffusion tensor imaging (DTI) MRI studies of the intervertebral disc,[26] and yielded an estimated minimum sample size of 24 participants. These

initial activity levels of low and high sedentary time were evaluated using the International Physical Activity Questionnaire Short Form (IPAQ-SF).[27] The participants signed informed consent documents as approved by the authors' Institutional Review Board. Basic information measured included height, weight, and blood pressure. Figure 1 provides a synopsis of the methods including prescreening, accelerometry, diagnostic tests, and MRI imaging. Participants' activity was tracked for 4 to 8 consecutive days including one weekend day using an Actigraph accelerometer (GT1M, Pensacola, FL) during their waking hours on their left hip with a requested minimum of 13 hours of data collecting time each day.[28] Four days were requested, some participants elected to provide more days, but there was not a difference in daily activity variability between those reporting 4 days and those reporting more. Activity type varied, with most recorded activity being running and brisk walking as well as work related activity. Activity data were evaluated using the ActiLife analysis program. Wear time averaged 14.3 hours per day, and any days with less than 11 hours per day were excluded. Activity data which indicated zeros for over one hour were considered nonwear time and were not included in the data analysis.[28] Sedentary groups were identified as high sedentary, with greater than 67% of recorded time as sedentary time, or low sedentary, with less than 67% of sedentary time per day, based on the IPAQ and accelerometer data collected. These cut-points are based on a modification of the quartile averages Dunstan et al. calculated using NHANES data.[12] This placed the individuals in the low sedentary group above the mean for the third quartile of activity and the individuals in the high sedentary group below the mean for the third quartile of activity. Vigorous activity was measured by presence or absence of any accelerometer-recorded activity at a cut point of 5625 counts per minute using 60-second epochs, which was identified as vigorous or very vigorous activity by Freedson.[29] The time interval of 30 minutes of physical

activity was selected based on the recommendations of the American Heart Association and the American College of Sports Medicine.[1] This represents any activity greater than 1952 counts per minute for 30 or more minutes per day and included both moderate and vigorous activity.[29]

The participants completed the Modified Oswestry Low Back Pain Disability Questionnaire to confirm that participants did not have back injury or chronic pain as well as to gain further understanding of their back health and any reasons they may have lower activity levels.[30] Range of motion and spinal stability testing was performed using standard protocols.[31] Range of motion tests included active and passive range of motion and segmental mobility. The subject was tested for presence of lumbar instability with the prone instability test. Nerve root involvement was tested by the straight leg raise test. Sacroiliac joint involvement was tested by the sacral thrust, posterior shear, compression and distraction tests. Initial questionnaire screening had already excluded participants with pain. No participants were found to have pain or instability during range of motion/instability testing, and range of motion was not significantly limited in any of the participants.

Participants' bone density was measured at both the hip and lumbar spine using a GE Lunar DEXA densitometer (Sunnyvale, CA) to evaluate relationships between physical activity, bone mineral density, and IVD health.[32] The participants received a DEXA scan of the lumbar and pelvic region to examine bone mineralization, determine bone density, T and Z scores, and categorize their bone density as being either normal for their age, osteopenic, or osteoporotic. DEXA uses low dose X-rays to emit photons at two different energy levels, and bone mineral density is calculated based on the differences between these energy levels by the number of photons reflected back in each level.[33] DEXA differentiates between bone and soft tissue, and measures small changes in bone mineral density over time with a precision of 0.5 to 2.0%. For

the exam, the participants lay on the scanning table and the arm of the scanner moved over their bodies. We measured both the hip and spine. The test is painless, uses a radiation dose that is one tenth that of a normal X-ray, is considered completely safe, and takes 5 to 10 minutes.[33]

The participants underwent an ultrasound evaluation of the carotid artery to measure carotid intima media thickness (IMT). Ultrasound is used clinically as a method of determining atherosclerosis.[34-36] Ultrasound imaging was performed at a location 1 cm proximal to the carotid bulb or bifurcation of both the left and right carotid arteries. Six measurements were performed, three on each side, for each subject and the values averaged. The test is considered safe for the participants as no negative effects have been found and uses high frequency sound waves to create an image of the carotid arteries.[37] Imaging was performed on a SonoSite 180+ Ultrasound portable system (Sonosite, Inc., Bothell, WA) and analyzed with SonoCalc software. The participants also had their blood pressure measured using a standard sphygmomanometer as an additional measure of arterial health. Cardiorespiratory fitness was assessed using the Ebbeling Single-Stage Submaximal Treadmill Walking Test.[38] The submaximal test is much lower impact and risk than the maximal test, and only involves walking with a minimal likelihood of a cardiac event. Individuals walked on a flat treadmill at a comfortable rate between 2 to 4.5 MPH that increased their heart rate to 50 to 70% of their estimated maximum. The incline was then increased to 5% and the individual walked for 4 minutes with heart rate measured at each 1-minute interval. Steady state heart rate values during the last two minutes were entered into Ebbeling's equation that estimated their VO_2max.[38]

Each participant received an MRI of the lumbar spine, focusing on the L5-S1 disc for diffusion tensor images (DTI). Participants were imaged in the late afternoon, allowing for the day's activities to exert their influence on the spine. Imaging was performed on a day reflective

of the participants' normal schedule and activity level. Imaging sequences were implemented on a whole-body MRI scanner (Siemens TIM-Trio 3.0T, Siemens Medical Systems, Erlangen, Germany) with a 4-channel surface coil. All appropriate MRI screening and safety measures were taken for imaging. Participants were imaged in a supine position with the surface coil placed below their lumbar spine. Foam supports were used to help the participants lay comfortably with their knees elevated to maintain an appropriate pelvic tilt and keep the lumbar spine flat against the surface coil. The imaging sequence included sagittal T2 sequences of the entire lumbar spine, and transverse T1 and DTI images of the L5-S1 disc. Imaging sequence details are provided (Table 1). MRI data were evaluated using OsiriX (Pixmeo SARL, Bernex, Switzerland) and apparent diffusion coefficient (ADC) and fractional anisotropy (FA) for the region of interest were examined. We used a 5 cm oval region of interest for the L5-S1 transverse image analysis. All MRI values were based on average signal intensity over the defined region of interest. In order to reduce variability due to signal-to-noise ratio (SNR) and field strength inhomogeneities, the same scanner and imaging protocol were used for all participants.

Hypotheses on sedentary time, VPA, and MVPA and combined groups were statistically tested independently. We performed analysis of variance and regression analysis to determine relationships between each activity level (independent variables) with spine and overall health metrics (dependent variables). These included spine health metrics, bone health measures, and intima media thickness along with post hoc T-tests for activity level groups by spine health metrics and all other covariates (i.e., age, gender, bone density, etc.) for each hypothesis. Normal distributions were assumed based on both Shapiro-Wilk and Kolmogorov-Smirnov tests (IBM

SPSS Statistics, version 24). Statistical significance was set at $p < 0.05$. Data analysis was performed using Excel (Microsoft, version 15.33).

RESULTS

The three hypotheses of the work were tested independently and results are grouped by hypothesis. Since the total subject group is relatively small (26 participants), Figure 2 presents a modified Venn diagram showing the overlaps among the analysis groups.

Hypothesis 1: Participants with any amount of daily vigorous physical activity have better disc health.

Participants were grouped according to presence (> 0%) or absence of vigorous physical activity as measured by accelerometer (Table 2). Participants with any amount of vigorous physical activity had significantly greater L5/S1 ADC values ($p = 0.002$, $t = 3.09$, $df = 24$), corresponding to higher freedom of diffusive movement for cellular nutrients and metabolic waste. Sagittal T2 values in the L5/S1 were also higher ($p = 0.004$, $t = 2.83$, $df = 24$), corresponding to a higher water content in the discs. Fractional anisotropy (FA) of the L5-S1 discs was higher in the group without daily vigorous activity, but did not reach statistical significance. A high FA corresponds to increased impediments to diffusion in one direction as compared to others and has been correlated with disc degeneration. Unexpectedly, participants with vigorous activity had lower average bone mineral densities (BMD), which was statistically significant at the femoral neck. Cardiovascular health indicators were better among those with daily vigorous activity, but none of the differences was statistically significant.

Hypothesis 2: Participants with greater than 30 minutes of daily moderate to vigorous physical activity have better disc health.

Participants were grouped by time spent in moderate and vigorous physical activity (Table 3) with a threshold of 30 minutes. Participants with more than 30 minutes of daily MVPA had significantly higher ADC values ($p = 0.03$, $t = 1.87$, $df = 24$), but differences in T2 and FA were not statistically significant. Similar to the observation noted above, participants with greater than 30 minutes MVPA had lower average bone mineral densities (BMD), which was statistically significant at the lumbar spine ($p = 0.01$, $t = ^{-}2.33$, $df = 24$). Cardiovascular health indicators were better among those with greater than 30 minutes MVPA, including a significantly higher VO2max ($p = 0.008$, $t = 2.55$, $df = 24$), with the exception of slightly higher systolic and diastolic blood pressure in this group.

Hypothesis 3: Participants with high levels of daily sedentary time (greater than 67% of daily awake time) have diminished disc health.

Participants were grouped by daily sedentary time (Table 4), with a threshold of 67% of their awake time. Participants with high sedentary time had significantly lower ADC values ($p = 0.03$, $t = 3.52$, $df = 24$), but differences in the other disc health indicators were not statistically significant. BMD measures were not significantly different. With the exception of maximum intima media thickness ($p = 0.04$, $t = ^{-}1.79$, $df = 24$), cardiovascular health indicators were not significantly different. Spinal function indicators were not significantly different between the two groups. BMI was significantly higher in the high sedentary time group ($p = 0.04$, $t = ^{-}1.82$, $df = 24$).

We then examined interactions between the activity groups. We first looked at the group of individuals ($n = 11$) who fell into all three high activity groups (Table 5). Disc health

indicators were not statistically significant, although ADC and T2 values in the L5/S1 disc were higher in the high activity group. There was significantly lower BMD for all three metrics in the high activity group (spine BMD $p = 0.007$, $t = 2.64$, femoral neck BMD $p = 0.003$, $t = 2.91$, and total hip BMD $p = 0.01$, $t = 2.30$, $df = 24$ for all). In evaluating cardiovascular factors, mean intimal thickness was significantly lower in the high activity group ($p < 0.0001$, $t = 4.68$, $df = 24$). Other cardiovascular health indicators were not significantly different. We then looked at individuals who fell into at least one of the three high activity groups and compared them with those who did not fall into any of the high activity groups. These participants had significantly higher ADC ($p = 0.003$, $t = 2.99$, $df = 24$) and T2 ($p = 0.01$, $t = 2.38$, $df = 24$) along with significantly lower BMI ($p = 0.04$, $t = {}^{-}1.74$, $df = 24$). There were no significant differences in intima media thickness (IMT) or bone mineral density measures.

Due to the relatively small sample size, a post hoc power analysis was performed. All of the statistically significant results were evaluated for power. All disc health-related results demonstrated a power above 98%, with the exception of the ADC comparison between the groups higher and lower than 30 minutes daily moderate-to-vigorous physical activity. BMD-related results demonstrated powers ranging from 67% to 89%.

DISCUSSION

We found there is a strong relationship between daily vigorous physical activity and IVD health, as evaluated by fluid movement using ADC values and T2 values. As low ADC is associated with IVD degeneration,[39] the higher ADC values found in participants with vigorous activity demonstrate the beneficial effects of activity, and particularly vigorous activity, on IVD health. As lower T2 is indicative of degenerative changes in the IVD,[40] the higher T2 values seen in the vigorous activity group indicate activity as a potential benefit to disc health in delaying

degenerative changes. Activity has been shown to benefit disc health in a rat model where running demonstrated increased extracellular matrix production with no cellular apoptosis, suggesting a positive effect for regular exercise on disc health.[7] Although genetics appears to play a large role in disc degeneration,[6] the strong associations seen in this study indicate a relationship between activity and disc health that may help us positively impact disc health despite the genetic factors beyond control. More research on the reasons for the positive relationship between exercise and disc health is warranted.

The participants who had at least 30 minutes of MVPA demonstrated significantly higher ADC values than those with less than 30 minutes of MVPA. The positive relationship seen between high ADC values and higher activity provide support to the American College of Sports Medicine recommendations to get at least 30 minutes of moderate activity 5 days per week or at least 20 minutes of vigorous activity 3 days per week.[1] Results of this study encourage the inclusion of at least some vigorous activity in one's exercise program, since the positive effects were greater on ADC with vigorous activity, but support all activity as beneficial to IVD health. Early research reported that short-term loading does not appear to alter solute transport,[20,41] but long-term exercise (e.g., 3 months) significantly increases nutrient flow, possibly due to the remodeling of the microcirculation.[8] More recently, Gullbrand reported a 16.8% increase in fluid transport in healthy discs and a 12.6% increase in degenerative discs with low rate cyclic loading.[42] In contrast, extreme or sudden increases in activity have a negative impact, as repetitive high strains may lead to fatigue failure of the collagen network and initiate degeneration.[43,44] The effects of chronic loading take time to manifest, so consistent, regular exercise is important in maintaining IVD health.

Individuals with lower sedentary time also demonstrated significantly higher ADC values than those with high sedentary time. When an individual spends extended periods of time in one position, it can negatively influence nutrient transport and IVD health.[45,46] As movement affects IVD fluid flow, high amounts of sedentary time may negatively impact the ability of disc cells to exchange nutrients and maintain disc matrix. Long term supine creep loading of the disc, which also occurs upright in prolonged sitting or standing in one position, has been shown to slow the transport of small solutes, requiring 3 hours of recovery time for 4.5 hours of loading to attain diffusion rates of unloaded discs.[47] Time spent in sedentary behavior is a new research focus for physical activity and health outcomes[12] as sedentary time is related to increased disability, independent of time spent in moderate or vigorous activity.[11] Decreasing sedentary time and the static loading it causes, as well as increasing activity appears beneficial in aiding IVD fluid flow and health.

The results of this study indicate a beneficial relationship between daily physical activity and IVD health. Epidemiologic studies show that physical activity levels correlate with the extent of disc degeneration,[48,49] although negative findings have also been published.[50] In the Finnish Twin Spine study, heavy leisure-time physical loading explained just 2% of lumbar disc degeneration variability.[51] Our findings are consistent with other studies examining the effects of mechanical loading on IVD fluid movement[52,53] and supportive of theoretical models examining dynamic and static compression. Using finite element models, dynamic compressions (i.e., active exercise) as opposed to static compressions (i.e., sitting) led to higher IVD cell density in degenerated discs,[54] increased oxygen concentration, and reduced lactate accumulation[55] with the effects dependent on load amplitude and frequency. Increases in glycosaminoglycan (GAG) synthesis is another known beneficial effect of disc loading that may be a factor in the more

active individuals. Static and diurnal loads of variable magnitudes have been found in a multiscale mathematical model [56] as well as in experimental models[57,58] to impact GAG synthesis. The results of this study motivate interest in further examining the relationships between physical activity and disc health to determine the beneficial mechanisms at work.

Multiple health factors were examined to evaluate the effects of lifestyle and overall health with the health of the IVD. We examined bone mineral density in its relationship to activity and disc fluid levels. Although most pathologies decrease nutrient perfusion, osteoporosis increases perfusion, as decreased bone mineralization increases the space available in the bone for fluid, allowing increased means for nutrient flow.[32] Osteoporosis also decreases endplate resistance, leading to reduced intradiscal compressive strain that can also increase diffusive transport, particularly of glucose, toward the disc.[32] Disc degeneration can alternatively lead to osteoporosis in elderly people, as degenerated discs alter the mechanics of the lumbar segments and decrease trabecular bone density when the disc nucleus degenerates.[59] In this study, we noted a consistently lower BMD in the more active, less sedentary groups, although only femoral neck and lumbar spine BMD were significantly lower in the high VPA and MVPA, respectively. When the individuals who fell into in all three higher activity groups were examined, their bone mineral density in all three measures was significantly lower in the more active, less sedentary participants. The results were unexpected as this was a healthy, nonelderly population with few participants having low bone mass (no osteoporosis, 23% with osteopenia). There was no relationship between BMD and expected confounders such as age, gender, or BMI although femoral neck and total hip BMI were related to weight. Activity type was inconsistent among participants, and was not heavily low-impact in the high activity group. Female athlete triad was considered as a possible explanation of the lower BMD in more active individuals but

cannot be confirmed as data was not collected on the presence of triad symptoms during adolescence.[60] Both male and female endurance runners have been shown to have lower BMD, which may be a factor in some of the participants in this study, but not all who had lower BMD were endurance runners.[61] There were no significant direct relationships correlating BMD and ADC. IMT was significantly related to femoral neck BMD, with lower mean IMT in individuals with lower BMD (Figure 3).

We examined cardiovascular health as a potential confounding factor in examining the relationship between disc health and activity. As anticipated, those who participated in 30+ minutes of MVPA had significantly higher VO_2max, reflecting the known beneficial effects of exercise on cardiovascular health.[1] We evaluated carotid artery ultrasound data as a measure of overall arterial health, and found a significant positive relationship between higher ADC and lower IMT thickness in this study (Figure 4). This is particularly significant as this was a healthy population without known cardiovascular disease and with all but two participants (borderline high) having normal IMT for their age. Cardiovascular health can potentially affect disc fluid flow by altering the availability of blood to vertebral capillary beds.[62] Spinal vertebrae are perfused by vertebral arteries and capillaries penetrating the subchondral plate[3] with blood flow highest in the cervical vertebrae and lowest in the lumbar vertebrae[41]; therefore, decreased arterial blood flow would affect the lumbar discs more than cervical discs. Atherosclerosis negatively impacts blood flow to the vertebrae and endplates, and abdominal aortic atherosclerosis has been associated with disc degeneration and back pain.[63] Similarly, Kurunlahti found lower ADC values correlated with lumbar arterial narrowing, demonstrating a relationship between disc degeneration and poor arterial health.[63] Our study likewise found a correlative

relationship between arterial health and ADC supporting the link between blood supply and disc health.

There are several limitations to the study. First, this study had a relatively small sample size from a single geographic area and, consequently, the results may not universally apply to a larger, more diverse population group. For example, the BMD differences we found were both significant and meaningful, representing large magnitude differences in bone density. However, the findings were counter-intuitive (high activity participants had significantly lower BMD). Further research with a larger, more geographically diverse sample would be beneficial, particularly as part of a prospective, randomized study. Second, there is not a consensus on which MRI IVD health metrics are most clearly correlated with pain. Correlating activity levels with Pfirmann rating, disc height measurements, high intensity zones, etc., could have clinical value.[2] Additionally, we were unable to collect Actigraph data from participants from the same day as the MR imaging, which may have provided a stronger correlation with instantaneous fluid flow metrics in the disc. A third significant limitation of the study is the sole reliance on Actigraph accelerometer data as a measure of participant activity. For example, accelerometers are incapable of recording resistance training and do not discriminate between activities that induce very high spinal loads or cardiovascular burdens. We did not discriminate between prolonged periods of exercise versus multiple shorter periods. For example, the EPILIFT study[22] showed that very high levels of endurance activities were detrimental to low back health, which was not seen in resistance activities. Activity modalities that provide a specific load on the spine such as isolated lumbar extension exercises have been shown in animal models to benefit disc health[2] and may play a greater role in humans more than overall activity, which should be

examined further. Differences in activity type might also be linked to the BMD findings noted above.

Spine health is an important element in examining health and wellness, and disc health, specifically, has been shown to depend on mechanical loading. This study is unique in quantifying the specific relationships between vigorous activity, moderate-vigorous physical activity, sedentary time, and quantitative MRI evaluation of IVD health.

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Table 1. MRI Settings for the T2 and DTI Sequence Performed on a Siemens TIM-Trio 3.0T Scanner with a 4-Channel Surface Coil

Two-dimensional DTI sequence	
Field of View (FOV) readout-phase	256 mm x 256 mm (phase with 100% oversample)
Matrix size kx-ky-slice	128 x 128 (with 6/8 phase partial Fourier) x 1
Voxel size x-y-slice thickness	2 mm x 2 mm x 5 mm
TR/TE/echo spacing	3000 msec/98 msec/0.73 msec

Other parameters:

- Average = 4, readout bandwidth = 1502 hz/pixel
- Diffusion direction = 64, b value = 1000 s/mm^2

Sagittal view two-dimensional T2 weighted turbo-spin echo sequence	
Field of View (FOV) readout-phase	280 mm x 280 mm
Matrix size kx-ky slice	384 x 288 (phase encode 100% oversample) x 20
Voxel size x-y-slice thickness	0.7 mm x 1 mm x 3 mm
TR/TE/Flip angle	3500 msec/99 msec/160 degree

Other parameters:

- Turbo factor 32, slice gap 3.6 mm,
- Average = 2, readout bandwidth = 260 Hz/pixel
- Flow compensation is applied in readout direction, fat suppression used

Table 2. Statistical Analysis Based on Presence/Absence of Daily Vigorous Activity, mean (SD)

	Demographics			***Cardiovascular Health***					***Bone Mineral Density***			***Spine Function***		***Disc Health***		
	N, M:F	Age (yrs)	BMI (kg/m^2)	Systolic BP (mmHg)	Diastolic BP (mmHg)	VO2 max (ml/kg/min)	Max IMT (mm)	Mean IMT (mm)	Femoral neck BMD (g/cm^2)	Hip total BMD (g/cm^2)	Lumbar Spine BMD (g/cm^2)	ROM (degrees)	ODI (%)	T2 Intensity (ms)	FA	ADC (mm^2/s)
With Vigorous Activity	15, 5:10	45.9 (6.5)	23.5 (3.5)	116 (9.1)	75.0 (8.5)	39.6 (3.2)	0.607 (0.05)	0.529 (0.05)	0.974 (0.11)	1.002 (0.13)	1.18 (0.15)	38.7 (11.5)	1.6 (3.0)	62.7 (24.1)	0.143 (0.06)	1.21 (0.47)
Without Vigorous Activity	11, 4:7	42.9 (6.4)	26.8 (6.1)	118 (12.3)	78.7 (10.2)	37.8 (3.7)	0.637 (0.06)	0.555 (0.06)	1.05 (0.08)	1.061 (0.08)	1.25 (0.16)	42.3 (9.8)	4.0 (09.7)	39.9 (13.2)	0.174 (0.11)	0.671 (0.37)
p-value		0.12	0.04*	0.3	0.16	0.1	0.08	0.1	0.03*	0.1	0.14	0.2	0.19	0.004**	0.18	0.002**

** $p \leq 0.01$ * $p \leq 0.05$

Table 3. Statistical Analysis Based on 30 Minutes of Daily Moderate-to-Vigorous Activity, mean (SD)

	Demographics			***Cardiovascular Health***					***Bone Mineral Density***			***Spine Function***		***Disc Health***		
	N, M:F	Age (yrs)	BMI (kg/m^2)	Systolic BP (mmHg)	Diastolic BP (mmHg)	VO2 max (ml/kg/min)	Max IMT (mm)	Mean IMT (mm)	Femoral neck BMD (g/cm^2)	Hip total BMD (g/cm^2)	Lumbar Spine BMD (g/cm^2)	ROM (degrees)	ODI (%)	T2 Intensity (ms)	FA	ADC (mm^2/s)
> 30 min MVPA	14, 6:8	46.1 (6.4)	24.3 (3.8)	119 (8.3)	77.1 (2.5)	40.3 (2.9)	0.658 (0.07)	0.527 (0.04)	0.979 (0.11)	1.001 (0.13)	1.146 (0.15)	37.5 (12.0)	4.5 (09.4)	55.8 (24.7)	0.147 (0.06)	1.145 (0.48)
< 30 min MVPA	12, 3:9	43.0 (6.5)	25.5 (6.2)	114 (12.3)	74.6 (10.6)	37.2 (3.3)	0.687 (0.06)	0.555 (0.06)	1.037 (0.08)	1.058 (0.09)	1.279 (0.13)	43.3 (8.6)	1.0 (1.9)	49.7 (21.4)	0.165 (0.11)	0.789 (0.49)
p-value		0.12	0.27	0.12	0.25	0.008**	0.14	0.09	0.08	0.11	0.014*	0.08	0.09	0.25	0.30	0.03*

** $p \leq 0.01$ * $p \leq 0.05$

Table 4. Statistical Analysis Based on Daily Sedentary Time, mean (SD)

	Demographics			***Cardiovascular Health***					***Bone Mineral Density***			***Spine Function***		***Disc Health***		
	N, M:F	Age (yrs)	BMI (kg/m^2)	Systolic BP (mmHg)	Diastolic BP (mmHg)	VO2 max (ml/kg/min)	Max IMT (mm)	Mean IMT (mm)	Femoral neck BMD (g/cm^2)	Hip total BMD (g/cm^2)	Lumbar Spine BMD (g/cm^2)	ROM (degrees)	ODI (%)	T2 Intensity (ms)	FA	ADC (mm^2/s)
< 67% sedentary time	16, 4:12	45.1 (6.7)	23.5 (3.45)	116 (8.5)	75.0 (8.4)	38.9 (3.5)	0.659 (0.07)	0.529 (0.05)	0.981 (0.35)	1.004 (0.13)	1.212 (0.18)	40.6 (12.1)	1.5 (2.9)	56.2 (22)	0.158 (0.07)	1.128 (0.45)
> 67% sedentary time	10, 5:5	43.9 (6.6)	27.0 (6.41)	119 (13.1)	79.1 (10.4)	38.9 (3.6)	0.708 (0.07)	0.559 (0.06)	1.046 (0.26)	1.064 (0.09)	1.199 (0.13)	39.5 (9.0)	4.4 (10)	48.0 (24.8)	0.151 (0.11)	0.748 (0.52)
p-value		0.33	0.04*	0.22	0.13	0.48	0.04*	0.07	0.06	0.1	0.18	0.4	0.14	0.20	0.42	0.03*

** $p \leq 0.01$ * $p \leq 0.05$

Table 5. Statistical Analysis for High Activity Groups vs Others, mean (SD)

	Demographics			***Cardiovascular Health***					***Bone Mineral Density***			***Spine Function***		***Disc Health***		
	N, M:F	Age (yrs)	BMI (kg/m^2)	Systolic BP (mmHg)	Diastolic BP (mmHg)	VO2 max (ml/kg/min)	Max IMT (mm)	Mean IMT (mm)	Femoral neck BMD (g/cm^2)	Hip total BMD (g/cm^2)	Lumbar Spine BMD (g/cm^2)	ROM (degrees)	ODI (%)	T2 Intensity (ms)	FA	ADC (mm^2/s)
All activity	11, 4:7	47.1 (6.7)	23.7 (3.8)	118 (8.5)	76.3 (8.4)	39.7 (2.9)	0.653 (0.07)	0.529 (0.05)	0.974 (0.11)	1.002 (0.13)	1.12 (0.12)	36.8 (12.3)	1.1 (2.1)	55.4 (20.4)	0.149 (0.06)	1.10 (0.48)
Not all activity	15, 5:10	42.9 (6.0)	25.8 (5.7)	116 (11.9)	76.7 (10.1)	38.2 (3.7)	0.696 (0.07)	0.629 (0.06)	1.05 (0.08)	1.061 (0.08)	1.27 (0.15)	42.7 (9.2)	3.7 (8.6)	47.3 (20.6)	0.16 (0.10)	0.89 (0.51)
p-value		0.05*	0.15	0.37	0.46	0.13	0.04*	<0.0001**	0.03*	0.1	0.007**	0.9	0.16	0.16	0.38	0.14

** $p \leq 0.01$ * $p \leq 0.05$

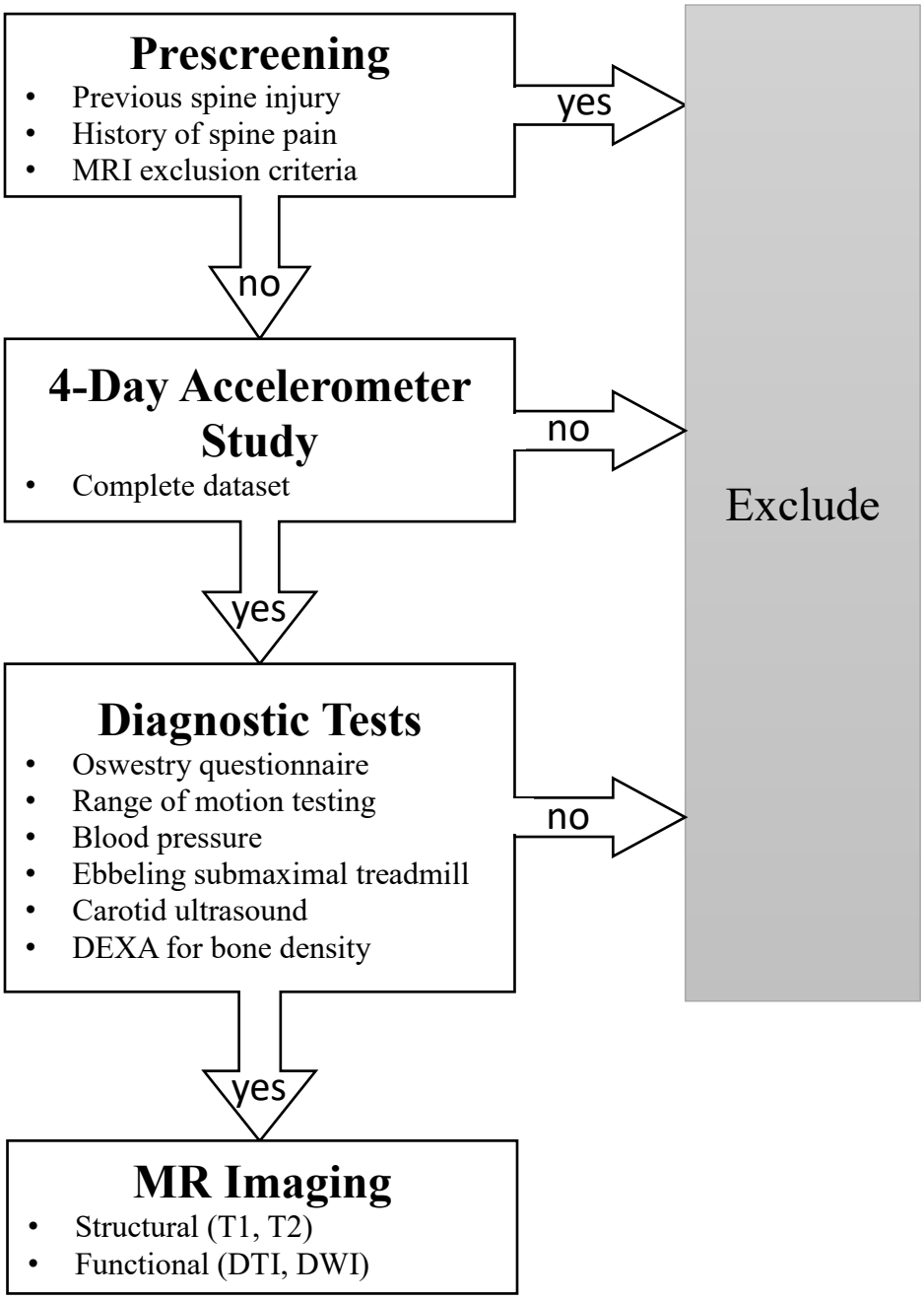

Figure 1. Flowchart of Research Methodology

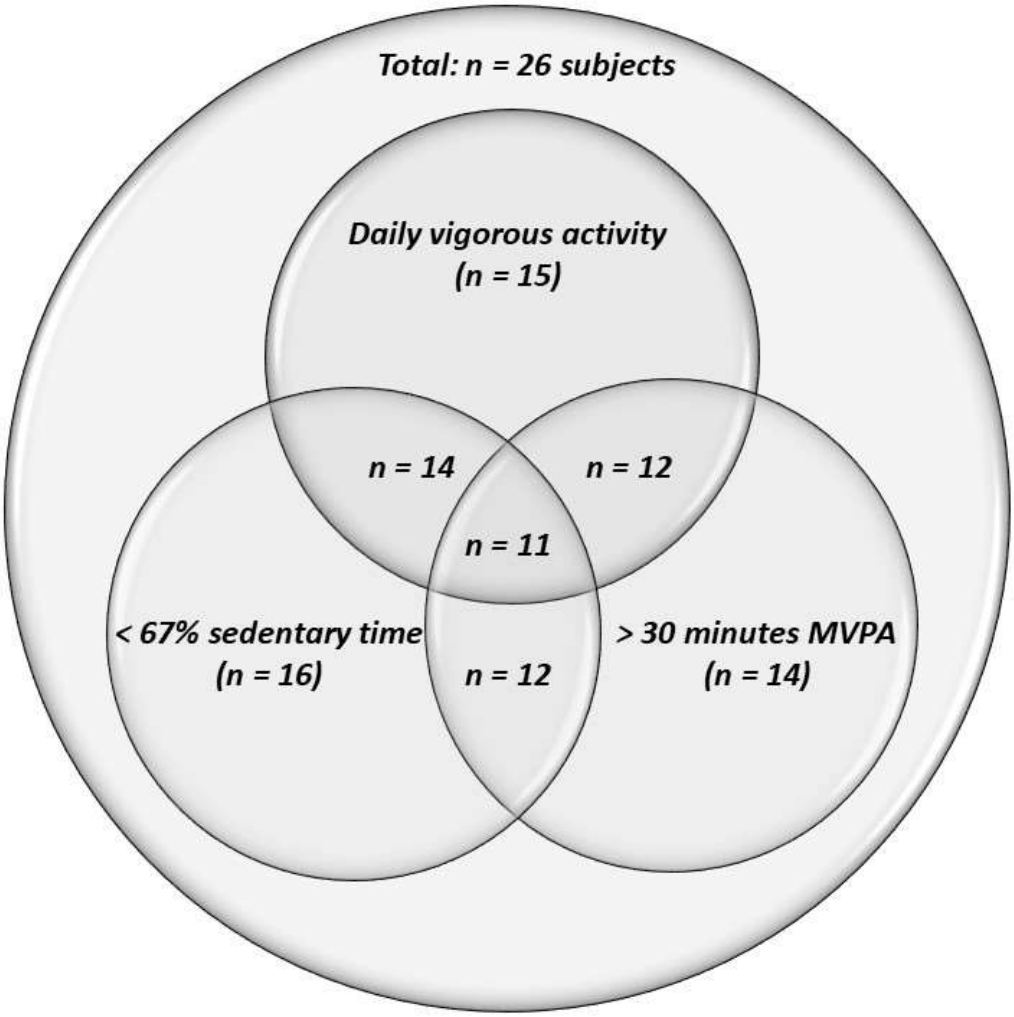

Figure 2. Modified Venn Diagram of Participants in Each Activity Group.

Note that in order to minimize confusion, the sample sizes (i.e., inclusive overlap totals, rather than exclusive overlap totals) are used in the diagram**.**

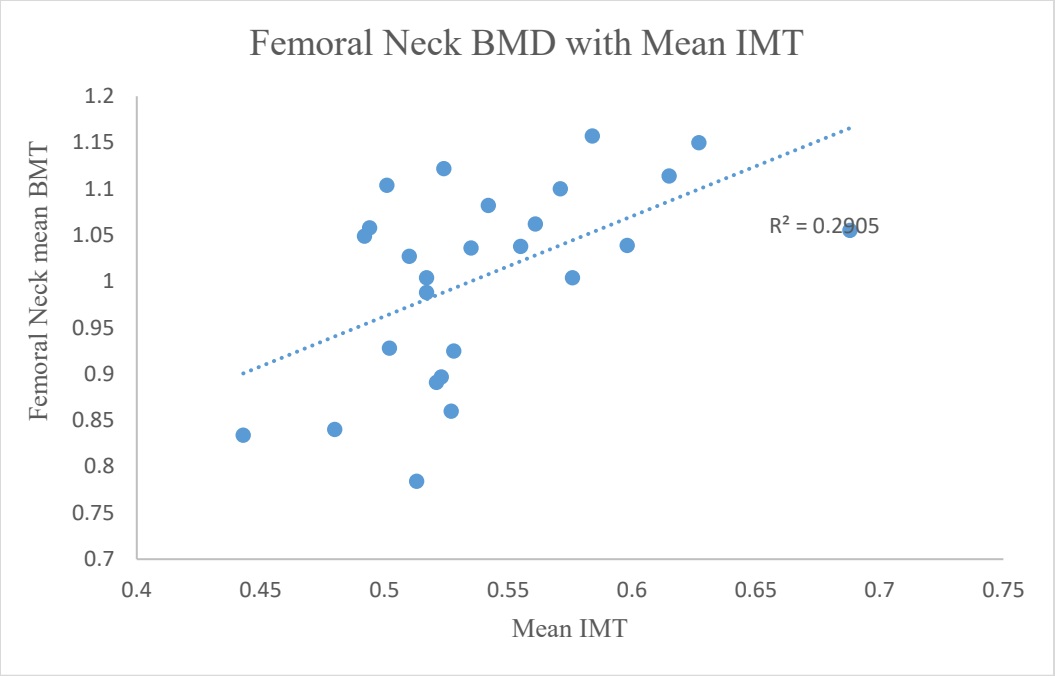

Figure 3. Relationship Between Femoral Neck BMD and Mean IMT (p = 0.004) Demonstrating A Lower IMT with Lower BMD

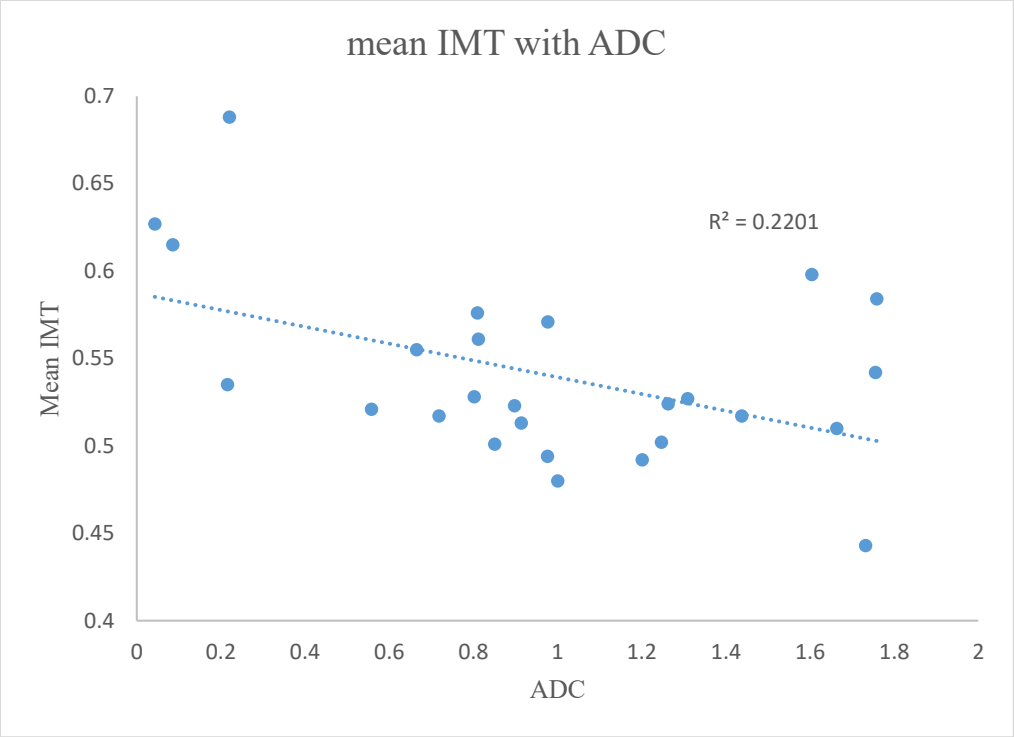

Figure 4. Relationship Between Mean IMT and ADC (p = 0.01) Demonstrating a Lower IMT in Individuals with Higher ADC

APPENDIX A. RESEARCH TOOLS

A.1 Oswestry Low Back Pain Disability Questionnaire

Oswestry Disability Index

Please complete this questionnaire. It is designed to tell us how your back pain affects your ability to function in everyday life. I have "Chronic Pain" or pain that has bothered me for 3 months or more: ☐Yes ☐No

Check one of the following: ☐Prior to Surgery ☐After Surgery 3 Months

☐After Surgery 1 year ☐After Surgery 6 weeks ☐After Surgery 6 Months

☐After Surgery 2 years

Please answer each section below by checking the One Choice that applies the most to you at this time. (You may feel that more than one of the statements relates to you at this time, but it is very important that you Please check only one choice that best describes your problem at this time.

Section 1: Pain Intensity

☐ I can tolerate the pain I have without having to use painkillers. [0 points]

☐ the pain is bad but I manage without taking painkillers. [1 point]

☐ Painkillers give complete relief from pain. [2 points]

☐ Painkillers give moderate relief from pain. [3 points]

☐ Painkillers give very little relief from pain. [4 points]

☐ Painkillers have no effect on the pain and I do not use them. [5 points]

Section 2: Personal Care

☐ I can look after myself normally without causing extra pain. [0 points]

☐ I can look after myself normally but it causes extra pain. [1 point]

☐ It is painful to look after myself and I am slow and careful. [2 points]

☐ I need some help but manage most of my personal care. [3 points]

☐ I need help every day in most aspects of self-care. [4 points]

☐ I do not get dressed wash with difficulty and stay in bed. [5 points]

Section 3: Lifting

☐ I can lift heavy weights without extra pain. [0 points]

☐ I can lift heavy weights but it gives extra pain. [1 point]

☐ Pain prevents me from lifting heavy weights off the floor but I can manage if they are conveniently positioned for example on a table. [2 points]

☐ Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned. [3 points]

☐ I can lift only very light weights. [4 points]

☐ I cannot lift or carry anything at all. [5 points]

Section 4: Walking

☐ Pain does not prevent me walking any distance. [0 points]

☐ Pain prevents me walking more than 1 mile. [1 point]

☐ Pain prevents me walking more than 0.5 miles. [2 points]

☐ Pain prevents me walking more than 0.25 miles. [3 points]

☐ I can only walk using a stick or crutches. [4 points]

☐ I am in bed most of the time and have to crawl to the toilet. [5 points]

Section 5: Sitting

☐ I can sit in any chair as long as I like. [0 points]

☐ I can only sit in my favorite chair as long as I like. [1 point]

☐ Pain prevents me sitting more than 1 hour. [2 points]

☐ Pain prevents me from sitting more than 0.5 hours. [3 points]

☐ Pain prevents me from sitting more than 10 minutes. [4 points]

☐ Pain prevents me from sitting at all. [5 points]

Section 6: Standing

☐ I can stand as long as I want without extra pain. [0 points]

☐ I can stand as long as I want but it gives me extra pain. [1 point]

☐ Pain prevents me from standing for more than 1 hour. [2 points]

☐ Pain prevents me from standing for more than 30 minutes. [3 points]

☐ Pain prevents me from standing for more than 10 minutes. [4 points]

☐ Pain prevents me from standing at all. [5 points]

Section 7: Sleeping

☐ Pain does not prevent me from sleeping well. [0 points]

☐ I can sleep well only by using tablets. [1 point]

☐ Even when I take tablets I have less than 6 hours sleep. [2 points]

☐ Even when I take tablets I have less than 4 hours sleep. [3 points]

☐ Even when I take tablets I have less than 2 hours of sleep. [4 points]

☐ Pain prevents me from sleeping at all. [5 points]

Section 8: Sex Life

☐ My sex life is normal and causes no extra pain. [0 points]

☐ My sex life is normal but causes some extra pain. [1 point]

☐ My sex life is nearly normal but is very painful. [2 points]

☐ My sex life is severely restricted by pain. [3 points]

☐ My sex life is nearly absent because of pain. [4 points]

☐ Pain prevents any sex life at all. [5 points]

Section 9: Social Life

☐ My social life is normal and gives me no extra pain. [0 points]

☐ My social life is normal but increases the degree of pain. [1 point]

☐ Pain has no significant effect on my social life apart from limiting energetic interests such as dancing. [2 points]

☐ Pain has restricted my social life and I do not go out as often. [3 points]

☐ Pain has restricted my social life to my home. [4 points]

☐ I have no social life because of pain. [5 points]

Section 10: Traveling

☐ I can travel anywhere without extra pain. [0 points]

☐ I can travel anywhere but it gives me extra pain. [1 point]

☐ Pain is bad but I manage journeys over 2 hours. [2 points]

☐ Pain restricts me to journeys of less than 1 hour. [3 points]

☐ Pain restricts me to short necessary journeys under 30 minutes. [4 points]

☐ Pain prevents me from traveling except to the doctor or hospital. [5 points]

Interpretation: Simply add up your points for each section and plug it in to the following formula in order to calculate your level of disability: point total / 50 X 100 = % disability (aka: 'point total' divided by '50' multiply by ' 100 = percent disability)
Example: on my last ODI I scored an 18. So, 18/50 x 100 = 36% disability.

ODI Scoring:
0% to 20% (minimal disability): Patients can cope with most activities of daily living. No treatment may be indicated except for suggestions on lifting, posture, physical fitness and diet. Patients with sedentary occupations (ex. secretaries) may experience more problems than others.

21% to 40% (moderate disability): Patients may experience more pain and problems with sitting, lifting and standing. Travel and social life are more difficult. Patients may be off work. Personal care, sleeping and sexual activity may not be grossly affected. Conservative treatment may be sufficient.

41% to 60% (severe disability): Pain is a primary problem for these patients, but they may also be experiencing significant problems in travel, personal care, social life, sexual activity and sleep. A detailed evaluation is appropriate.

61% to 80% (crippled): Back pain has an impact on all aspects of daily living and work. Active treatment is required. 81% to 100%: These patients may be bed bound or exaggerating their symptoms. Careful evaluation is recommended.

A.2 International Physical Activity Questionnaires (IPAQ)

IPAQ: SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT
FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health related physical activity.

Background on IPAQ
The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken in 12 countries (14 sites) across 6 continents during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages. IPAQ is suitable for use in regional, national and international monitoring and surveillance systems and for use in research projects and public health program planning and evaluation. International collaboration on IPAQ is on-going and an international prevalence study is under development.

Using IPAQ
Worldwide use of the IPAQ instruments for monitoring and research purposes is encouraged. It is strongly recommended, to ensure data quality and comparability and to facilitate the development of an international database on health-related physical activity, that
· no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments,
· if additional questions on physical activity are needed they should follow the IPAQ items,
· translations are undertaken using the prescribed back translation methods (see website)
· new translated versions of IPAQ be made available to others via the web site to avoid duplication of effort and different versions in the same language,
· a copy of IPAQ data from representative samples at national, state or regional level be provided to the IPAQ data storage center for future collaborative use (with permission) by those who contribute.

More Information
Two scientific publications presenting the methods and the pooled results from the IPAQ reliability and validity study are due out in 2002.
More detailed information on the IPAQ process, the research methods used in the development of the IPAQ instruments, the use of IPAQ, the published papers and abstracts and the on-going international collaboration is available on the IPAQ web-site.

www.ipaq.ki.se

International physical activity questionnaire Ipaq: short last 7 days self-administered format
For use with young and middle-aged adults
Note: examples of activities may be replaced by culturally relevant examples with the same mets values (see Ainsworth et al., 2000).

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. This is part of a large study being conducted in many countries around the world. Your answers will help us to understand how active we are compared with people in other countries. The questions are about the time you spent being physically active in the last 7 days. They include questions about activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Your answers are important.
Please answer each question even if you do not consider yourself to be an active person.
THANK YOU FOR PARTICIPATING.

In answering the following questions:

vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal.

moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

1a. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling?
Think about only those physical activities that you did for at least 10 minutes at a time.
_____ days per week › or _____ None

2a. Again, think only about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.
_____ days per week › or _____ None

3a. During the last 7 days, on how many days did you walk for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did solely for recreation, sport, exercise or leisure.
_____ days per week › or _____ None

The last question is about the time you spent sitting on weekdays while at work, at home, while doing course work and during leisure time. This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television.

4. During the last 7 days, how much time in total did you usually spend sitting on a weekday?

____ hours _____ minutes

This is the end of questionnaire, thank you for participating

A.3 The Single Stage Treadmill Walking Test (Ebbeling et al. 1991)

The single stage treadmill walking test is a submaximal aerobic fitness test that estimates VO_2 max. It is suitable for low risk, apparently healthy, nonathletic adults 20 to 59 years of age. The walking pace required throughout the test also makes it appropriate for participants who experience problems such as knee pain when exercising at a jogging pace. The test can be administered to moderate sized groups of participants with low to moderate fitness levels and requires only a treadmill and a HR monitor.
Protocol:
The walking speed for the test is individually determined based on the participant's gender, age, and fitness level

1. Estimate the participant's age-predicted HRmax (220 − age) __ bpm then calculate; 50% __ bpm and 70% __ bpm of his/her HRmax.

2. Have the participant warm-up for 4 minutes at a 0% grade and a walking speed that brings the HR to between 50% and 70% of his/her HRmax. (The recommended walking speed is from 3.4 to 4 mph). If the HR is not in this range after the first minute, adjust the speed accordingly.

3. Following the warm-up, keep the participant at the same speed for an additional 4 minutes at a grade of 5%, then record the steady-state HR (SS HR) from the average of the final 30 sec of the last two minutes at the 5% grade. (Note; to achieve steady-state, the HR from the last two minutes must not differ by more than 5 bpm. If the HR differs by more than 5 bpm, extend the test by an additional minute and record the SS HR from the new final two minutes.) SS HR = bpm.

4. Enter this SS HR into the equation below to estimate VO_2 max (ml/kg/min).

5. Allow the participant to cool down at a slow walk and 0% grade for 2 to 5 min.
Estimated VO_2max (ml/kg/min) =
15.1 + 21.8 (speed in mph) – 0.327 (SS HR in bpm) – 0.263 (speed x age in years) + 0.00504 (SS HR in bpm x age in years) + 5.98 (gender; female = 0, male = 1)
15.1 + 21.8 (___) – 0.327 (___) – 0.263 (__ X __) + 0.00504 (__ X __) + 5.98 (__) =
_____ (ml/kg/min)
Example: A 30-year-old male walked at 3.6 mph at a grade of 5 % with a SS HR of 159 bpm. (HRmax = 190 bpm; 50% HRmax = 95 bpm; 70 % HRmax = 133 bpm):
Estimated VO_2max =
15.1 + 21.8 (3.6) – 0.327 (159) – 0.263 (3.6 x 30) + 0.00504 (159 x 30) + 5.98 (1) = 43.2 (ml/kg/min)