Association of exercise participation levels with cardiometabolic health and quality of life in individuals with hepatitis C

Kate Hallsworth,1,2,3 Shion Gosrani,1 Sarah Hogg,1 Preya Patel,1 Aaron Wetten,1 Rachael Welton,1 Stuart McPherson2,1, Matthew D Campbell4,5

ABSTRACT
Objective Hepatitis C virus (HCV) infection is associated with an increased risk of cardiovascular disease (CVD) and reduced health-related quality of life (HRQoL). Although physical activity (PA)/exercise has been shown to reduce CVD risk and improve HRQoL in patients with liver disease, there is limited data in HCV. We aimed to explore the association between PA/exercise levels, CVD risk and HRQoL in patients with HCV and assess individuals’ attitudes to PA/exercise.

Design Cross-sectional observational study recruiting consecutive patients with HCV from viral hepatitis clinics. Data were collected on CVD risk factors, anthropometry, HRQoL and the Exercise Benefits and Barriers Scale (EBBS).

Results 86 patients were recruited (71% men, 94% white, age 52±13 years); 49% of the cohort self-reported to be currently active. Although HRQoL was reduced across the cohort, patients that were regularly ‘active’ reported significantly higher HRQoL scores across Short-Form 36v2 domains compared with their inactive counterparts (p<0.05). Metabolic and cardiovascular characteristics were no different between groups stratified by PA/exercise status (p>0.05). EBBS scores were similar in the ‘active’ versus ‘inactive’ groups, however, patients categorised as ‘active’ scored significantly higher on the psychological outlook and social interaction subscales (p<0.05) than those that were ‘inactive’. There were significant associations between EBBS scores and HRQoL (p<0.05).

Conclusions PA/exercise is associated with increased HRQoL in patients with HCV irrespective of clinical parameters. Addressing specific motivators/barriers to exercise for patients will be key to designing effective PA/exercise interventions in this patient population to ensure maximum uptake and adherence.

INTRODUCTION
Hepatitis C virus (HCV) infection is a major cause of chronic liver disease affecting an estimated 71 million people worldwide.1 The disease causes numerous extrahepatic manifestations resulting in a high burden of comorbidity, including increased risk of cardiovascular disease (CVD)2–7 and neuropsychiatric disorders and depression8–10 even after successful antiviral treatment. Health-related quality of life (HRQoL) is also significantly reduced compared with non-HCV infected individuals.11 12

Recently, we developed a holistic care bundle to identify and target modifiable clinical parameters and health behaviours in individuals with HCV in order to improve overall health status and clinical prognosis.7 A central component of this work was the assessment of exercise participation levels, which showed that fewer individuals with HCV meet current physical activity (PA) recommendations than the general population.13 We also showed...
that sedentary behaviour was associated with reduced HRQoL.

Although others have previously shown PA/exercise to improve HRQoL in patients with liver disease, few studies have assessed the strength of this association in patients with HCV, or explored individual’s attitudes to PA/exercise. This information is fundamental for developing effective strategies for engaging individuals with HCV identified as sedentary in lifestyle improvement programmes. Therefore, we aimed to explore the association between sedentary behaviour and HRQoL and assess individuals’ attitudes to PA/exercise using the Exercise Benefits and Barriers Scale (EBBS). Our specific aims were to: (1) determine whether individuals with HCV who engage in regular PA/exercise have fewer cardiometabolic risk factors than sedentary individuals; (2) define the perceived benefits and barriers to PA/exercise in this cohort; (3) determine whether there is a relationship between attitudes to PA/exercise and HRQoL in this cohort.

METHODS
Study design
This cross-sectional, observational study recruited consecutive patients with HCV (treated or untreated) attending the viral hepatitis clinics at The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK. This was a substudy of the previously reported ENHANCE study and included 86 patients (out of 100) who had complete EBBS data. Unfortunately, 14 of the patients did not complete the EBBS survey or did not complete is fully so were excluded from the analysis. Their clinical and demographic data was similar to the main cohort.

Patients
Individuals aged 18 years or older were included if they had chronic HCV infection (defined as HCV RNA detectable in blood for >6 months) or had achieved sustained virological response (SVR=cure of infection) 2–3 months after antiviral treatment. Exclusions were: currently on antiviral treatment for HCV or within 3 months of the end of treatment; coinfection with hepatitis B or HIV; history of significant mental health disorder (eg, psychosis, active substance use, current suicidal ideation) or of ‘significant’ mental health disorder was defined as one where pharmacological treatment was used for its treatment.

HRQoL was determined using the Hepatitis Quality of Life Questionnaire (HQLQv2), a survey constructed to assess the functional health and well-being of patients with HCV, using the Short-Form 36v2 (SF36v2) Health Survey and 15 additional hepatitis-specific questions relevant in assessing the impact of hepatitis. SF36v2 scores presented in this study were normalised to the US general population to have a mean of 50 and SD of 10. Therefore, SF36v2 scores below 50 were considered reduced HRQoL in this study. Scores were normalised to US data because this is more recent than UK data, by 12 years and there has been a marked change in HRQoL over that time. US and UK populations have similar HRQoL. For the hepatitis specific scores, the Hepatitis Distress scale (HD), Positive Wellbeing (PWB), Hepatitis Specific Limitations scale (HLIM) and Hepatitis Specific Health Distress scale (HHD), scores ranged from 0 to 100 (not normalised to the US population) with higher scores indicating better HRQoL.

Details about each patients’ current self-reported PA/exercise levels were recorded as sedentary, engaging in regular moderate PA/exercise (≥150 min/week of activity that leads to faster breathing, increased heart rate and feeling warmer (eg, walking 3–4 m/hour and household tasks, like mowing the lawn or vacuuming)) or regular vigorous PA/exercise (≥75 min/week of activity that leads to very hard breathing, shortness of breath, rapid heartbeat and should leave a person unable to maintain a conversation comfortably (eg, running at 6–8 m/hour or cycling 12–14 m/hour)). Patients completed the EBBS which provides a measurement of the perceived benefits and barriers to participating in PA/exercise, and has been demonstrated to be a valid tool in a range of clinical cohorts in adults with chronic diseases.

Clinical and laboratory data
All clinical and laboratory data were collected at the time of enrolment including age, gender, ethnicity, weight, waist circumference, waist to hip ratio and body mass index. Body composition was measured using 8-point Bioelectrical Impedance Analysis (SECA BIA mBCA 525 Machine, SECA, UK). Blood tests were taken including: full blood count, liver enzymes, HbA1c, lipids, glucose, vitamin D, thyroid stimulating hormone and HCV RNA, which were analysed in an accredited NHS clinical laboratory. A detailed medical history, including a list of current prescribed medications, was recorded and cross-referenced with information from primary care. Details about each individual’s history of HCV infection was also collected including: suspected route of infection, previous antiviral treatment and outcomes, and current status (active HCV viraemia or SVR). Stage of liver fibrosis was assessed using transient elastography and cirrhosis was defined as a liver stiffness measurement >12.5 kPa, liver biopsy demonstrating cirrhosis or imaging evidence of cirrhosis with portal hypertension.

Details of any history of CVD including ischaemic heart disease, cerebrovascular disease, peripheral vascular disease or atrial fibrillation were recorded. We used the QRISK3 (www.qrisk.org) to determine an individual’s estimated risk of a major cardiovascular event in the next 10 years. Smoking history was documented as never smoked, current smoker or previous smoker (for >1 year). The metabolic syndrome and its individual features were defined according to the International Diabetes Federation criteria. Information on past or current history of mental health disorders was also collected. A history of ‘significant’ mental health disorder was defined as one where pharmacological treatment was used for its treatment.
EBBS contains 43 statements pertaining to ‘ideas about exercise’ and is scored on a Likert-scale with responses ranging from 4 (strongly agree) to 1 (strongly disagree). Twenty-nine statements relate to perceived benefits of exercise and 14 relate to perceived barriers. Scores for the total instrument range from 45 to 172 with higher scores representing a more positive attitude towards PA/exercise.

A measure of socioeconomic status/deprivation was assessed by mapping the home postcode for each patient onto the English Indices of Deprivation using the Index of Multiple Deprivation (IMD). The lower layer super output area (LSOA) was calculated for each individual patient postcode. The LSOA with a rank of 1 is the most deprived and the LSOA with a rank of 32844 is the least deprived. Deciles for the IMD are calculated by ranking the 32844 LSOAS in England into 10 equal groups (1 being the most deprived area decile and 10 the least deprived).

**Statistical analysis**

Descriptive information for each variable was derived and the distribution assessed to determine normality. Metric and normally distributed variables are reported as mean±SD, non-normally distributed variables are reported as median and IQR, and categorical variables are reported as frequency (percentage) unless otherwise stated. The cohort was stratified according to activity level (‘inactive’ vs engaging in moderate or vigorous PA/exercise (termed ‘active’)), with differences between dichotomised variables assessed using independent t-tests, Mann-Whitney U tests or Fisher’s exact tests. Differences between EBBS scores were assessed using a general linear model with multiple comparisons adjusted using Bonferroni correction. Multiple linear regression models were used to investigate the associations between clinical characteristics and EBBS scores. Models were fit to estimate associations with sequential adjustment for age, gender and participation in exercise. Data analysis was performed with SPSS (IBM SPSS Statistics V.25, IBM Corp) with statistical significance inferred at a two-tailed p<0.05; 95% CIs and β coefficients are presented where relevant.

**RESULTS**

**Baseline clinical characteristics**

A total of 86 patients (42 active and 44 inactive) were included in the analysis. The clinical characteristics of all patients are presented in tables 1 and 2. The gender, ethnicity and socioeconomic status distributions were similar between active and inactive patients (table 1; p>0.05). Metabolic and cardiovascular characteristics, as well as blood biochemistry, were also similar between patient groups stratified by PA/exercise status (table 2). The prevalence of a psychological comorbidity was high.
in both groups and greatest in those characterised as inactive (inactive: 57% vs active 41%, p = 0.031).

**Self-reported exercise participation and EBBS scores**
Self-reported exercise participation and EBBS scores are presented in **Table 3**. From our sample of 86 patients, 49% (n=42) of the cohort self-reported to be currently active, of which 14% (n=12) self-reported regular participation in vigorous PA/exercise. Of those patients classified with cirrhosis (n=30, (35%)), 43% (n=13) were physically active, compared with 52% (n=29) of those classified as non-cirrhotic. Of those patients with active viraemia (28%, n=24), 50% were classified as physically active;
Table 3  Self-report Exercise Benefit and Barrier Scale (EBBS) scores

|                          | Exercise status | P value               |
|--------------------------|-----------------|-----------------------|
|                          | All patients    | Inactive | Active |               |
| Total EBBS score         | 122.69±16.46    | 117.66±15.91 | 127.95±15.52 | 0.416*     |
| Combined benefit items   | 83.24±13.67     | 79.61±14.96 | 87.05±11.13 | 0.189*     |
| Combined barrier items   | 39.44±6.34      | 38.05±6.06 | 40.90±6.37 | 0.744*     |

Perceived benefit items

**Life enhancement subscale**

25: My disposition is improved by exercise 2.85±0.66 2.77±0.77 2.93±0.51 0.253*
26: Exercising helps me sleep better at night 2.85±0.69 2.75±0.78 2.95±0.58 0.110*
29: Exercise helps me decrease fatigue 2.62±0.72 2.50±0.79 2.74±0.63 0.290*
32: Exercise improves my self-concept 2.92±0.65 2.77±0.68 3.07±0.60 0.175*
34: Exercising increases my mental alertness 2.90±0.69 2.77±0.74 2.02±0.60 0.302*
35: Exercise allows me to carry out normal activities without becoming tired 2.81±0.64 2.73±0.62 2.90±0.66 0.649*
36: Exercise improves the quality of my work 2.71±0.63 2.64±0.69 2.79±0.56 0.137*
41: Exercise improves overall body function 2.93±0.66 2.86±0.70 3.00±0.62 0.315*

**Physical performance subscale**

7: Exercise increases my muscle strength 3.08±0.72 2.98±0.73 3.19±0.71 0.262*
15: Exercises increases my level of physical fitness 3.12±0.71 3.05±0.71 3.19±0.71 0.696*
17: My muscle tone is improved with exercise 3.06±0.64 2.89±0.69 3.24±0.53 0.035* †
18: Exercising improves functioning of my cardiovascular system 3.06±0.62 2.86±0.67 3.26±0.50 0.020* †
22: Exercise increases my stamina 3.14±0.65 3.02±0.73 3.26±0.54 0.330*
23: Exercise improves my flexibility 3.09±0.71 3.02±0.79 3.17±0.62 0.449*
31: My physical endurance is improved by exercise 3.03±0.66 2.91±0.68 3.17±0.62 0.214*
43: Exercise improves the way my body looks 2.99±0.68 2.93±0.76 3.05±0.58 0.452*

**Psychological outlook subscale**

1: I enjoy exercise 2.80±0.78 2.50±0.85 3.12±0.55 0.001* †
2: Exercise decreases feelings of stress and tension for me 2.85±0.78 2.66±0.83 3.03±0.70 0.136*
3: Exercise improves my mental health 2.77±0.75 2.57±0.76 2.98±0.68 0.018* †
8: Exercise gives me a sense of personal accomplishment 2.90±0.85 2.73±0.90 3.07±0.78 0.257*
10: Exercising makes me feel relaxed 2.83±0.69 2.66±0.78 3.00±0.54 0.095*
20: I have improved feelings of well-being from exercise 2.93±0.73 2.80±0.79 3.07±0.64 0.283*

**Social interaction subscale**

11: Exercising lets me have contact with friends and persons I enjoy 2.49±0.72 2.30±0.73 2.69±0.64 0.032* †
30: Exercising is a good way for me to meet new people 2.70±0.63 2.61±0.65 2.79±0.61 0.200*
38: Exercise is good entertainment for me 2.76±0.77 2.68±0.83 2.83±0.70 0.539*
39: Exercise increases my acceptance by others 2.40±0.74 2.39±0.84 2.40±0.63 0.252*

**Preventive health subscale**

5: I prevent heart attacks by exercising 2.93±0.70 2.82±0.72 3.05±0.66 0.505*
13: Exercising increases my levels of physical fitness 2.91±0.57 2.77±0.60 3.05±0.49 0.148*
27: I will live longer if I exercise 2.85±0.69 2.68±0.77 3.02±0.56 0.114*

Perceived barrier items

Continued
of those patients without active viraemia (72% (n=62)), 51% were classified as physically active.

Across the whole cohort, the highest scoring exercise benefit subscale was physical performance, and the social interaction subscale was scored lowest (tables 3 and 4). Preventive health, psychological outlook and life enhancement subscales were largely comparable (tables 3 and 4). Physical performance was negatively associated with social interaction (r=−0.251; p=0.020). The highest scoring individual benefit item was ‘exercise improves my flexibility’ and the lowest was ‘exercise increases my acceptance by others’. Family discouragement and time expenditure were rated similarly as the main overarching barriers to exercise (tables 3 and 4), with patients scoring ‘exercise takes too much time from family relationships’ as the highest individual barrier item. The lowest scoring barrier subscale was physical exertion, with patients scoring ‘exercise tires me out’ as the lowest individual barrier item. Overall, the perceived benefits (mean±SD: 2.87±0.47) and barriers (mean±SD: 2.82±0.45) to exercise were equally weighted (p=0.386) in a 1:1 ratio. Mean scores for all benefits and barriers were between 2 and 3, which, equated to between ‘agree’ and ‘disagree’ on the EBBS scoring scale. Stratification by PA/exercise status did not reveal statistically significant between-group differences in overall EBBS scores, however, patients categorised as active scored significantly higher on the psychological outlook and social interaction subscales (table 3). Specifically, active patients scored ‘Exercise improves my mental health’ and ‘Exercise lets me have contact with friends and persons I enjoy’ significantly greater than inactive patients (table 3).

**Relationship between HRQoL and PA**

HRQoL was reduced with mean scores for all SF36v2 domains below that of the general population (data shown...
Previously). However, patients categorised as active demonstrated significantly higher HRQoL scores (signifying better HRQoL) across SF36v2 domains, including: Physical Functioning (41±11 vs 48±11, p=0.031), General Health (37±11 vs 45±11, p=0.001), Vitality (39±10 vs 48±12, p<0.001), Social Functioning (35±14 vs 46±13, p=0.003), Mental Health (37±14 vs 48±11, p=0.003), Physical Component Score (41±12 vs 47±10, p=0.003), Mental Component Score (36±15 vs 46±33, p=0.003), Hepatitis Distress (42±33 vs 65±33, p=0.005), Physical Wellbeing (40±28 vs 64±23, p=0.017), for inactive versus active individuals, respectively.

### Discussion

Our findings show that patients with a history of HCV infection (treated or untreated) who regularly undertake PA/exercise report significantly higher HRQoL scores compared with their inactive counterparts, irrespective of CVD risk and comorbidity. Collectively, these findings suggest that PA/exercise should be promoted as a potential therapeutic tool to improve HRQoL in patients with HCV, even if participation may not result in improved cardiometabolic and biochemical parameters.

The clinical picture of HCV and recovery from treatment is characterised by a highly comorbid state coupled with reduced life expectancy. We have previously shown a high prevalence of cardiometabolic risk in this cohort of patients with HCV, however, the finding that increased cardiometabolic risk is ubiquitous within this patient group irrespective of PA/exercise participation was somewhat unexpected. Participation in regular PA/exercise is widely recognised to reduce cardiometabolic risks in both the general population and those with chronic disease. Our observational data would suggest that PA/exercise participation may have little impact on cardiometabolic characteristics in HCV, although in a relatively small sample size. However, it is worth noting that within our ‘active’ HCV cohort, rates of statin and antihypertensive prescribing were low (14% and 32%, respectively), and smoking rates were very high (39% current smokers vs 14% in the UK general population), which collectively, may have negated the potential benefits of regular PA/exercise participation on cardiometabolic parameters. It is important to note however, that we investigated the associations between clinical parameters and self-reported PA/exercise participation at a single time point, and therefore longitudinal and interventional studies are required to fully establish whether PA/exercise has a therapeutic role in modifying cardiometabolic risk in this patient group. It is widely accepted that PA/exercise is an important and effective therapy for improving the pathology and symptoms related to specific liver diseases with studies demonstrating that moderate PA is beneficial in maintaining functional capacity, improving body composition, glucose homeostasis, dyslipidaemia and hypertension, as well as reducing hepatic steatosis and improving liver function.

### Table 4

| Perceived benefit items | 1   | 2   | 3   | 4   | 5   |
|-------------------------|-----|-----|-----|-----|-----|
| 1: Life enhancement     | –   | <0.001*** | 0.984 | <0.001*** | 0.994 |
| 2: Physical performance | –   | <0.001*** | <0.001*** | <0.001*** | 0.994 |
| 3: Psychological outlook| –   | –   | 0.002*** | 0.957 |
| 4: Social interaction   | –   | –   | <0.001*** |
| 5: Preventive health    | –   | –   | –   |

| Perceived barrier items | 1   | 2   | 3   | 4   |
|-------------------------|-----|-----|-----|-----|
| 1: Exercise milieu      | –   | 0.952 | <0.001*** | 0.957 |
| 2: Time expenditure     | –   | <0.001*** | 0.996 |
| 3: Physical exertion    | –   | –   | <0.001*** |
| 4: Family discouragement| –   | –   | –   |

*Between item difference at p<0.05; **between item difference at p<0.01; ***between item difference at p<0.001; post-hoc comparisons adjusted using Bonferroni corrections.
Our data support previous research highlighting patients with HCV have a significantly reduced HRQoL. Although such benefits are often assumed to apply to individuals with HCV, there is little available empirical evidence to support this. In addition, although it was beyond the scope of the present analysis, it would be of interest to assess the mediating impact of viraemic status as well as other prevalent clinical characteristics on PA levels given that recent data demonstrates that HCV increases fatigue and that fatigue is improved following SVR.

The present study extends this work, showing that patients with HCV who are regularly active report significantly higher HRQoL, across SF36v2 domains, compared with inactive counterparts. The main motivator for exercising was to improve physical performance, with those that exercised regularly indicating that improving muscle tone, stamina and cardiovascular fitness as being most important. This supports a rationale for practitioners to encourage patients with HCV to undertake regular PA/exercise as a way to improve HRQoL beyond simply targeting liver health. Furthermore, we show that individuals with HCV who were active report higher scores on the EBBS indicating a more positive perception towards PA/exercise, with psychological outlook and social interaction scoring significantly higher in those active compared with non-active HCV individuals. This is important given that a significant proportion of patients with HCV present with mental health disorders and would suggest that PA/exercise participation may be an effective tool to specifically address this within this cohort.

Overall, patients with HCV placed equal weighting on the perceived benefits and barriers to exercise. It is therefore important to acknowledge that this ‘equipoise’ may be unlikely to lead to behaviour change within the setting of current clinical practice, which focuses on simply promoting PA/exercise. It is therefore important for healthcare professionals (HCPs) to communicate to patients that the benefits of PA/exercise, extend beyond liver-health. Indeed, linking exercise participation to tangible improvements in HRQoL may be perceived as more important for patients with HCV than linking exercise participation to routine clinical biomarkers. Given that the benefits of PA/exercise need to be perceived as of high enough importance for patients to want to overcome the barriers of changing PA/exercise behaviours, HCPs also need to assess barriers in this population to enable the development of successful lifestyle interventions.

| Table 5 Linear regression analysis between EBBS scores with self-report hepatitis quality of life scores |
|---------------------------------|---------------------------------|---------------------------------|
| Model 1 | Model 2 | Model 3 |
| β (95% CI) | P value | β (95% CI) | P value | β (95% CI) | P value |
| **Total EBBS score** | | | | | | |
| PCS | 0.242 (0.097 to 0.387) | 0.001** | 0.255 (0.113 to 0.396) | 0.001** | 0.213 (0.067 to 0.359) | 0.005** |
| MCS | 0.295 (0.111 to 0.480) | 0.002** | 0.287 (0.102 to 0.471) | 0.003** | 0.216 (0.029 to 0.403) | 0.024* |
| HD | 0.892 (0.468 to 1.316) | <0.001*** | 0.884 (0.466 to 1.303) | <0.001*** | 0.747 (0.321 to 1.173) | 0.001** |
| PWB | 0.633 (0.282 to 0.984) | 0.001** | 0.615 (0.264 to 0.967) | 0.001** | 0.446 (0.099 to 0.794) | 0.012** |
| HLD | 0.783 (0.438 to 1.128) | <0.001*** | 0.793 (0.444 to 1.142) | <0.001*** | 0.737 (0.372 to 1.102) | <0.001*** |
| HHD | 0.422 (−0.006 to 0.849) | 0.053 | 0.406 (−0.084 to 1.044) | 0.094 | 0.358 (−0.099 to 0.806) | 0.116 |

Models were fit to estimate associations with sequential adjustment for age and gender (model 2), and exercise status (model 3).

*Significant association at p<0.05; **significant association at p<0.01; ***significance association at p<0.001.

HD, Hepatitis Distress; HHD, Hepatitis-specific Health Distress; HLIM, Hepatitis-specific Limitations; MCS, Mental Health Component; PCS, Physical Health Component; PWB, Positive Wellbeing.
The greatest barriers to exercise were time, with patients in both groups indicating that taking time away from family for PA/exercise was prohibitive, and that family members discouraged PA/exercise. Both of these barriers need to be addressed to design a successful PA/exercise intervention for this patient population and thus future research should seek to establish the attitudes of family members early in the design stage. In the present study, other commonly perceived barriers such as cost and accessibility to PA/exercise were perceived no differently in those that did and did not exercise regularly. Although this is somewhat of a surprising finding, it is likely attributable to a lack of difference in socioeconomic status between the two groups with patients in this study.

**Study limitations**

The main limitations to the study are firstly the use of self-reporting to ascertain PA levels at a single time point, which lacks the precision of objective methods and may result in over-reporting or under-reporting of PA/exercise duration and intensity and may also not reflect historic activity levels. Future studies should seek to employ objective measures of PA (such as accelerometry) to provide a detailed description of 24-hour activity levels (including intensity) over a 7-day period. Second, the EBBS asks patients to ‘score’ their attitudes towards exercise on a scale of 1–4 but does not allow patients to elaborate on their responses. A more in-depth qualitative analysis of patient (and their families/friends) perceptions of benefits and barriers to exercise participation may be warranted prior to designing a targeted intervention for patients with HCV. Third, we were unable to ascertain whether the association between PA/exercise and reduced HRQoL was ‘cause’ or ‘effect’. Fourth, the sample size was relatively small and consisted of predominately relatively older white men who were seen in secondary care which may limit generalisability and may be a factor accounting for our findings showing no association between PA/activity and cardiometabolic risk. Further larger studies in more diverse cohorts should be undertaken to confirm or refute these findings.

In conclusion, PA/exercise could be an important tool for improving HRQoL in patients with HCV irrespective of improvements in clinical parameters. Addressing specific motivators/barriers to exercise for patients will be key to designing effective PA/exercise interventions in this patient population to ensure maximum uptake and adherence.

**Competing interests** SMcP: consultancy/speaker fees from Abbvie, Allergan, BMS, Cambivox, Gilead, Intercept, MSD, Novartis and Sequana. MDC: consultancy/speaker fees from Dexcelom, Eli-Lilly, MSD, Novonordisk, Sanofi.

**Patient consent for publication** Not required.

**Ethics approval** The study was approved by the North East – Tyne and Wear South Research Ethics Committee (16/NE/0239) and all patients provided written informed consent before enrolment.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. Data are available on request from stuart.mcpherson2@nhs.net.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

**ORCID iD**

Stuart McPherson http://orcid.org/0000-0002-5638-2453

**REFERENCES**

1. WHO. Global hepatitis report. World Health Organisation, 2017.

2. Lee KK, Steilze D, Bing R, et al. Global burden of atherosclerotic cardiovascular disease in people with hepatitis C virus infection: a systematic review, meta-analysis, and modelling study. *Lancet Gastroenterol Hepatol* 2019;4:794–804.

3. Badawi A, Di Giuseppe G, Arora P. Cardiovascular disease risk in patients with hepatitis C infection: results from two general population health surveys in Canada and the United States (2007-2017). *PLoS One* 2018;13:e208839.

4. Fabiani S, Fallahi P, Ferrari SM, et al. Hepatitis C virus infection and development of type 2 diabetes mellitus: systematic review and meta-analysis of the literature. *Rev Endocr Metab Dist* 2018;19:405–20.

5. Butt AA, Yan P, Shuaib A, et al. Direct-Acting antiviral therapy for HCV infection is associated with a reduced risk of cardiovascular disease events. *Gastroenterology* 2019;156:987–96.

6. Rossi C, Jeong D, Wong S, et al. Sustained virological response in interferon-based hepatitis C regimen is associated with reduced risk of extrahepatic manifestations. *J Hepatol* 2019;71:1116–25.

7. McPherson S, Gosrani S, Hogg S, et al. Increased cardiovascular risk and reduced quality of life are highly prevalent among individuals with hepatitis C. *BMJ Open Gastroenterol* 2020;7:e000470.

8. Petta S, Craxi A. Extrahepatic manifestations of chronic viral C hepatitis. *Gastroenterol Clin North Am* 2020;49:547–60.

9. Louie KS, St Laurent S, Forsseen UM, et al. The high comorbidity burden of the hepatitis C virus infected population in the United States. *BMC Infect Dis* 2012;12:86.

10. Barreira DP, Marinho RT, Bichò M, et al. Psychosocial and neurocognitive factors associated with hepatitis C – implications for future health and wellbeing. *Front Psychol* 2019;9:2666.

11. Cossais S, Schwarzinger M, Pol S, et al. Quality of life in patients with chronic hepatitis C infection: severe comorbidities and disease perception matter more than liver-disease stage. *PLoS One* 2019;14:e0221556.

12. Younossi ZM, Stepanova M, Reddy R, et al. Viral eradication is required for sustained improvement of patient-reported outcomes in patients with hepatitis C. *Liver Int* 2019;39:54–9.

13. NHS Digital. Health survey for England 2016: physical activity in adults, 2016.

14. Ahmad A, Ali H. Comparative effects of two exercise training programs on health-related quality of life in middle-aged women with non-alcoholic fatty liver disease. *Advances in Rehabilitation* 2020;34:1–10.

15. Abdelbasset WK, Tantawy SA, Kamel DM, et al. A randomized controlled trial on the effectiveness of 8-week high-intensity interval exercise on intrahepatic triglycerides, visceral lipids, and health-related quality of life in diabetic obese patients with nonalcoholic fatty liver disease. *Medicine* 2019;98:e14918.

16. Moya-Nájera D, Moya-Herraiz Ángel, Compte-Torroro L, et al. Combined resistance and endurance training at a moderate-to-high intensity improves physical condition and quality of life in liver transplant patients. *Liver Transpl* 2017;23:1273–81.
17 Alberti KGMM, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International diabetes Federation Task force on epidemiology and prevention; National heart, lung, and blood Institute; American heart association; world heart Federation; international atherosclerosis Society; and international association for the study of obesity. Circulation 2009;120:1640–5.

18 Ware JE, Bayliss MS, Mannocchia M, et al. Health-Related quality of life in chronic hepatitis C: impact of disease and treatment response. The Interventional therapy group. Hepatology 1999;30:550–5.

19 Maruish M, Kosinski M, Bjorner J, et al. User’s manual for the SF36v2 Health Survey. Quality Metric Incorporated 2011.

20 Sechrist KR, Walker SN, Pender NJ. Development and psychometric evaluation of the exercise benefits/barriers scale. Res Nurs Health 1987;10:357–65.

21 Government U. English indices of deprivation 2019. National Statistics, 2019.

22 Tian D, Meng J. Exercise for prevention and relief of cardiovascular disease: prognoses, mechanisms, and approaches. Oxid Med Cell Longev 2019;2019:1–11.

23 Thompson P, Buchner D, Pina I. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on clinical cardiology (Subcommittee on exercise, rehabilitation, and prevention) and the Council on nutrition, physical activity, and metabolism (Subcommittee on physical activity). Circulation 2003;107.

24 Hillmeister P, Tadic M, Ngare N, et al. Exercise and cardiovascular diseases. Acta Physiol 2020;229.e13476.

25 NHS Digital. Statistics on smoking England 2019. NHS Digital, 2019.

26 Galant LH, Forgariarini Junior LA, Dias AS, et al. Functional status, respiratory muscle strength, and quality of life in patients with cirrhosis. Rev Bras Fisioter 2012;16:30–4.

27 Konishi I, Hiasa Y, Tokumoto Y, et al. Aerobic exercise improves insulin resistance and decreases body fat and serum levels of leptin in patients with hepatitis C virus. Hepatol Res 2011;41:928–35.

28 McKenna O, Blake C. Management of hepatitis C: the potential benefits of exercise. Physical Therapy Reviews 2007;12:271–6.

29 Nobili V, Carter-Kent C, Feldstein AE. The role of lifestyle changes in the management of chronic liver disease. BMJ Med 2011;9:70.

30 Pattullo V, Duarte-Rojo A, Soliman W, et al. A 24-week dietary and physical activity lifestyle intervention reduces hepatic insulin resistance in the obese with chronic hepatitis C. Liver Int 2013;33:410–9.

31 Vázquez-Vandyck M, Roman S, Vázquez JL, et al. Effect of Breathwalk on body composition, metabolic and mood state in chronic hepatitis C patients with insulin resistance syndrome. World J Gastroenterol 2007;13:6213–8.

32 Zucker DM. An intervention to prevent symptoms associated with hepatitis C: a pilot study. Appl Nurs Res 2010;23:116–20.

33 Keating SE, Hackett DA, George J, et al. Exercise and non-alcoholic fatty liver disease: a systematic review and meta-analysis. J Hepatol 2012;57:157–66.

34 Hashida R, Kawauchi T, Bekki M, et al. Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: a systematic review. J Hepatol 2017;66:142–52.

35 Hallsworth K, Adams LA. Lifestyle modification in NAFLD/NASH: facts and figures. JHEP Reports 2019;1:468–79.

36 St George A, Bauman A, Johnston A, et al. Effect of a lifestyle intervention in patients with abnormal liver enzymes and metabolic risk factors. J Gastroenterol Hepatol 2009;24:399–407.

37 Catania VE, Malaguarnera G, Fiorenza G, et al. Hepatitis C virus infection increases fatigue in health care workers. Diseases 2020;8:37.

38 Senmo N, Müllhaupt B, Ruckstuhl L, et al. A prospective, multicenter, post-marketing observational study to measure the quality of life of HCV genotype 1 infected, treatment naïve patients suffering from fatigue and receiving 3D regimen: the HEMATITE study. PLos One 2020;15:e0241267.