The associations between physical activity intensity, cardiorespiratory fitness, and non-alcoholic fatty liver disease

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Catherine J. Kerr
School of Sport, Rehabilitation, and Exercise Sciences, University of Essex, Essex, UK

Sally P. Waterworth
School of Sport, Rehabilitation, and Exercise Sciences, University of Essex, Essex, UK

David Brodie
Department of Health, Buckinghamshire New University, Bucks, UK

Gavin R. H. Sandercock
School of Sport, Rehabilitation, and Exercise Sciences, University of Essex, Essex, UK

Lee Ingle
Department of Sport, Health & Exercise Sciences, University of Hull, Hull, UK

Abstract:

Background and Aim: High levels of physical activity and cardiorespiratory fitness may protect against non-alcoholic fatty liver disease. We investigated whether different physical activity intensities, and cardiorespiratory fitness, were independent predictors of non-alcoholic fatty liver disease.

Methods: We included healthy adults with no prior diagnosis of liver dysfunction. Non-alcoholic fatty liver disease prevalence was estimated based on fatty liver index scores. We created tertiles of self-reported low, moderate, and vigorous physical activity. Participants completed an incremental treadmill test to estimate cardiorespiratory fitness, and data were subsequently separated into quintile groups (Q1 [least fit] through Q5 [most fit]).

Results: Non-alcoholic fatty liver disease prevalence in our sample of 7,111 adults was 28.3% in males, and 6.5% in females. Logistic regression showed the relative odds of non-alcoholic fatty liver disease were 42% lower if >60 min per week of vigorous physical activity was maintained (OR=0.58 CI: 0.49-0.68). There was a negative dose-response association between cardiorespiratory fitness and non-alcoholic fatty liver disease between Q1-Q4. Compared with Q1, odds were 39% (OR=0.61, CI: 0.51-0.73) lower in Q2, through to 51% lower in Q5 (OR=0.49, CI: 0.41-0.60). Moderate physical activity did not reduce the odds of non-alcoholic liver disease.

Conclusions: We found the lowest prevalence of non-alcoholic fatty liver disease in adults achieving >60 min per week of vigorous physical activity. However, a stronger dose-response relationship existed between cardiorespiratory fitness and non-alcoholic fatty liver disease. Improving cardiorespiratory fitness as a potential therapeutic target for treatment and prevention of non-alcoholic fatty liver disease warrants further investigation.

Word count: 250

Keywords: fatty liver, physical activity, physical exertion, cardiorespiratory fitness

Introduction

Non-alcoholic fatty liver disease (NAFLD) affects around 25% of the European adult population.[1] The condition is defined by fatty infiltration of the liver amounting to greater than 5% of the liver weight, in the absence of other causes of fatty liver, for example, excessive alcohol consumption.[2] NAFLD is a progressive disorder which may lead to liver fibrosis and cirrhosis, conditions associated with significant morbidity and mortality.[3] Epidemiological and clinical studies have identified NAFLD in the development of a range of cardiovascular conditions including left ventricular dysfunction, atherosclerosis, and ischaemic stroke, and may be independent of traditional risk factors of cardiovascular disease.[4-6] While formal diagnosis of NAFLD requires evidence of hepatic steatosis from imaging, at-risk individuals can be identified from the non-invasive "fatty liver index" (FLI), which is based on simple anthropometric data and standard blood biomarkers.[7,8]

The prevalence of NAFLD continues to increase in parallel with other conditions including obesity and type 2 diabetes mellitus.[9] Guidelines for the long-term treatment of NAFLD focus on weight loss and dietary control, and there is a lack of evidence regarding other positive lifestyle behaviours including the adoption of increased physical activity (PA) and the role of cardiorespiratory fitness (CRF) which are both associated with improved cardiometabolic profiles.[10,11] A poor quality diet and over-reliance on saturated and trans-fats, processed meat, and sugar-sweetened beverages, and fructose, are risk factors associated with NAFLD.[12,13] Relatively small amounts of weight loss can lead to significant reductions in liver fat, improved cardiometabolic risk profiles factors, and enhanced longer-term health outcomes.[2]

CRF is a strong predictor of cardiovascular morbidity and all-cause mortality, independent from PA.[14-16] Only in recent years have studies investigated the potential value of high levels of CRF in patients with NAFLD.[17,18] Palve and colleagues[17] reported that CRF was associated with a lower risk of NAFLD after adjustment for age and sex in 463 Finnish adults. Participants who were obese but fit (based on CRF) had a lower prevalence of NAFLD than participants who were obese and unfit (11.7% vs 34.8%, *P*=0.0003). Recently, Croci et al (18) reported that in 15,781 adults from the Hunt Study, low levels of CRF were associated with an increased risk of premature death in adults with NAFLD, and was strongly associated with a higher likelihood of the presence of NAFLD.

The relationship between PA and CRF is a complex one; although increases in PA are associated with concomitant increases in CRF,[19,20] the association is modest, with explained variance ranging between 1-36%.[21,22] Current PA guidelines indicate that individuals should be aiming to achieve 150 min of moderate intensity PA, or 75 min of vigorous intensity PA per week.[10] However, it is unclear whether PA intensity plays a role in the development of NAFLD. No previous studies have examined the associations between PA intensities and CRF in individuals with NAFLD. Therefore, we aimed to determine the relationship of different PA intensities and examine whether PA and CRF are independent predictors of NAFLD in a large sample of apparently healthy men and women in the United Kingdom.

Methods

Participants

Ethical approval was granted by the Faculty of Society & Health ethics committee, Buckinghamshire New University. Participants attended one of five Health & Wellbeing clinics for a three-hour preventative health assessment between 2000 and 2009. All participants completed a comprehensive medical and pre-participation questionnaire, which included self-report lifestyle-related questions, related to PA, diet, smoking status, alcohol intake and stress levels. Participants were 'apparently' healthy, free from any known illness or medical condition. Area level deprivation was determined by home postal codes using the English Indices of Deprivation (EID).[23] Each participant gave written, informed consent to which was countersigned by the duty medical officer.

Anthropometric measurements

Body mass was measured using digital scales (Marsden, UK) and recorded in kilograms (kg) to the nearest 0.1 kg wearing light clothing but without shoes and participants were encouraged to evacuate their bladder before weighing. Scales were calibrated daily with a known weight and bi-annually by the manufacturer. Stature was measured using a stadiometer (Seca, Hamburg, Germany) and recorded in centimeters (cm) to the nearest 0.1 cm. Participants stood on the stadiometer platform (without shoes) with feet together and head in the Frankfort plane. Buttocks and scapulae were in contact with the back of the stadiometer, shoulders relaxed, hands

and arms placed loosely at the sides. The measurement was taken on full inhalation.[23] Body mass index (BMI) was calculated as ($kg \cdot m^{-2}$). Waist circumference was measured to the nearest 0.1 cm using a flexible anthropometric tape, and taken midway between the lowest rib and iliac crest at minimal inspiration.[24]

Physical activity (PA) assessment

Level of PA was assessed using a semi-structured interview in which trained practitioners asked participants to report the number of bouts of moderate PA (MPA) they normally performed each week.[25] A bout of moderate activity was described lasting at least 30 min and being equivalent to brisk walking. Participants then reported the number of bouts of vigorous PA (VPA) usually performed each week. A bout of vigorous activity was defined as lasting for at least 20 min; typically comprising structured exercise or sporting activity.

Cardiorespiratory fitness (CRF) assessment

Each participant was instructed to avoid any form of VPA, alcohol and caffeinated beverages within the 24 hours prior to their assessment. After 5 min of rest in the supine position, a 12-lead electrocardiogram (ECG) (Marquette CASE, GE Healthcare, UK) was performed, which was reviewed by the duty medical officer. Participants walked on a treadmill (T2100, GE Healthcare Ltd., Buckinghamshire, UK) using the Bruce protocol (3 min incremental stages) and were discouraged from holding the handrails. At the end of each minute, heart rate was monitored, and recorded every three minutes. Blood pressure was monitored at the second minute of each stage using the automatic Tango stress test BP monitor (Suntech Medical, Oxfordshire, UK). Participants exercised until volitional termination or if they met any of the American College of Sports Medicine (ACSM) test termination criteria.[26] Peak oxygen uptake was estimated and reported in $ml \cdot kg^{-1} \cdot min^{-1}$.

Venous blood sampling

Participants presented in a fasted state (for the previous 12 hours) but ate a snack (fruit or muesli bar) prior to the exercise test. At the start of each assessment, fasted venous blood samples were

obtained using vacutainer tubes and heparinised whole blood analyzed using the Piccolo blood chemistry analyzer (Abaxis, USA). We measured the liver enzymes gamma-glutamyltransferase (GGT), alanine aminotransferase (ALT), and aspartate transaminase (AST), and serum triglycerides which were used in subsequent analysis (see *Data treatment* below).

Dietary antioxidant intake assessment

A skin carotenoid score was detected by resonance Raman spectrophotometry (Bio Photonic scanner S3 Scanner, Pharmanex, Provo, UT, USA) in order to assess antioxidant levels. Carotenoid levels were measured in the skin via the palm of the hand. Lower scores (<2,000) were associated with poorer dietary quality, for example, lower daily fruit and vegetable (FV) intake, and/or a history of smoking, and higher stress levels; higher scores are associated with higher likely FV intake (25,000-30,000, 3-5 portions; >30,000, 5+ portions; >40,000, 8+ portions).

Data treatment

Inclusion & exclusion criteria

We included male and female adults between ages 40-60 years with complete health assessment data including CRF, PA assessment and all measures needed to calculate NAFLD. We included only individuals with verified fasted status, verified achievement of 85% HR maximum during the exercise test, and those unlikely to have alcoholic fatty liver disease [a reported alcohol intake of moderate or less (<20 g per day, women and <30 g per day, men), and AST/ALT ratio <2.0].[27] We defined the presence of NAFLD based on the fatty liver index (FLI) which has a predictive accuracy of 0.84 (95% CI 0.81–0.87).[28] The formulae used to calculate FLI is:

$$FLI = (e^{0.953*\log e(\text{triglycerides}) + 0.139*BMI + 0.718*\log e(ggt) + 0.053*\text{waist circumference} - 15.745}) / (1 + e^{0.953*\log e(\text{triglycerides}) + 0.139*BMI + 0.718*\log e(GGT) + 0.053*\text{waist circumference} - 15.745}) * 100$$

A FLI < 30 (negative likelihood ratio = 0.2) excludes, and a FLI ≥ 60 (positive likelihood ratio = 4.3) is used to identify NAFLD.[28]

Metabolic syndrome

The presence of Metabolic Syndrome (MetS) was defined according to the harmonised criteria set forth by a joint scientific multisocietal committee in 2009[29]: Waist circumference ≥102 cm in men and ≥88 cm in women; serum triglycerides >1.7 mmol·l^{-1}; HDL-cholesterol: < 1.0 mmol·l^{-1} for men and <1.03 mmol·l^{-1} for women; systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; fasting serum glucose >5.6 mmol·l^{-1} or current treatment for diabetes. Presence of ≥3 components was used to indicate presence of the MetS.

Data analysis

To determine potential benefits of VPA and MPA, the following categories were used: No MPA (0); Low MPA (0-60 min per week); Moderate MPA (>60-120 min per week); High MPA (>120 min per week); No VPA; Low VPA (0-30 min per week); Moderate VPA (>30-60 min per week); High VPA (>60 min per week). Binary logistic regression was employed to calculate odds ratios (OR, 95% CI) for both MPA and NAFLD, and for VPA and NAFLD. Estimates were adjusted for age, sex, smoking, and alcohol consumption, smoking status, and dietary antioxidant intake score.

To calculate odds ratios (OR, 95%CI) using binary logistic regression for NAFLD and CRF, participant data were categorized into quintiles. Estimates were adjusted for age, sex, alcohol consumption, smoking status, dietary antioxidant intake score, MPA, and VPA. All analyzes were performed using SPSS version 25.0 (SPSS an IBM Company, IBM Ltd. NY, USA).

Results

We included 7,111 apparently healthy men (mean age, 49.1 ± 8.3 years; BMI, 26.9 ± 3.4 kg·m^{-2}) and women (mean age, 47.0 ± 8.6 years; mean BMI, 24.5 ± 3.8 kg·m^{-2} , mean area-level deprivation score: low) in our analysis. NAFLD prevalence was 28.3% in males, and 6.5% in females (Table 1).

Binary logistic regression (adjusted for age, sex, smoking status, alcohol consumption and dietary antioxidant intake score) showed that the relative odds of NAFLD was 42% lower if VPA was high (>60 min per week, OR=0.58 CI: 0.49-0.68) (Table 2, Figure 1), with more modest reductions in risk of 17% and 15%, respectively, if VPA was moderate (>30-60 min per wek, OR=0.83 CI: 0.70-0.98) or low (0-30 min per week), OR=0.86 CI: 0.72-1.01). MPA did not impact upon the relative risk of NAFLD in this population at any level.

Table 3 and Figure 2 show the likelihood of NAFLD by quintiles of CRF (referent group - least fit; quintile 5 (Q5)-highest fit; adjusted by age, smoking status, alcohol consumption, dietary antioxidant intake score, weekly MPA and weekly VPA). There was a negative dose-response association between CRF and NAFLD from comparison Q1 to Q2, Q2 to Q3, and Q3 to Q4, but thereafter (Q4 to Q5) there was no further risk reduction in the highest fitness quintile**.** The likelihood of NAFLD was 39% (OR=0.61, CI: 0.51-0.73) lower in Q2 compared to Q1, through to 51% lower in Q5 (highest fit; OR=0.49, CI: 0.41-0.60). When comparing the likelihood of NAFLD in CRF quintiles, the largest benefits occurred when comparing Q1 to Q2, although less pronounced risk reductions occurred between Q2 and Q3 (4%) and between Q3 and Q4 (8%). This relationship was not altered after adjusting for physical activity level (weekly MPA or VPA).

Discussion

Our study identifies the associations between PA intensity and risk of NAFLD, and CRF and risk of NAFLD in a large sample of apparently healthy men and women. We identified 28.3% of males and 6.5% of females with NAFLD based on the FLI. We found that the relative odds of NAFLD were 42% lower if VPA was >60 min per week (OR=0.58 CI: 0.49-0.68), 17% lower if VPA was >30 to 60 min per week (OR=0.83 CI:0.70-0.98), and 15% if VPA was up to 30 min per week (OR=0.86 CI: 0.72-1.0) after adjustment for age, sex, smoking status, alcohol consumption and dietary antioxidant intake score. There was no association between MPA and risk of NAFLD. There was a negative dose-response association between CRF and NAFLD between quintiles 1-4, with no further apparent benefit conferred in the highest fitness category (Q5); odds of NAFLD were 51% lower in the highest fit quintile (OR=0.49, CI: 0.41-0.60).

Improving CRF presents a potential therapeutic target for treatment and prevention of NAFLD. Indeed, Croci and co-workers[18] showed that an improvement in CRF of 1-MET reduced the risk of mortality by 13% in healthy men and women, which equates to a risk reduction comparable to a decrease in waist circumference of 7 cm, a decrease in plasma glucose of 1 $mmol \cdot L^{-1}$, and a decrease in systolic blood pressure of 5 mmHg.[15] These findings highlight the importance of advocating exercise training aimed at improving CRF in NAFLD, independent of an effect on liver

disease.[18] Our finding that estimated CRF is strongly negatively associated with the likelihood of being identified with NAFLD is in agreement with others.[18] Like us, Croci et al[18] found that compared to individuals with high CRF, individuals with low CRF were more likely to have elevated liver enzymes and a greater prevalence of NAFLD.

The most substantial difference in the odds of NAFLD occurred between CRF quintiles 1 and 2, with a 39% relative reduction occurring in Q2. Considerably smaller reductions occurred when comparing differences between higher CRF groups; Q2 to Q3 (4%) and Q3 to Q4 (8%). The importance of targeting individuals in lower CRF categories supports previous findings showing that a reclassification in CRF from unfit to the next CRF quintile confers the most benefit in terms of reduction in mortality risk (44%).[31]

Our findings highlight that the intensity of PA is a key consideration for determining the risk of NAFLD in apparently healthy individuals. There was no association between MPA or lower levels of VPA, and odds of NAFLD, but, in individuals with a high VPA level (>60 mins per week), the odds of NAFLD were reduced by 42%, and by more modest levels of 17% and 15% respectively, when reported VPA was at moderate levels (30-60 min per week), or lower levels (0-30 min per week) . However, in terms of CRF, we found a more consistent odds reduction for NAFLD when comparing individuals in the lowest fitness quintile (Q1) with higher sub-groups. For example, a 39% odds reduction in Q2, 43% in Q3, and 51% in Q4, with no further benefit in Q5 These reductions were upheld despite adjustment for MPA and VPA levels. The association between PA and CRF is complex and has been reported in previous studies. The intensity of PA is a stronger determinant of CRF than the duration of PA.[32] Therefore, the implementation of PA guidelines which are designed to improve CRF, rather than a focus on PA intensity *per se*, should be an important driver in the management of NAFLD.

Previous studies have shown that exercise interventions are effective for reducing liver fat, even in the absence of significant weight loss[33] or dietary intervention.[34] The largest randomized controlled exercise training intervention[35] to date included 220 participants (68% females) with NAFLD and central obesity. The study aimed to characterize the 'dose–response' relationship between exercise intensity and reduction in liver fat following a 12-month exercise intervention. Both moderate exercise training and moderate–vigorous exercise training were similarly effective

in reducing liver fat when compared with controls. The authors[35] concluded that these improvements were largely mediated by weight loss as, after adjustment for weight loss, net changes in liver fat were similar between the intervention group and controls. The implications of this large study indicate that regular exercise is beneficial in preventing and treating NAFLD but that the mode, intensity or volume of exercise is less critical. Combined aerobic and resistance training has also proven to be effective for reducing the prevalence of individuals with NAFLD, though different exercise modalities (aerobic exercise, resistance training, or high intensity interval training) independently appear to have a similar positive effect on the condition.[36]

Our study is not without its limitations. Data are drawn from an opportunistic sample of men and women attending private health screening at entry to a preventive health program and may not be representative of the general or current population, since data were collected between 2000-2009. The mean area-level deprivation score for the sample was low, indicating participants lived in relatively affluent areas. NAFLD is positively associated with higher levels of deprivation, so the prevalence may be higher in a more nationally representative sample. The fact that all participants were voluntarily participating in a preventive healthcare program may have biased the sample either towards health conscious individuals who would likely produce a lower prevalence of NAFLD than expected. Alternatively, the preventive screening and healthcare may have attracted individuals with existing health concerns or those advised to improve their health by family, friends or a medical practitioner. Despite such potential biases, the sample means for health indicators such as blood pressure, BMI and the proportion of overweight and obese, are very similar to values from nationally representative cohort samples reported previously.[37] The use of estimated peak oxygen uptake is also a limitation of the study. There is some reference data in UK adults derived from estimated CRF values,[38] however, it is unclear how these values differ from objectively collected data from maximal treadmill testing registries such as FRIEND.[39] The use of self-report PA questionnaires may provide questionable validity and reliability. Measurement error could be inflated due to issues of accurate recall. Objective monitoring of PA using accelerometers or activity trackers would provide more reliable data, however this is not generally undertaken in large epidemiological studies due to trial complexity and associated costs. We also acknowledge that we have identified NAFLD through the non-invasive FLI method which

uses simple measures of body composition and laboratory blood biomarkers. The FLI has a predictive accuracy of 0.86, but has not been validated against tissue histology.[2] FLI was developed in a cohort of patients where just over 50% were suspected of having liver disease most likely steatosis due to alcohol or NAFLD[40] and this may have affected our ability to accurately identify individuals with NAFLD. However, the FLI is recommended by the European Association for the Study of the Liver.[41]

In conclusion, we found the lowest incidence of NAFLD in adults achieving >60 minutes of VPA per week. However, we found a stronger dose-response relationship between CRF and NAFLD which remained significant after adjusting for age, sex, smoking, alcohol consumption and PA. Improving CRF as a potential therapeutic target for treatment and prevention of NAFLD, and its effectiveness alongside effective weight management, warrants further investigation.

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	Males	*n*=5515	Female	*n*=1596	All	*n*=7111
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Age (y)	49.1	8.3	47.0	8.6	48.6	8.4
BMI (kg/m^2)	26.9	3.4	24.5	3.8	26.4	3.6
WC (cm)	93.6	9.6	79.6	10.4	90.4	11.4
ALT (IU/L)	30.9	10.6	21.1	8.3	28.7	11.0
AST (U/L)	28.9	7.8	24.5	7.2	27.9	7.9
Triglycerides ($mmol \cdot L^{-1}$)	1.4	0.83	1.0	0.44	1.4	0.8
GGT ($\mu g \cdot L^{-1}$)	31.2	19.3	31.0	19.32	31.1	19.3
Alcohol (units)	12.4	7.8	8.8	6.9	11.6	7.7
Weekly MPA (min)	61.6	58.9	70.7	56.8	63.7	58.6
Weekly VPA (min)	33.3	31.8	27.0	28.2	31.9	31.2
VO_2 peak ($ml \cdot kg^{-1} \cdot min^{-1}$)	38.7	9.2	36.8	10.3	38.3	9.5
Fatty Liver Index Score	44.8	23.4	22.1	19.1	39.7	24.4
	Males		Female		All	
	%	n	%	n	%	n
Smoking (Current)	6.3%	348	8.4%	134	6.8%	482
Fatty Liver Index>60	28.3%	1559	6.5%	104	23.4%	1663
Metabolic Syndrome	23.0%	1271	7.2%	115	19.5	1386
Moderate Physical Activity						
None	25.2%	1389	19.7%	315	24.0%	1704
Low	20.5%	1132	16.6%	265	19.6%	1397
Mod	35.1%	1934	39.8%	635	36.1%	2569
High	19.2%	1060	23.9%	381	20.3%	1441
Vigorous Physical Activity						
None	32.7%	1802	41.9%	669	34.7%	2471
Low	17.6%	969	14.7%	235	16.9%	1204
Mod	20.9%	1150	19.7%	314	20.6%	1464
High	28.9%	1594	23.7%	378	27.7%	1972

Table 1 Title: Demographic and clinical data of the cohort.

Table 1 Legend. MPA, moderate physical activity. None (No MPA) n=1704; Low (0-60 min/week) n=1379; Moderate (60-120 min/week) n=2569; High (>120 min/week) n=1441

VPA, vigorous physical activity. None (No VPA) n=2471; Low (0-30 min/week) n= 1204; Moderate (30-60 min/week) n=1464; High (>60 min/week) n=1972.

Age (continuous, years); Alcohol (continuous, Units per week); Metabolic Syndrome (Y, yes), defined according to the harmonised criteria set forth by a joint scientific multisocietal committee.[29]

	β	se	Wald	P	OR	95%CI	
MPA Groups			10.9	=0.012			
MPA (None)					1.00		
MPA (Low)	0.19	0.09	4.34	=0.037	1.21	1.01	1.46
MPA (Mod)	0.20	0.08	5.77	=0.016	1.22	1.04	1.44
MPA (High)	-0.01	0.10	0.02	=0.882	0.99	0.82	1.19
VPA Groups			43.6	<0.001			
VPA (None)					1.00		
VPA (Low)	-0.16	0.09	3.21	=0.073	0.86	0.72	1.01
VPA(Mod)	-0.19	0.08	5.08	=0.024	0.83	0.70	0.98
VPA (High)	-0.55	0.08	43.1	<0.001	0.58	0.49	0.68
Age	0.001	0.001	0.21	=0.649	1.00	0.99	1.01
Sex (Female)	-1.69	0.11	238	<0.001	0.18	0.15	0.23
Smoking (Yes)	0.15	0.12	1.57	=0.210	1.16	0.92	1.46
Alcohol (units)	-0.01	0.00	5.13	=0.024	0.99	0.98	1.00
Dietary Antioxidant Intake	-1.39	0.10	203	<0.001	0.25	0.21	0.30
Constant	14.89	1.03	210	<0.001			

Table 2 Title: Binary logistic regression for the association of moderate intensity and vigorous intensity physical activity with non-alcoholic fatty liver disease in N=7111 adults.

Table 2 Legend. Odds ratios (OR, 95% confidence intervals, CI) from binary logistic regression analysis adjusted for age, sex, alcohol consumption (units per week), smoking status (current/non-smoker) and dietary antioxidant intake score.

MPA, moderate physical activity. None (No MPA) n=1704; Low (0-60 min/week) n=1379; Moderate (60-120 min/week) n=2569; High (>120 min/week) n=1441;

VPA, vigorous physical activity. None (No VPA) n=2471; Low (0-30 min/week) n= 1204; Moderate (30-60 min/week) n=1464; High (>60 min/week) n=1972.

Sex, Male = 1 Female =2; Smoking status, Non-smoker = 1, Current smoker = 2; Age (continuous, years); Alcohol (continuous, units per week); Dietary antioxidant intake (continuous, antioxidant score).

	β	se	Wald	P=	OR	95% CI	
Fitness Quintiles			72.1	<0.001			
Fitness Q1 (Ref)					1.00		
Fitness Q2	-0.49	0.09	29.2	<0.001	0.61	0.51	0.73
Fitness Q3	-0.55	0.09	33.8	<0.001	0.57	0.47	0.69
Fitness Q4	-0.70	0.09	52.4	<0.001	0.49	0.41	0.59
Fitness Q5	-0.70	0.09	50.7	<0.001	0.49	0.41	0.60
Age	-0.003	.004	.652	=0.419	0.99	0.99	1.00
Sex (Female)	-1.79	0.11	261	<0.001	0.16	0.13	0.21
Smoking (Yes)	0.13	0.12	1.22	=0.268	1.14	0.90	1.44
Alcohol (units)	-0.01	.004	2.79	=0.094	0.99	0.99	1.00
Dietary Antioxidant Intake	-1.34	0.09	187	<0.001	0.26	0.22	0.32
MPA (min/week)	-.001	.001	1.99	=0.158	0.99	0.99	1.00
VPA (min/week)	-.007	.001	45.5	<0.001	0.99	0.99	0.99
Constant	15.37	1.03	221	<0.001			

Table 3 Title: Binary logistic regression for the association of cardio-respiratory fitness with non-alcoholic fatty liver disease in N=7111 adults

Table 3 Legend. Odds ratios (OR, 95% confidence intervals, CI) from binary logistic regression analysis, adjusted for age, sex, alcohol consumption (units per week), smoking status (current/non-smoker) and dietary antioxidant intake score.

Fitness – cardiorespiratory fitness measured as $\dot{V}O_{2peak}$ from maximal treadmill exercise. Fitness Quintiles: Q1- Quintile 1 (<20th percentile) n=1397; Quintile 2 (20-40th percentile) n=1423; Quintile 3 (40-60th percentile) n= 1423; Quintile 4 (60-80th percentile) n=1420; Quintile 5 (>80th percentile) n=1424.

MPA, moderate physical activity (min/week); VPA, vigorous physical activity (min/week);

Sex, Male = 1 Female =2; Smoking status, Non-smoker = 1, Current smoker = 2; Age (continuous, years); Alcohol (continuous, units per week); Dietary antioxidant intake (continuous, antioxidant score).

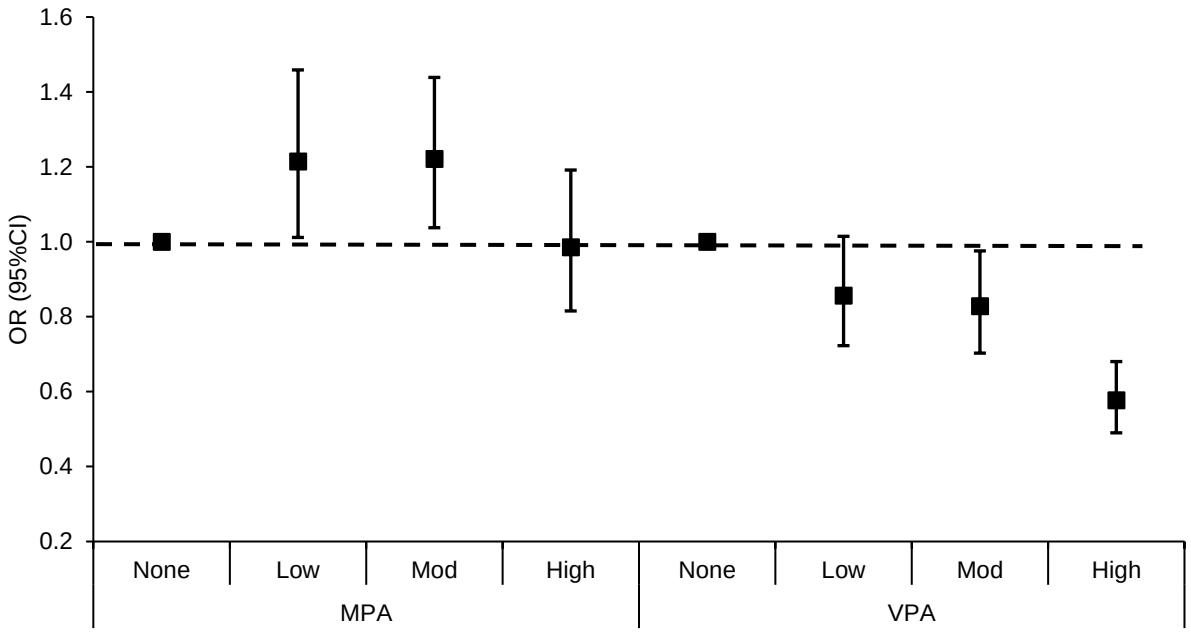

Figure 1 Title: Binary logistic regression showing the association of moderate intensity (MPA) and vigorous intensity physical activity (VPA) with non-alcoholic fatty liver disease in 7,111 adults.

Figure 1 Legend: Values shown are odds ratios (OR, 95% confidence intervals, CI) from binary logistic regression analysis adjusted for age, sex, alcohol consumption (units per week), smoking status (current/non-smoker) and dietary antioxidant intake score.

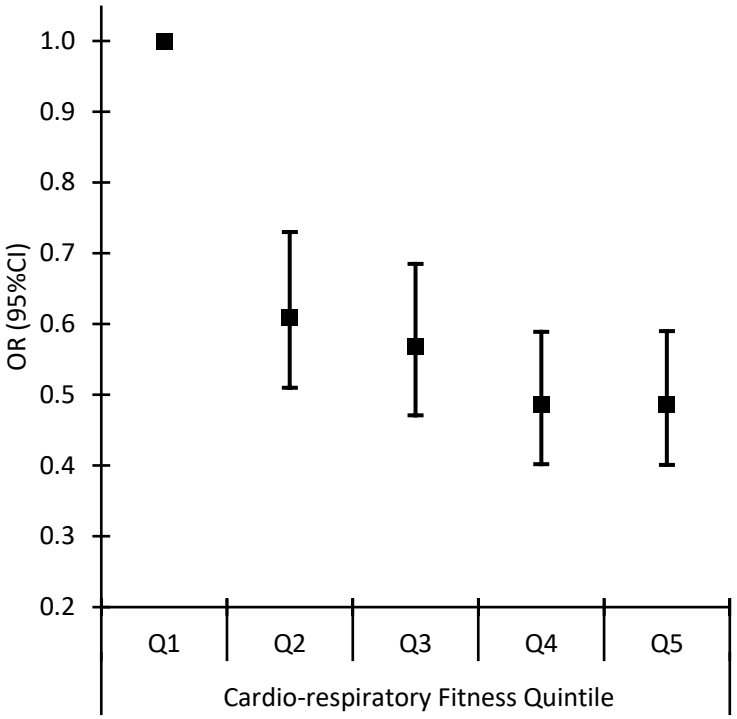

Figure 2 Title: Binary logistic regression showing the association of cardiorespiratory fitness with non-alcoholic fatty liver disease in 7,111 adults.

Figure 2 Legend: Values shown are odds ratios (OR, 95% confidence intervals, CI) from binary logistic regression analysis adjusted for age, sex, alcohol consumption (units per week), smoking status (current/non-smoker) and dietary antioxidant intake score, weekly time (min per week) spent in moderate physical activity and vigorous physical activity.