Exercise-based interventions for people with long term conditions: an overview of systematic reviews

Supplementary files

Contents

1. Search strategy
Search 1

Medline search 23rd March 2022
Ovid MEDLINE(R)

1	(LONG* TERM CONDITION* or CHRONIC DISEAS* or MULTIMORBIDITY or CHRONIC CONDITION* or LONG* TERM ILLNESS* or CHRONIC ILLNESS*).ab,kw,ti.
2	(long adj3 (covid* or ncov* or novel coronavirus or novel betacoronavirus or sars-ncov-2 or sars-cov-2)).mp.
3	((chronic* or longterm or long term or long-term) adj3 (post covid or post-covid or postcovid)).mp.
4	(covid adj2 (consequence* or impact or post-acute or chronic or prolonged or persist*)).ab,kw,ti.
5	Chronic Disease/
6	Rehabilitation/ or Exercise/ or Exercise therapy/
7	(rehabilit* or exercise*).ab,kw,ti.
8	(exercise adj therapy).ab,kw,ti.
9	(physical* adj (fit* or train* or therap* or activ*)).ab,kw,ti.
10	(train* adj (strength* or resistance or aerobic* or exercise*)).ab,kw,ti.
11	((exercise* or fitness) adj3 (treatment or intervent* or program*)).ab,kw,ti.
12	((lifestyle or life style) adj5 (interven* or program* or treatment*)).ab,kw,ti.
13	((behavior* or behaviour*) adj5 (modify or modificat* or therap* or change)).ab,kw,ti.
14	Physical Fitness/
15	(fitness or capacity or function*).ab,kw,ti.
16	(oxygen consumption or oxygen uptake).ab,kw,ti.
17	Oxygen consumption/
18	(VO2 adj (peak or max)).ab,kw,ti.
19	(physical* adj (fit* or train* or therap* or activ*)).ab,kw,ti.
20	"six min* walk* test".ab,kw,ti.
21	(incremental shuttle walk or ISWT).ab,kw,ti.
22	Physical Endurance/
23	(endurance or speed or distance).ab,kw,ti.
24	"Activities of Daily Living"/
25	(activities of daily living or ADL).ab,kw,ti.
26	Muscle Strength/
27	(strength or force or power).ab,kw,ti.
28	(Balance or frailty or mobility or gait or falls).ab,kw,ti.
29	"Quality of Life"/
30	(quality of life or QOL or HRQOL or symptom* or burden or qaly or short form* or SF12 or SF36 or euroqol or eq5d).ab,kw,ti.
31	Mortality/
32	(mortality or Hospital* or admission or inpatient or Disability or activity limitation or Physical activ* or pedometer or accelerometer or IPAQ or steps or energy expenditure or EE).ab,kw,ti.
33	1 or 2 or 3 or 4 or 5
34	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
35	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
36	33 and 34 and 35
37	MEDLINE.tw.
38	systematic review.tw.
39	meta-analysis.pt.
40	intervention$.ti.
41	37 or 38 or 39 or 40
42	36 and 41
43	randomized controlled trial.pt.
44	42 not 43
45	limit 44 to yr="2000 -Current"

Search 2

Medline search 1st June 2022
Ovid MEDLINE(R)

1	Alcohol-Related Disorders/ or Fatigue Syndrome, Chronic/ or Depression/ or Bulimia/ or Anorexia Nervosa/ or Irritable Bowel Syndrome/ or Peripheral Vascular Diseases/ or Thyroid Diseases/ or Anxiety/ or Liver Diseases/ or Diverticular Diseases/ or Anemia, Pernicious/ or Constipation/ or Meniere Disease/ or Polycystic Ovary Syndrome/ or Dyspepsia/ or Sinusitis/ or Epilepsy/ or Migraine Disorders/ or Prostatic Diseases/ or Hepatitis, Viral, Human/ or Atrial Fibrillation/ or Glaucoma/ or Eczema/ or Coronary Disease/ or Osteoporosis/ or Substance-Related Disorders/ or Dementia/ or Hypertension/ or Schizophrenia/ or Bipolar Disorder/
2	Rehabilitation/ or Exercise/ or Exercise therapy/
3	(rehabilit* or exercise*).ab,kw,ti.
4	(exercise adj therapy).ab,kw,ti.
5	(physical* adj (fit* or train* or therap* or activ*)).ab,kw,ti.
6	(train* adj (strength* or resistance or aerobic* or exercise*)).ab,kw,ti.
7	((exercise* or fitness) adj3 (treatment or intervent* or program*)).ab,kw,ti.
8	((lifestyle or life style) adj5 (interven* or program* or treatment*)).ab,kw,ti.
9	((behavior* or behaviour*) adj5 (modify or modificat* or therap* or change)).ab,kw,ti.
10	Physical Fitness/
11	(fitness or capacity or function*).ab,kw,ti.
12	(oxygen adj consumption).ab,kw,ti.
13	(oxygen adj uptake).ab,kw,ti.
14	Oxygen consumption/
15	(VO2 adj (peak or max)).ab,kw,ti.
16	(physical* adj (fit* or train* or therap* or activ*)).ab,kw,ti.
17	"six min* walk* test".ab,kw,ti.
18	(incremental shuttle walk or ISWT).ab,kw,ti.
19	Physical Endurance/
20	(endurance or speed or distance).ab,kw,ti.
21	"Activities of Daily Living"/
22	(activities of daily living or ADL).ab,kw,ti.
23	Muscle Strength/
24	(strength or force or power).ab,kw,ti.
25	(Balance or frailty or mobility or gait or falls).ab,kw,ti.
26	"Quality of Life"/
27	(quality of life or QOL or HRQOL or symptom* or burden or qaly or short form* or SF12 or SF36 or euroqol or eq5d).ab,kw,ti.
28	Mortality/
29	(mortality or Hospital* or admission or inpatient or Disability or activity limitation or Physical activ* or pedometer or accelerometer or IPAQ or steps or energy expenditure or EE).ab,kw,ti.
30	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
32	MEDLINE.tw.
33	systematic review.tw.
34	meta-analysis.pt.
35	intervention$.ti.
36	32 or 33 or 34 or 35
37	randomized controlled trial.pt.
38	36 not 37
39	1 and 30 and 31
40	38 and 39
41	limit 40 to yr="2000 -Current"

2. Supplementary Table 1 - List of included LTCs adapted from the Cambridge Multimorbidity Score and Barnett 2012

Alcohol problems	Chronic fatigue syndrome	Depression	Inflammatory bowel disease	Parkinson's disease	Stroke or transient ischaemic attack (TIA)
Anorexia nervosa or bulimia	Chronic kidney disease	Diabetes mellitus	Irritable bowel syndrome	Peripheral vascular disease	Thyroid disease
Anxiety	Chronic liver disease	Diverticular disease	Long-COVID	Pernicious anaemia	Treated constipation
Arthritis	Chronic obstructive pulmonary disease (COPD)	Endometriosis	Meniere's disease	Polycystic ovarian syndrome	Treated dyspepsia
Asthma	Chronic sinusitis	Epilepsy	Migraine	Prostate disorders	Viral hepatitis
Atrial fibrillation	Connective tissue disease	Glaucoma	Multiple sclerosis	Psoriasis or eczema	
Bronchiectasis	Coronary heart disease	Heart failure	Osteoporosis	Psychoactive substance misuse	
Cancer	Dementia	Hypertension	Painful condition	Schizophrenia or bipolar affective disorder	

3. List of eligible but not selected reviews

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4. Primary study overlap

Total primary studies included across all selected systematic reviews and supplementary RCT studies = 1,218. Of these, 990 were RCTs that met our inclusion criteria. The primary studies listed in the table below overlapped across the listed systematic reviews (non-overlapping primary studies and systematic reviews not shown). Blue studies met our inclusion criteria and were considered in our results, orange studies were not eligible (non-RCT) and did not contribute to our results/conclusions. The total corrected covered area (CCA) was calculated as 0.02%.

LTC / **Primary Study**	**Cancer** (haem; Knips 2019) 18 studies included	**Anaemia** (Courneya 2009) Single RCT	**Cancer** (advanced metastatic; Chen 2020) 15 studies included	**Alcohol Problems** (Gur 2020) 10 studies included	**Psychoactive substance abuse** (Dowla 2022) 42 studies included	**Arthritis** (osteo-hip; Fransen 2014) 10 studies included	**Arthritis** (osteo-knee; Fransen 2015) 54 studies included
Courneya 2009	x	x					
Chang 2008	x		x				
Gur 2017				x	x		
Giesen 2016				x	x		
Hallgreen 2014				x	x		
Abbott 2013						x	x
Van Baar 1998						x	x

5. Supplementary Table 2 – Characteristics of LTC participants across selected SRs and RCTs as reported by authors

LTC	Population definition	Comorbidities considered	Age (mean age range unless otherwise stated)	Sex (median % female, unless otherwise stated)	Diversity information (eg. SES, ethnicity)
Alcohol problems	All participants had a diagnosis of AUD based on Diagnostic and Statistical Manual of Mental Disorders (DSM)-I, DSMII, DSM-III, DSM-III-R, DSM-IV, DSM-V, the International Classification of Disease, Tenth Revision (ICD-10), the Alcohol Use Disorders Identification Test (AUDIT), or guidelines of the National Institute on Alcohol Abuse and Alcoholism. We excluded studies with a heterogeneous sample consisting of AUD participants (eg, SUBs and post-traumatic disorders)."	No	20.1 to 48.2 years	33.3%	Not reported
Anaemia*	Eligible patients had a histologically confirmed nonmyleoid cancer diagnosis, an Hb level of 80-110 g/l, an Eastern Cooperative Oncology Group performance status score of 0-2, completed definitive surgery, an expected survival duration ≥3 months, and were English speaking and ≥18 years of age.	Participants had cancer diagnoses alongside mild-to-moderate anaemia. Exclusion criteria included: iron deficiency (ferritin <12µg/l), had received an erythropoiesis-stimulating agent (ESA) within 4 weeks of randomization, or had uncontrolled hypertension, cardiac abnormalities, a psychiatric illness, a known hematologic disorder causing anaemia, substantial lung, pleural, or pericardial disease, pre-existing bone metastases at high risk for fracture, or contraindications to maximal exercise testing.	Mean age 56 years	81.8%	Completed university: 43.6% Income >$60,000/year: 25.5%
Anorexia	Patients with anorexia nervosa	Exclusion criteria: "other diagnoses", not specified further	20 to 29 years	99% female	"predominantly Caucasian females"
Anxiety	Participants had elevated anxiety symptoms using a validated assessment instrument or were diagnosed with an anxiety disorder	Some of the studies allowed individuals to participate if they had either elevated anxiety or another condition (e.g., depression, medical comorbidities). Studies that did not provide data on anxiety related outcomes specifically for the participants with elevated pre-treatment anxiety were excluded	19 to 64 years	range across included studies: 11-100%	Not reported
Arthritis (osteo-, hip)	Adults, men or women, with either an established diagnosis of hip OA according to accepted criteria or self reporting hip OA on the basis of chronic anterior joint pain (without radiographic confirmation).	No	58 to 70 years	range 75-80% female (only reported in 3 studies)	Not reported
Arthritis (osteo-, knee)	Male and female adults given an established diagnosis of knee OA according to accepted criteria (Altman 1991), or	"Many study cohorts comprised participants who were overweight	53 to 75 years	range 42-100% female	Not reported

	who self reported knee OA on the basis of chronic joint pain (with or without radiographic confirmation).	(body mass index (BMI) 25 to 29.9 kg/m2) or obese (BMI ≥ 30 kg/m2)."			
Arthritis (rheumatoid)	Patients with RA and did not have other serious diseases	Inclusion criteria – without other serious diseases	41.4 to 66.6 years	range 62 to 83% female	Not reported
Asthma	Human adults (≥18 years) with a clinical diagnosis of asthma as the primary respiratory disease	No	22 to 68 years	Range 36 to 98%	Not reported
Atrial fibrillation	Adults with atrial fibrillation (aged 18 and over with no upper limit). Specified populations (permanent AF, persistent AF, paroxysmal AF, chronic AF)	No	Not reported	65%	Not reported
Bronchiectasis	Individuals diagnosed with non-CF bronchiectasis according to physician diagnosis or clinical evidence or high resolution computed tomography	No	Not reported	Range 19-52%	Not reported
Cancer (solid tumour)	Included adult patients (aged ≥18), patients diagnosed with cancer, patients who had completed their main treatment for cancer but might be still undergoing hormonal treatment	No	Mean 55 (range 39-74) years	range 0-100%	Not reported
Cancer (haematological)	Adults (18 years and over) with confirmed diagnoses of haematological malignancies	No	20.8 to 58.8 years	Not reported	Not reported
Cancer (advanced metastatic)	Cancer that has spread to other places in the body and usually cannot be cured or controlled with treatment	No	47.5 to 72.4 years	27 to 67%	Not reported
Chronic fatigue syndrome	Male and female participants over the age of 18 years, irrespective of cultures and settings. Included studies in which participants fulfilled the following diagnostic criteria for CFS or ME: • Fatigue, or a symptom synonymous with fatigue, was a prominent symptom; • Fatigue was medically unexplained (i.e. other diagnoses known to cause fatigue such as anorexia nervosa or sleep apnoea could be excluded); • Fatigue was sufficiently severe to significantly disable or distress the participants; • Fatigue persisted for at least 6 months.	Inclusion criteria: studies involving participants with co-morbid physical or common mental disorders were eligible for inclusion only if the co-morbidity did not provide an alternative explanation for fatigue. Depression ranged from 18-39% participants	33 to 44.6 years	range 65-78%	34-39% working or studying at least part time (where reported)
Chronic kidney disease	Chronic kidney disease, single or both genders of age ≤80 years. Included haemodialysis and non dialysis dependent CKD patients (stages not specified)	No	18 to 75 years	Not reported	Not reported
Chronic liver disease	Participants with cirrhosis of any age or sex, irrespective of the severity or aetiology. Included %range: Alcohol 7.7-86% Chronic hepatitis C 5-38.5% Non-alcoholic steatohepatitis 0-33.3%	No	51 to 65.5 years	16.7 to 50%	Not reported
Chronic obstructive pulmonary disease	Clinical diagnosis of COPD according to the Global Obstructive Lung Disease Initiative criteria (Global Strategy for the Diagnosis, Management and Prevention of COPD)	No	52 to 77.6 years	0-70%	Not reported
Connective tissue disease	Interstitial lung disease of any origin, diagnosed according to investigator definitions	No	36 to 72 years	28-67%	Not reported

Coronary heart disease	Adult (≥18 years) men and women, in either hospital-based or community-based settings, who have had a myocardial infarction (MI), or who have undergone revascularisation (CABG, PCI) or who have angina pectoris or coronary artery disease defined by angiography.	No	47 to 77 years	<15% overall	Not reported
Dementia	Primary diagnosis of mild cognitive impairment or dementia	No	65.3 to 89.2 years	Not reported	Not reported
Depression	Adults with a primary diagnosis of major depressive disorder (MDD) according to established criteria (e.g., Diagnostic and Statistical Manual of Mental Disorders (DSM)(American PsychiatricAssociation,1994, 2013) or International Classification of Diseases (ICD) (World Health Organization, 1993) or those with increased depressive symptoms determined by a validated screening measure (e.g., Hamilton Rating Scale for Depression, (HAM-D), (Hamilton,1967), Beck Depression Inventory (BDI)(Beck etal.,1961), Geriatric Depression Scale (GDS) (Yesavage,1988) or other) according to the author's criteria. Also included studies meeting criteria that included some participants with other related diagnoses, such as dysthymia. This decision was based on the fact that dysthymia is categorized as a chronic and milder disorder within the depressive disorder spectrum (American PsychiatricAssociation, 2013)"	One study included participants with depression and participants with additional co-morbid diagnoses, such as cardiovascular diseases	38.8 to 76.4 years	50-100%	Not reported
Diabetes mellitus	Males and females with type 2 diabetes. Ideally, the diagnostic criteria for type 2 diabetes mellitus should have been described in the trial. To be consistent with changes in classification and diagnostic criteria of diabetes through the years, the diagnosis should have been established using the standard criteria valid at the beginning of the trial. Acceptable diagnostic criteria included those described by: the National Diabetes Data Group standards (NDDG 1979), the World Health Organisation standards (WHO 1980; WHO 1999) or the American Diabetes Association standards (ADA 1997b).	No	45 to 65 years	0-70%	Not reported
Endometriosis	Women with any degree of endometriosis as diagnosed with an imaging or surgical modality, who presented with pain in the pelvic region (including dysmenorrhea, dyspareunia, or CPP).	No	Not reported	100%	Not reported
Epilepsy	Eligible participants were people with all types of epilepsy, of all age groups, and both genders.	No	19.7 to 25.8 years	72%	Not reported
Glaucoma	Primary open angle glaucoma	No	Not reported	Not reported	Not reported
Heart failure	Adults aged 18 years of older with HF. Participants were predominantly HFrEF and NYHA classes II and III.	2 studies reported rates of comorbidity	51 to 81 years	Median 21%	Only 10 trials reported on ethnicity – 47-100% white
Hypertension	Hypertensive, SBP>130 mmHg or DBP >80 mmHg, following the American College of Cardiology/American Heart Association	No	52.2 to 76 years	0-100%	Not reported

Inflammatory bowel disease	**Adults ≥18 years diagnosed with either Chron's disease or ulcerative colitis.**	**No**	**Not reported**	**Not reported**	**Not reported**
Irritable bowel syndrome	Inclusion criteria Not reported Diagnostic criteria of included participants: Rome II (n=3 studies) Rome III (n=8 studies)	No	19.6 to 53.6	Not reported	Not reported
Long-COVID	Adults (>18 years) diagnosed with COVID-19 at least four weeks before study enrollment, according to the definition of PACS	Exclusion criteria in eligible study: uncontrolled hypertension, uncontrolled chronic disease, cerebrovascular disease within 6 months, Intra-articular drug injection or surgical treatment of lower extremities within 6 months, Inability to walk independently with assistive device, History of severe cognitive or mental disorder or substance abuse"	49.2 to 69.4 (over all studies including non-eligible)	Mean 45% (over all studies including non-eligible)	Not reported
Migraine	Patients older than 18 years old and diagnosed with primary headaches based on the International Classification of Headache Disorders (ICHD), and referred by a physician were included	No	25.1 to 48 years	85%	Not reported
Multiple sclerosis	Adults aged>18 years with a definite diagnosis of MS, regardless of sex, disease duration, MS phenotype, or level of disability were considered eligible for inclusion	No	31.3 to 56 years	range 0-100%	Not reported
Osteoporosis	Persons (women and men) as community dwellers (not hospitalized) over the age of 45 diagnosed with osteoporosis (defined as a T-score≤−2.5 SD) with or without a fracture and with osteopenia (defined as a T-score between−1.0 and−2.5 SD) below the norm mean for a healthy female young adult.	Only mentioned that there was considerable diversity in the presence of comorbidities and medication use across studies	56 to 82 years	94.9% (based on all included trials – some ineligible)	"There was considerable diversity in terms of the socio demographic factors of participants." No further information provided
Painful condition (chronic back pain)	Adult participants with chronic nonspecific low back pain of more than 12 weeks' duration (defined as meaning back pain duration of the study group was greater than or equal to 12 weeks)	No	43.7 (95% CI 35.8 to 44.9)	59.7% (95% CI 55.1 to 64.2%)	Not reported
Painful condition (fibromyalgia)	Adults with fibromyalgia in studies that used published criteria for diagnosis (or classification) of fibromyalgia. Diagnosis could be based on ACR 1990 criteria - the preliminary diagnostic tool (Wolfe 1990), ACR 2010 criteria (Wolfe 2010), or a follow-up survey questionnaire (Wolfe 2011).	No	43.2 to 59 years	98%	Not reported
Parkinson's disease	Studies had to investigate people with PD according to established criteria, include people with PD scoring 1–3 on the Hoehn and Yahr scale	No	mean 65 years (range 59-76 years)	M:F ratio 2.1 : 1	Not reported
Peripheral vascular disease	Symptomatic intermittent claudication due to atherosclerotic disease. Intermittent claudication may be diagnosed objectively by an ABI < 0.9 or evidence of PAD on Doppler ultrasound or angiography, or both, or by questionnaire or	No	44 to 71 years	range 0-100%	Not reported

	clinically if objective measures such as ABI or imaging were not used or reported				
Polycystic ovarian syndrome	Reproductive-aged women with a diagnosis of polycystic ovary syndrome (PCOS) based on the National Institute of Health (NIH) diagnostic criteria (1990), the Rotterdam ESHRE/ASRM (2003) diagnostic criteria or the AE-PCOS Criteria (2006). We also included trials where the PCOS diagnosis had been verified by a general practitioner or specialist clinician.	Participants with T2DM, fasting hyperglycaemia, or glucose intolerance were explicitly excluded in 9 trials (50%), and 9 trials also excluded participants with any diagnosed CVD.	21.8 to 35.2 years	100%	Not reported
Prostate disorders	Diagnosed with prostate cancer	No	Not reported	0%	Not reported
Psychoactive substance misuse	Participants seeking treatment for substance use disorder (including patients who were engaged in a drug or alcohol treatment or had received a Diagnostic and Statistical Manual of mental disorders, fifth edition diagnosis for alcohol or any illicit or prescription drug) Included alcohol use disorder (n=7), polysubstance use (6), stimulant type drugs (6), opioid (3), heroin (3)	4 studies excluded participants with additional substance use disorders (additional to alcohol use disorder)	27 to 55 years	22%	Not reported
Schizophrenia	Patients with schizophrenia-spectrum disorder (SSD) or first episode of psychosis (FEP). SSD encompassed ICD-10 codes F20-F29: schizophrenia (SCZ), schizotypal, delusional, and other non-mood psychotic disorders. Schizophrenia only (n=25), any SSD diagnosis (n=3), FEP only (n=3), mixed FEP + SSD (n=7), other conditions included Schizoaffective disorder (SAD), Delusional disorder (DD), Acute and transient psychosis (ATP), Schizophreniform (SCZPH)	No	18 to 63 years	range 0-100%	Not reported
Stroke or TIA	Adult stroke survivors who were considered suitable for fitness training by the studies' authors; we used the study authors' definition of stroke. Participants were considered eligible irrespective of the time since stroke onset.	People with comorbidities excluded in 14 studies	Approximately 62 years	Range 13-85%	1 study included people with below 'per capita' income, below minimum wage was an inclusion criteria
Treated constipation	Study participants were adults (≥18 years), diagnosed with non-drug or other disease-induced constipation; the participants were able to exercise without assistance	Exclusion criteria: patients with mental illnesses or cognitive disorders. 6 studies excluded due to constipation caused by disease	33.25 to 86.15 years	Not reported	Not reported
Viral hepatitis*	Study 1: Cirrhotic adults aged 18–65 with a Child-Turcotte-Pugh (CTP) score ≤ 6 were eligible for inclusion. Cirrhosis was diagnosed using computed tomography or magnetic resonance imaging, transient elastography with liver stiffness measurement ≥ 13 kPa, or liver biopsy (Metavir fibrosis score = 4). The etiologies of cirrhosis included chronic hepatitis B (CHB) on antiviral drugs with virological suppression, chronic hepatitis C (CHC) with the sustained virological response (SVR), alcohol with abstinence ≥ 1 year, or non-alcoholic steatohepatitis (NASH). Patients were excluded if they had one or more of	Study 1: Exclusion criteria: significant comorbid diseases, such as cardiac diseases (coronary artery disease, cardiac arrhythmia, impaired ejection fraction < 60%, or positive exercise stress test ≥ 1 mm ST depression), chronic renal failure on dialysis, hematologic diseases (hemoglobin < 11 g/dL or platelet count < 50,000 cell/mm3), myopathy, or chronic lung	55.5 to 56.3 years	range 14-35%	Not reported

	the following conditions: (1) body mass index (BMI) ≥ 28 kg/m2; (2) large esophageal varices (EV) or uncontrolled EV or gastric varices; (3) active malignancy, including hepatocellular carcinoma; or, (4) significant comorbid diseases, such as cardiac diseases (coronary artery disease, cardiac arrhythmia, impaired ejection fraction < 60%, or positive exercise stress test ≥ 1 mm ST depression), chronic renal failure on dialysis, hematologic diseases (hemoglobin < 11 g/dL or platelet count < 50,000 cell/mm3), myopathy, or chronic lung diseases (severe asthma and chronic obstructive pulmonary disease). Study 2: All registered adults in the Midwest area of the Health Services Executive, Ireland, who had contracted hepatitis C through contaminated blood products were eligible. Candidates younger than 18 years and those infected through alternative means were excluded.	diseases (severe asthma and chronic obstructive pulmonary disease). Study 2: Total number of comorbidities (median, range) 2 (0-5). Comorbidities not described. "A simple count of medical diagnoses was used to quantify the level of comorbid disease in the cohort.

*RCT evidence only identified. CI: confidence interval; NR: not reported; SES: socioeconomic status.

6. Supplementary Table 3 – Characteristics of exercise interventions of selected SRs and RCTs as reported by authors

Condition	N Exercise only / multi-component [a]	Exercise frequency (sessions/ week)	Exercise intensity	Duration (per session)	Exercise type/mode	Resistance/ strength training included	Overall duration (range)	Setting/ delivery method	Modi-fications for co-morbidities?	Intervention reporting quality assessment (Tidier/CERT – mean score)
Alcohol problems	0/5	1 to 3	55-90% HRmax or <40-<60% VO2 peak	20-90 mins	Aerobic	No	8 to 24 weeks	Centre-based (hospital/ clinic)	Not reported	Not done
Anaemia (RCT only)	1	3	60-100% baseline peak power output	Not reported	Aerobic, cycle ergometry	No	12 weeks	Not reported	Individually tailored to each participant	CERT – total score = 8[c]
Anorexia	2/1	2 to 4	Not reported	60 mins	Flexibility, anaerobic and resistance/ strength, low/high impact aerobic, yoga, recreational games	Yes – included in 3 studies	2.5 weeks to 3 months	Eating disorder outpatient clinic, eating disorder unit, residential eating disorder	Not reported	Not done
Anxiety	8/4	1 to 5	50-90% HRmax or work output	16-90 mins	Aerobic (n=8), aerobic + resistance (n=2), mindfulness-based stretching (n=1), participants choice (n=1)	Yes – included in 2 studies	2 weeks – 6 months	supervised exercise (n=8), partially supervised (n=2), unsupervised (n=2)		Not done
Arthritis (osteo-, hip)	8/2	1 to 3	Not reported	30-60 mins	Aerobic, resistance, flexibility, tai chi, range of movement	Yes – included in 6 studies	6-12 weeks	2 described as provided by physiotherapist	Not reported	Not done
Arthritis (osteo-, knee)	41/16[b]	1 to 5	moderate, 60-80% HRmax, 50-80% 1RM, 50-85% HRreserve	20-60 mins	Strength, combination (strength + aerobic), aerobic, tai chi, baduanjin	Yes – included in 37 studies	1 to 24 months	Concurrent clinic/home (n=4); home based (n=7); classes (n=25); individual (n=18)	Not reported	Not done
Arthritis (rheumatoid)	13/0	1 to 7	30-100% max load, aerobic Not reported	5-80 min	Aerobic (water based, walking), combination, tai chi, resistance	Yes – included in 8 studies	3-24 weeks	Not reported	Not reported	Not done
Asthma	12/11[b]	1 to 5	60-90% HRmax, 60-90% VO2 peak, RPE 7-8(/10) or 12-14(/20), 60-100% max power output	20-90 min	Aerobic (walking, circuit training, bodyweight HIIT), resistance, yoga	Yes – included in 3 studies	4 weeks -12 months	Community, outpatient clinic, lab. Supervised by exercise physiologists, physicians, respiratory therapist.	Not reported	Not done
Atrial fibrillation	12/0	1 to 3	30-95% HRmax or 40-70% max	30-90 min	Aerobic, anaerobic, combination (aerobic	Yes – included in 4 studies	8 weeks – 6 months	Not reported	Not reported	Not done

			exercise capacity		+ anaerobic), qigong, yoga, resistance					
Bronchiectasis	0/4	2 to 7	75-85% VO2 max, 80% HR peak, RPE 12-14, 60-80% 1RM	20-45 min	Aerobic (treadmill walking, cycling, stair climbing, ski machine), resistance training	Yes – included in 3	8 weeks	Hospital outpatient or inpatient	Not reported	Not done
Cancer (solid tumour)	34/0	1 to 7	25-85% HRmax, 60-75% VO2 peak, moderate-vigorous, RPE 10-16	10-90 min	Aerobic (walking, cycling), strength/ resistance training	Yes – included in 4 studies	Median 13 weeks, range 3-60 weeks	Not reported	Not reported	Not done
Cancer (haematological)	15/3	2 to 5	Low to high, 50-70% HR reserve, 60-75% peak power output	10-70 min	Aerobic (walking, cycling), resistance	Yes – included in 4 studies	5-15 weeks	Not reported	Not reported	Not done
Cancer (advanced metastatic)	15/0	2 to 8	55-95% HRmax, >3 MET hours/ week, 60-80% VO2 peak, 30-80% max work rate, 40-70% 1RM, ≥13 RPE	20-120 min	Endurance, strength, walking, Nordic walking, yoga	Yes – included in 9 studies	0.5-6 months	Supervised by certified physiotherapist or instructor in 14 studies	Not reported	Not done
Chronic fatigue syndrome	7/2[b]	3 times per week to several times per day	40-75% VO2max	5-90 min	Aerobic (graded exercise training)	No	12-26 weeks	"most of the included studies encouraged participants to exercise at home"	Not reported	Not done
Chronic kidney disease	11/0	3 to 4	50-70% HR max, 40% 1RM; 11-15 RPE, mild to moderate	Not reported	Aerobic, resistance, combination (aerobic and resistance), inspiratory muscle training	Yes – included in 6 studies	8-24 weeks	9 intradialytic, 2 non-dialysis. Home based mentioned in 1 study	Not reported	Not done
Chronic liver disease	3/3	2 to 3	moderate to high, 60-80% VO2 peak	30-70 min	Aerobic, combination, resistance	Yes – included in 3 studies	8-14 weeks	One home based, otherwise Not reported. Delivered by exercise specialist, physiotherapist, nurses, cardiologist	Not reported	Not done
Chronic obstructive pulmonary disease	0/39	Not reported	Not reported	Not reported	yoga, tai chi, conventional exercises	Not reported	Not reported	Not reported	Not reported	Not done

Connective tissue disease	9/12	2 to 7	moderate to vigorous	30-120 min	endurance, pulmonary rehabilitation	Yes – included in 13 studies	5-48 weeks	Outpatient (n=18), inpatient (n=1), home-based (n=1), tele-rehab (n=1)	Not reported	Not done
Coronary heart disease	38/47	1 to 7	50-90% max/peak HR or HRR, 50-95% VO2 max, 11-16 RPE	20-90 min	most often aerobic including static cycling, walking or circuit training	Yes – included in 22 studies	Median 6 months, range 3 weeks to 42 months	21 home based programmes	Not reported	Not done
Dementia	30/8	1 to 7	30-70% VO2 max, "gentle", moderate to high, 40-85% HR reserve, 70-80% 1RM, 60% HRmax	15-150 min	aerobic, walking, dual-task, multimodal, ADL/functional training, strengthening, others	Yes – included in 3 studies	single session to ≥12 months	Institution (n=21), hospital (n=1), community (n=13), outpatient (n=2). Delivered by nurses, physiotherapist, researcher, physician, exercise scientist, occupational therapist, students, social centre staff	Not reported	Not done
Depression	0/6	2 to 5	light to moderate	Not reported	aerobic, mixed (yoga, tai chi, qigong)	No	3-32 weeks	outpatient (n=5), inpatient (n=1). Most studies supervised by exercise professionals	Not reported	Not done
Diabetes mellitus	11/3	1 to 7	65-75% HR reserve, 50-85% VO2max/ peak, up to 85% HR peak, low-moderate	30-120 min	aerobic, resistance, combination training, qigong	Yes – included in 7 studies	8 weeks-12 months	Not reported	Not reported	Not done
Endometriosis	0/2	2 to 4	50-70% HR max	40-120 min	cardio-fitness, flexibility, yoga	No	8-24 weeks	Not reported	Not reported	CERT – total score 12
Epilepsy	1/1	2 per day	Not reported	20-30 min	Yoga	No	5 weeks-6months	Trained instructor	Not reported	Not done
Glaucoma	0/1	7	Not reported	30 min	Not reported	No	Not reported	Not reported	Not reported	Not done
Heart failure	30/14	1 to 7	40-80% HRmax, 50-85% VO2 max, RPE 11-18	10-120 min	Aerobic, or aerobic + resistance	Yes – included in 14 studies	8-120 weeks	Centre-based, combination, or home-based (n=10)	Not reported	Not done
Hypertension	23/0	2 to 7	60-90% HRreserve, 45-75% VO2max, 50-80% 1RM, 11-13 RPE	20-210 min	Aerobic (walking, cycling, circuits), resistance (band, full body, upper/lower limbs & trunk)	Yes – included in 14 studies	6-36 weeks	Not reported	Not reported	Not done

Inflammatory bowel disease	5/2	1 to 7	60% VO2 max, 60% HR max	20 min – 6 hours	Aerobic, resistance, mind-body therapy (including yoga), lifestyle intervention	Yes – included in 3 studies	8 weeks- 1 year	1 reported as home based	Not reported	Not done
Irritable bowel syndrome	11/1[b]	2 per week to 2 per day	low to moderate	20-120 min	yoga, physical activity, Tai Ji, mountaineering	No	6-24 weeks	Not reported	Not reported	Not done
Long-COVID	0/2	1 to 4	40-80% HRmax	5-90 min	Aerobic + strength, pulmonary rehabilitation	Yes – included in 1 studies	6 weeks	Home-based	Not reported	Not done
Migraine	12/7	2 per week to every 2-3 hours	45-85% VO2 max, 70-95% HRmax, 13-16 RPE, 70-80% 12RM, ventilatory threshold	10-60 min	Aerobic, strength, combination, yoga	Yes – included in 8 studies	3 weeks – 6 months	Not reported	Not reported	TIDieR – total percentage 50%
Multiple sclerosis	22/0	1 to 5	60% VO2 max, RPE 8, 40-80% peak power output, 40-95% HRmax, 60-75% Wmax, 50-80% 1RM	27-69 min	Aerobic, resistance	Yes – included in 8 studies	3-26 weeks	Not reported	Not reported	Not done
Osteoporosis	15/1	1 to 7	50-80% 1RM	30-90 min	Gait, balance, functional, strength/ resistance, tai chi, multicomponent	Yes – included in 8 studies	5-52 weeks	Not reported	Not reported	Not done
Painful condition (chronic back pain)	<50%/>50 %	Not reported	“low dose”	Not reported	Resistance training, mixed, pilates, stretching, aerobic	Yes – included in 85 studies	0.14-26 weeks	Not reported	Not reported	Not done
Painful condition (fibromyalgia)	17/6	1 to 7	40-85% HRmax	45-180 min	Aerobic (walking, jogging, stationary bike), resistance (isotonic/ isometric), flexibility, belly dance, agility, co-ordination, balance	Yes – included in 19 studies	4-26 weeks	2 primarily home-based	Not reported	Not done
Parkinson’s disease	33/0	mean 2.7	60-85% HRmax, 30-90% 1RM	16-45 min	Treadmill, cycle, resistance – whole body programmes	Yes – included in 18 studies	4-104 weeks	Some home-based	Not reported	Not done
Peripheral vascular disease	30/2	2 to 7	Not reported	26-60 min	aerobic (walking, treadmill, arm cranking), resistance and combined training	Yes – included in 3 studies	2 weeks – 12 months	Primarily supervised and some included home-based exercise	Not reported	Not done
Polycystic ovarian syndrome	14/6[b]	3 to 5	40-95% HR max, 40-70% VO2 max/peak,	25-60 min	aerobic, resistance or combined	Yes – included in 6 studies	8-48 weeks	Not reported	Not reported	Not done

			1050-4200 kJ/week, 40-75% 1RM, 5-6/10 RPE							
Prostate disorders	16/0	2 to 7	55-100% HR max, 9-13 RPE, 3.0-6.0 METs, 55-100% VO2 peak, 500-1000 MET min/week	20-45 min	aerobic (walking, running), resistance or combined	Yes – included in 7 studies	8-36 weeks	Supervised (n=5), home-based (n=3), mix of supervised and home-based (n=4), supervised with suggested home-based (n=2)	Not reported	Not done
Psycho-active substance misuse	25/0	1 per week to 2 per day	Not reported	10-150 min	Aerobic, mind-body exercise (yoga/tai chi/qigong), aerobic + strength, strength only	Yes – included in 7	single session – 1 year	Inpatient addiction treatment facility/ rehabilitation centre/ residential treatment programme (n=15), outpatient unit/ treatment centre/clinic/AA/ community (n=5), withdrawal management (n=1)	Not reported	Not done
Schizophrenia	31/7	1 to 7	light to vigorous	20-360 min	aerobic, anaerobic, mind-body exercise (e.g. yoga), mixed (combination of aerobic + anaerobic or aerobic + mind-body)	Yes – included in 7	3-52 weeks	Inpatient (n=12), outpatient (n=26)	Not reported	Not done
Stroke or TIA	75/0	2 to 7	40-85% HR max, 40-70% HR reserve, 60-75% VO2 peak, 30-50% maximum effort, RPE ≤13, 40-100% 1RM	7-120 min	aerobic, resistance, mixed/combination	Yes – included in 43	2-24 weeks	Rehab centre/outpatient (n=34), community (n=10), hospital (n=12), home (n=5), mixed setting (n=3), exercise lab (n=1) Delivered by therapist, certified trainer, or PI assisted by physio students	Not reported	Not done
Treated constipation	9/0	2 to 7	Not reported	20-60 min	aerobic, resistance	Yes – included in 1 study	30 days – 24 weeks	Not reported	Not reported	Not done

Viral hepatitis (RCT only)	1/1	2 to 4	60-85% HR max	40-60 min	aerobic, resistance	Yes – included in 1 study	6-12 weeks	Centre based (n=1), home based (n=1). Delivered by sport scientist or physiotherapist	Not reported	CERT – total score 11

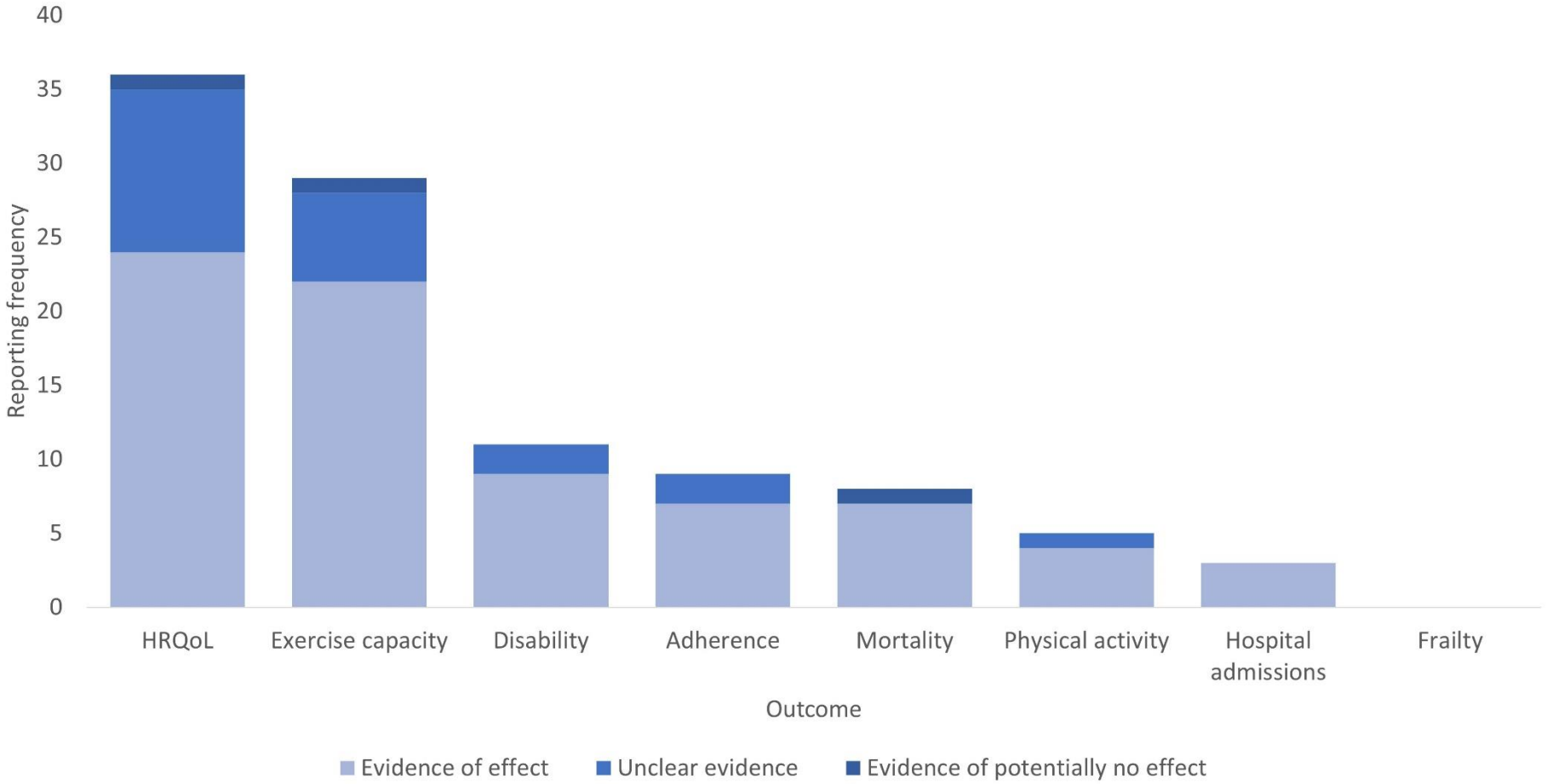
[a]Multicomponent = exercise + other (e.g., diet, education, psychological, medication); [b]: some studies had multiple intervention arms; [C]based on our own assessment
HR: heart rate; 1RM: one repetition max; VO2: oxygen consumption; RPE: rating of perceived exertion; TIDieR: Template for Intervention Description and Replication; CERT: Consensus on Exercise Reporting Template

7. Supplementary Table 4 – AMSTAR assessments for selected SRs

Condition	Q1	Q2*	Q3	Q4*	Q5	Q6	Q7*	Q8	Q9*	Q10	Q11*	Q12	Q13*	Q14	Q15*	Q16	Overall rating
Alcohol problems	Y	PY	N	N	N	Y	PY	PY	Y/N	N	N	N	N	Y	Y	Y	Low
Anorexia	Y	PY	N	N	Y	N	PY	PY	Y/N	N	Y	N	Y	Y	N	Y	Critically low
Anxiety	Y	N	N	N	Y	Y	N	PY	Y	N	NA	NA	Y	N	NA	Y	Low
Arthritis (osteo-, hip)	Y	Y	N	PY	Y	Y	Y	PY	Y	N	Y	N	Y	Y	Y	Y	Moderate
Arthritis (osteo-, knee)	Y	Y	N	PY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Arthritis (rheumatoid)	Y	N	N	N	Y	Y	PY	PY	Y	N	Y	N	Y	Y	Y	Y	Low
Asthma	Y	Y	N	N	Y	Y	PY	Y	Y/N	N	Y	N	Y	Y	N	Y	Critically low
Atrial fibrillation	Y	N	N	PY	N	N	N	PY	Y	N	Y	N	N	Y	Y	Y	Critically low
Bronchiectasis	Y	Y	N	PY	Y	Y	PY	N	Y	N	N	N	Y	N	N	N	Critically low
Cancer (solid tumour)	N	N	Y	PY	Y	Y	PY	N	Y	N	Y	Y	N	Y	Y	Y	Critically low
Cancer (haematological)	Y	Y	N	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Moderate
Cancer (advanced metastatic)	Y	N	N	Y	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	N	Y	Low
Chronic fatigue syndrome	Y	Y	N	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Moderate
Chronic kidney disease	Y	N	N	N	Y	N	PY	PY	PY	N	N	N	N	N	N	Y	Critically low
Chronic liver disease	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	N	N	Y	Moderate
COPD	N	N	N	PY	N	Y	PY	N	Y	N	Y	N	N	Y	Y	Y	Critically low
Connective tissue disease	Y	Y	N	PY	Y	Y	Y	PY	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Coronary heart disease	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
Dementia	Y	N	N	PY	Y	N	PY	Y	PY	N	Y	Y	Y	Y	Y	Y	Low
Depression	Y	N	N	PY	Y	Y	Y	Y	PY	N	Y	N	Y	Y	Y	Y	Low
Diabetes mellitus	Y	Y	N	PY	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Moderate
Endometriosis	Y	Y	N	PY	Y	Y	N	PY	Y	N	NA	NA	Y	Y	NA	Y	Low
Epilepsy	Y	Y	N	Y	Y	N	Y	PY	Y	N	N	N	Y	Y	N	Y	Low
Glaucoma	N	N	N	N	Y	N	N	N	N	N	NA	NA	N	N	NA	Y	Critically low
Heart failure	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
Hypertension	Y	N	N	N	N	N	Y	PY	Y	N	Y	N	N	N	Y	Y	Critically low
Inflammatory bowel disease	N	N	N	N	Y	Y	N	N	N	N	NA	NA	N	N	NA	Y	Critically low
Irritable bowel syndrome	N	N	N	N	Y	Y	N	N	Y	N	NA	NA	N	N	NA	Y	Critically low
Long-COVID	Y	PY	N	PY	Y	Y	PY	PY	Y	N	NA	NA	N	Y	NA	Y	Low
Migraine	Y	PY	N	PY	Y	Y	PY	PY	Y	N	N	N	Y	Y	Y	Y	Low
Multiple sclerosis	Y	Y	N	PY	Y	Y	PY	PY	Y	N	Y	N	N	Y	N	N	Low
Osteoporosis	Y	Y	N	PY	Y	N	PY	N	Y	N	Y	Y	Y	Y	N	Y	Moderate
Painful condition (chronic back pain)	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
Painful condition (fibromyalgia)	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
Parkinson's disease	Y	PY	N	Y	Y	Y	Y	PY	PY	N	Y	N	N	N	N	Y	Critically low
Peripheral vascular disease	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	Y	Y	Moderate
Polycystic ovarian syndrome	Y	Y	N	PY	Y	N	Y	PY	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Prostate disorders	Y	Y	N	Y	Y	Y	PY	Y	Y	N	Y	Y	Y	N	N	Y	Low
Psychoactive substance misuse	Y	PY	N	PY	Y	Y	PY	PY	N	N	N	N	Y	N	N	Y	Critically low
Schizophrenia	Y	Y	N	PY	Y	Y	PY	PY	Y	N	Y	Y	Y	Y	Y	N	Moderate
Stroke or TIA	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Treated constipation	N	N	N	PY	Y	Y	PY	PY	Y	N	N	N	Y	Y	N	Y	Critically low

*Critical domains. Y: yes, PY partial yes; N: no; NA: not applicable; Y/N: yes (sub domain one), no (sub domain two)

8. Supplementary Figure 1 – Frequency of outcome reporting across included studies



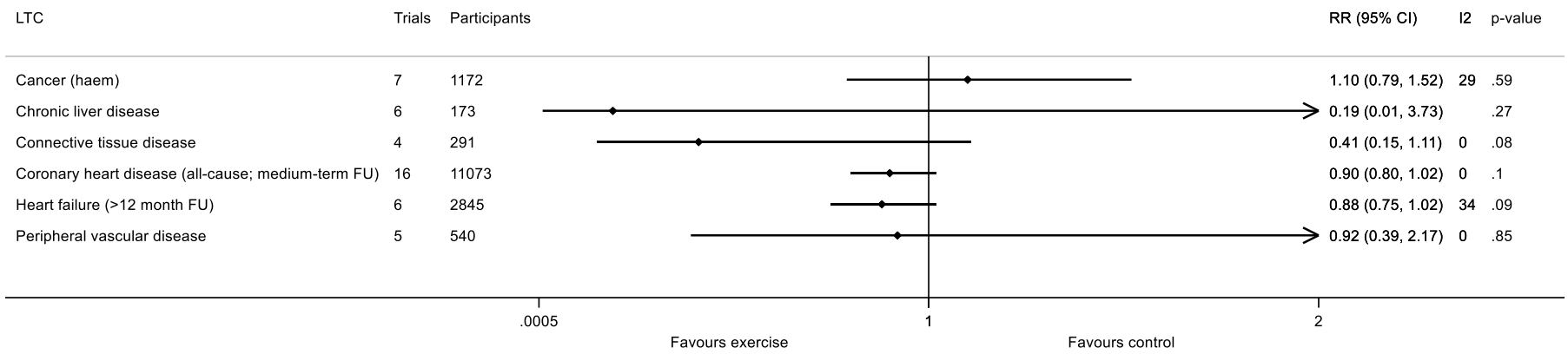
9. Supplementary Table 5 – Summary of exercise-based intervention vs control mortality by LTC

LTC	Effect estimates ***Follow-up***	N trials	N participants	N events Intervention vs Control	Exercise vs control effect RR (95% CI)	I^2	P-value	GRADE rating*
Bronchiectasis	Risk ratio *Follow-up NR*	1	NR	NR	3.0 (0.74 to 12.7)	NA	NR	NA
Cancer (haem)	Risk ratio *Follow-up NR*	7	1172	97 vs 87	1.10 (0.79 to 1.52)	29%	0.59	Low
Chronic liver disease	Risk ratio *Follow-up NR*	6	173	0 vs 2 (5 studies had 0 deaths in both groups)	0.19 (0.01 to 3.73)	NA	0.27	Moderate
Connective tissue disease	Odds ratio *6-12 months* Risk ratio†	4 4	291 291	5 vs 12	0.40 (0.14 to 1.12) 0.41 (0.15 to 1.11)	0%	0.08	Low
Coronary heart disease	Risk ratio **All cause:** *6-12 months* *>12-36 months* *>36 months* **CV mortality:** *6-12 months* *>12-36 months* *>36 months*	 26 16 11 15 5 8	 8823 11,073 3828 5360 3614 1392	 228 vs 242 467 vs 498 476 vs 493 109 vs 114 199 vs 239 56 vs 100	 0.87 (0.73 to 1.04) 0.90 (0.80 to 1.02) 0.91 (0.75 to 1.10) 0.88 (0.68 to 1.14) 0.77 (0.63 to 0.93) 0.58 (0.43 to 0.78)	 0% 0% 35% 0% 5% 0%	 0.13 0.10 0.34 0.34 0.008 0.0004	 Moderate NR NR NR NR NR
Heart failure	Risk ratio *<12 months* *>12 months*	 27 6	 2596 2845	 67 vs 75 244 vs 280	 0.89 (0.66 to 1.21) 0.88 (0.75 to 1.02)	 0% 34%	 0.47 0.09	 Low NR
Peripheral vascular disease	Risk ratio *Follow-up NR*	5	540	8 vs 9	0.92 (0.39 to 2.17)	0%	0.85	Moderate
Stroke/TIA	Risk difference **Cardiorespiratory training** *End of intervention (months NR)* *End of follow-up (months NR)* **Resistance training** *End of intervention* *End of follow-up* **Mixed training** *End of intervention*	 32 6 20 5	 1631 360 803 251	 2 vs 2 1 vs 1 1 vs 1 2 vs 2	 0.0 (-0.01 to 0.01) 0.0 (-0.03 to 0.03) 0.0 (-0.02 to 0.02) 0.0 (-0.04 to 0.04)	 0% 0% 0% 0%	 NA NA 0.99 0.97	 Low NR NR NR

	End of follow-up	23 13	1231 906	4 vs 9 4 vs 10	-0.0 (-0.02 to 0.01) -0.01 (-0.03 to 0.01)	0% 0%	0.5 0.22	NR NR

*GRADE rating as reported in SR. †Converted OR to RR by overview team. CV: cardiovascular; NA: not applicable; NR: not reported by SR authors

10. Supplementary Figure 2 – mortality forest plot comparing exercise-based intervention vs control



11. Supplementary Table 6 – Summary of exercise-based intervention vs control for hospital admissions by LTC

LTC	Effect estimate *Follow-up*	N trials	N participants	N events Intervention vs control	Exercise vs control effect RR (95% CI)	I^2	P-value	GRADE rating*
Bronchiectasis	Relative risk	1	NR	NR	1.5 (0.75 to 3.0)	NA	NR	NR
Coronary heart disease	Risk ratio **All cause:**							
	6-12 months	14	2030	130 vs 209	0.58 (0.43 to 0.77)	42%	0.0001	Moderate
	>12-36 months	9	5995	392 vs 417	0.92 (0.82 to 1.03)	0%	0.14	NR
	CV hospital admission: *6-12 months*	6	1087	40 vs 42	0.80 (0.41 to 1.59)	53%	0.53	Low
	>12-36 months	3	943	129 vs 141	0.92 (0.76 to 1.12)	0%	0.40	NR
Heart failure	Risk ratio **All cause:**							
	<12 months	21	2182	180 vs 258	0.70 (0.60 to 0.83)	19%	0.001	Moderate
	>12 months	6	2691	772 vs 825	0.70 (0.47 to 1.05)	66%	0.08	NR
	Disease specific: *<12 months*	14	1114	40 vs 61	0.59 (0.42 to 0.84)	11%	0.003	Low

*GRADE rating as reported in SR. NR: not reported by SR authors; CV: cardiovascular

12. Supplementary Table 7 – Summary of exercise-based intervention vs control for aerobic exercise capacity outcomes by LTC

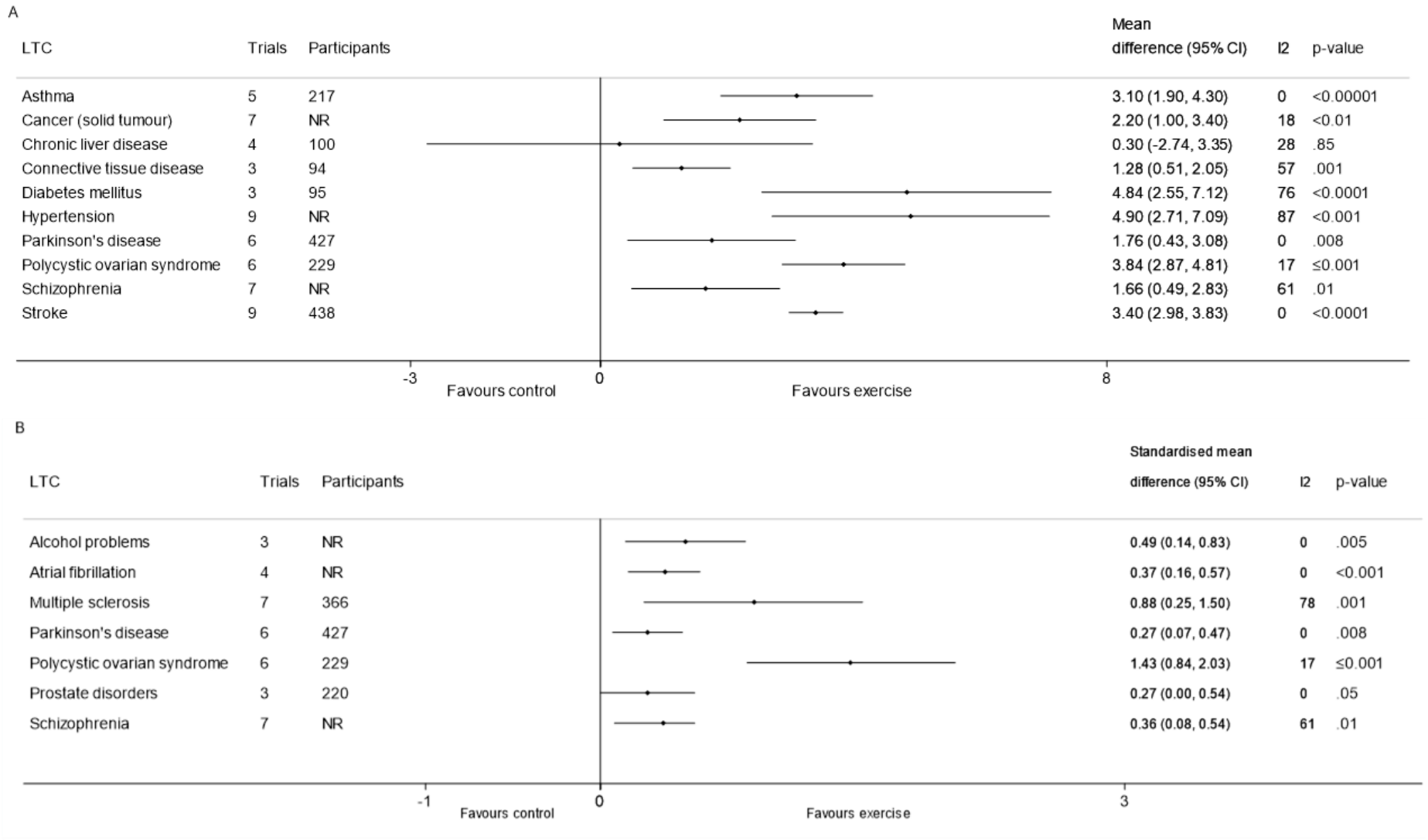
LTC	Unit of analysis	N trials	N participants	Exercise vs control effect SMD (95% CI)	Exercise vs control effect MD (95% CI)	I^2	p-value	Vote counting* or qualitative statement by authors	GRADE rating†
$VO_{2max/peak}$									
Alcohol problems	SMD	3	NR	0.487 (0.144 to 0.830)	-	0%	0.005	-	NR
Anaemia	mL/kg/min	1	55	-	-	-	-	1/1 trial favours exercise	NR
Asthma	mL/kg/min	5	217	-	3.1 (1.9 to 4.3)	0%	<0.00001	-	NR
Atrial fibrillation	SMD	4	NR	0.37 (0.16 to 0.57)	-	0%	<0.001	-	NR
Cancer (solid tumour)	mL/kg/min	7	NR	-	2.2 (1.0 to 3.4)	18%	<0.01	-	NR
Chronic liver disease	mL/kg/min	4	100	-	0.30 (-2.74 to 3.35)	28%	0.85	-	Low
Connective tissue disease	mL/kg/min	3	94	-	1.28 (0.51 to 2.05)	57%	0.001	-	NR
Diabetes mellitus	mL/kg/min	3	95	-	4.84 (2.55 to 7.12)	76%	<0.0001	-	NR
Hypertension	mL/kg/min	9	NR	-	4.90 (2.71 to 7.09)	87%	<0.001	-	NR
Multiple sclerosis	SMD (aerobic studies only)	7	366	0.88 (0.25 to 1.50)	-	78%	0.001	-	NR
Parkinson's disease	SMD & mL/kg/min Aerobic studies only Resistance studies only	 6 3	 427 75	 0.27 (0.07 to 0.47) -0.10 (-0.56 to 0.36)	 1.76 (0.43 to 3.08) NR	 0% 0%	 0.008 0.67	-	 NR NR
Polycystic ovarian syndrome	SMD & mL/kg/min post-intervention change from baseline	6 6	184 229	1.19 (0.40 to 1.99) 1.43 (0.84 to 2.03)	5.01 (3.48 to 6.54) 3.84 (2.87 to 4.81)	42% 17%	 ≤0.001 ≤0.001	-	NR NR
Prostate disorders	SMD	3	220	0.27 (-0.00 to 0.54)	-	0%	0.05	-	NR
Schizophrenia	SMD & mL/kg/min	7	NR	0.36 (0.08 to 0.63)	1.66 (0.49 to 2.83)	61%	0.011	-	NR
Stroke/TIA	mL/kg/min Cardiorespiratory training (end of intervention) Mixed training (end of intervention)	 9 2	 438 140	-	 3.40 (2.98 to 3.83) 1.40 (-0.19 to 2.99)	 0% 35%	 <0.0001 0.08	-	 Moderate Low
Viral hepatitis	mL/kg/min	1	22	-	-	-	-	1/1 trial favours exercise	NR
Other aerobic/overall									
Anaemia	Peak workload (Watts)	1	55	-	-	-	-	1/1 trial favours exercise	NR
Anxiety	"Fitness levels"	7	NR	-	-	NA	NA	4/7 (57%) trials favour exercise 3/7 (45%) neutral	NR
Asthma	Overall health-related physical fitness	12	477	0.67 (95% CI 0.46 to 0.89)	-	16%	p<0.0001	-	NR

Cancer (solid tumour)	Peak power output (W)	3	NR	-	21.0 (13.0 to 29.1)	0%	<0.01	-	NR
Cancer (haem)	Aerobic capacity/CV fitness measures	8	NR	-	-	-	-	11/14 (79%) results favour exercise 3/14 (21%) neutral	NR
Connective tissue disease	Peak work rate (W)	4	159	-	9.04 (6.07 to 12.00)	89%	<0.00001	-	Low
Prostate disorders	Submaximal aerobic capacity	6	346	0.49 (0.12 to 0.85)	-	61%	0.01	-	NR
Psychoactive substance abuse	Aerobic fitness	1	-	-	-	-	-	"As assessments and interventions varied greatly between each study, it is not possible to observe any trends in results"	NR
Schizophrenia	Peak power output (SMD & Watts)	2	NR	0.11 (-0.29 to 0.51)	25.01 (-67.93 to 117.95)	0%	0.604	-	NR
Stroke/TIA	Max cycling work rate (watts)	6	336	-	10.60 (1.88 to 19.33)	85%	0.02	-	NR

*'favours exercise': exercise better than control (P≤0.05); neutral: 'no difference' between exercise and control (P>0.05); 'favours control': control better than exercise (P≤0.05). †GRADE rating as reported in SR

MD: mean difference; SMD: standardised mean difference; CI: confidence interval; NR: not reported

13. Supplementary Figure 3 – Forest plot showing meta-analysis results for VO2max/peak. Panel A shows results reported as ml/min/kg with mean differences and as standardised mean differences on panel B.



14. Supplementary Table 8 – Summary of exercise-based intervention vs control for functional exercise capacity outcomes by LTC

LTC	Unit of analysis	N trials	N participants	Exercise vs control effect SMD (95% CI)	Exercise vs control effect MD (95% CI)	I^2	p-value	Vote counting* or qualitative statement by authors	GRADE rating†
6MWT									
Atrial fibrillation	SMD	5	NR	0.69 (0.19 to 1.19)	-	70.6%	0.007	-	NR
Cancer (solid tumour)	m	5	NR	-	29 (4 to 55)	20%	0.03		NR
Chronic Kidney disease	SMD (aerobic)	2	61	0.99 (0.45 to 1.54)		64%	0.003	-	NR
	m (combination training)	2	69		63.56 (43.44 to 83.68)	0%	<0.0001		
Chronic liver disease	m	4	105	-	56.06 (-9.14 to 121.26)	64%	0.09	-	Very low
COPD	m	34	NR	-	36.34 (26.51 to 46.17)	92%	<0.001	-	NR
Connective tissue disease	m, post-intervention	13	585	-	40.07 (32.70 to 47.44)	26%	<0.00001	-	Moderate
	m, long-term FU	5	297		32.43 (15.58 to 49.28)	43%	0.0002		Moderate
Dementia	m	7	402	-	50 (18 to 81)	79%	0.002	-	Moderate
Long-COVID	post-intervention	1	120	-	-	-	-	1/1 trial favours exercise	NR
	follow-up	1	120					1/1 trial favours exercise	
Painful condition (fibromyalgia)	m			-				-	
	short-term FU	5	306		52.77 (34.11 to 71.43)	0%	<0.0001		NR
	long-term FU	3	145		61.71 (15.37 to 108.1)	59%	0.01		NR
Parkinson's disease	SMD and m	5	250	0.89 (0.17 to 1.62)	69.2 (28.9 to 109.5)	83%	0.02	-	NR
Schizophrenia	SMD and m	3	NR	0.86 (0.15 to 1.56)	67.41 (36.21 to 98.62)	50%	0.018	-	NR
Stroke/TIA	m			-				-	
	cardiorespiratory training (end of intervention)	16	882		33.41 (19.04 to 47.78)	31%	<0.0001		High
	cardiorespiratory training (end of FU)	5	283		38.29 (7.19 to 69.39)	32%	0.02		NR
	resistance training (end of intervention)	5	238		24.98 (11.98 to 37.98)	0%	0.00		Low
	resistance training (end of FU)	2	117		22.41 (-27.87 to 72.69)	0%	0.38		NR
	mixed training (end of intervention)	10	720		35.00 (15.91 to 54.09)	28%	0.00		Low

	mixed training (end of FU)	4	464		47.48 (23.72 to 71.23)	0%	<0.0001		NR
Viral hepatitis	m	1	40	-	-	-	-	1/1 neutral	NR
Other functional/walking tests									
Arthritis (rheumatoid)	50ft walk test (SMD)	4	134	-0.64 (-0.99 to -0.28)	-	0%	NR	-	NR
Asthma	Walking distance (m)	7	139	-	40.5 (26.6 to 54.5)	0%	<0.00001	-	NR
Bronchiectasis	ISWT (m)	3	135	-	66.52 (51.57 to 81.68)	38%	<0.00001	-	NR
Cancer (solid tumour)	Sit and reach (cm)	2	NR	-	2 (-3 to 8)	0%	0.36	-	NR
Cancer (haem)	6MWD, 12 min walking test, balance, sit-to-stand - narrative	4	NR	-	-	-	-	5/6 results favour exercise 1/6 (17%) neutral	NR
Dementia	Timed-up-and-go (s)	11	606	-	-1.0 (-2 to 0)	18%	0.05	-	Moderate
	Walking speed (m/s)	7	568		0.13 (0.03 to 0.24)	90%	0.01		Moderate
Multiple sclerosis	Short walking test (aerobic trials only)	3	124	0.33 (-1.49 to 2.06)	-	69%	0.202	-	NR
	Short walking test (resistance trials only)	5	132	0.27 (0.07 to 0.47)		0%	0.000		NR
	Long walking test (aerobic trials only)	7	291	0.37 (-0.04 to 0.78)		43%	0.026		NR
	Long walking test (resistance trials only)	4	169	0.36 (-0.35 to 1.08)		48%	0.108		NR
Osteoporosis	Mobility	16	1065	-0.72 (-1.00 to -0.44)	-	77%	<0.00001	-	NR
Parkinson's disease	Timed up-and-go (SMD and s)							-	
	Aerobic studies only	6	255	-0.21 (-0.46 to 0.04)	-0.51 (-1.16 to 0.15)	0%	0.1		NR
	Resistance studies only	8	309	-0.62 (-1.01 to -0.24)	-1.45 (-2.56 to -0.34)	53%	0.002		NR
Peripheral vascular disease	Maximum walking distance (m)	10	500	-	120.36 (50.79 to 189.92)	89%	0.00	-	High
	Pain-free walking distance (m)	9	391		82.11 (71.73 to 92.48)	40%	<0.0001		High
	Max walking time (min)	12	577		4.51 (3.11 to 5.92)	82%	<0.0001		High
Psychoactive substance abuse	Functional capacity	2	-	-	-	-	-	"As assessments and interventions varied greatly between each	NR

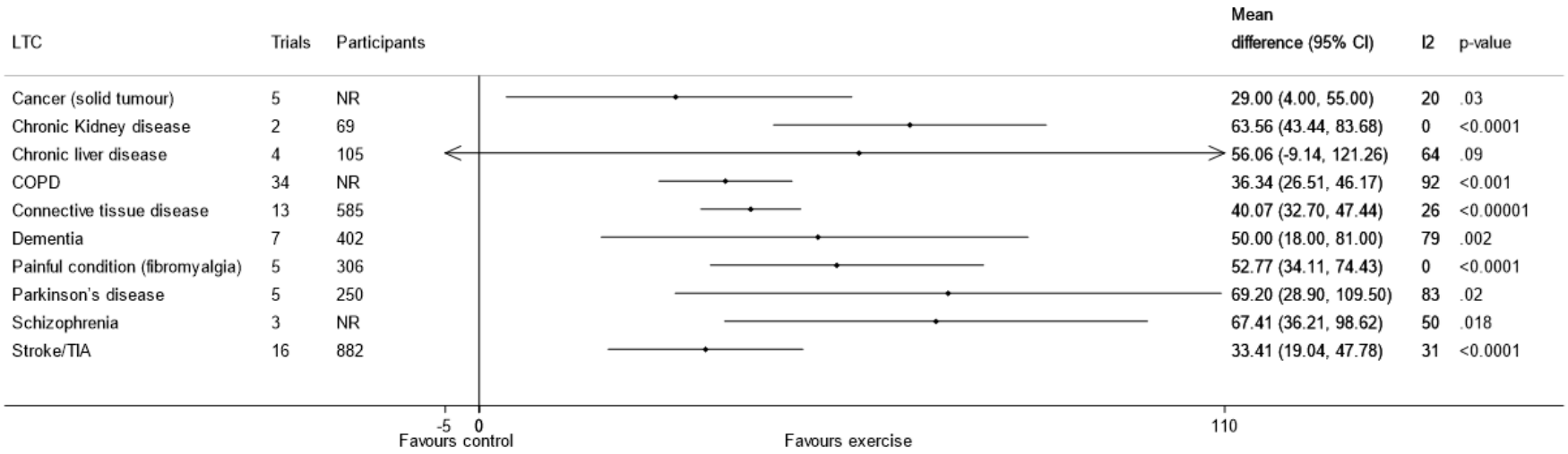
								study, it is not possible to observe any trends in results"	
Stroke/TIA	**Functional ambulation categories**							-	
	Cardiorespiratory training (end of intervention)	2	73		0.53 (0.21 to 0.85)	0%	0.00		NR
	Walking maximal speed (over 5-10m)								
	Cardiorespiratory training (end of intervention)	17	782		7.66 (3.65 to 11.68)	66%	0.00		NR
	Walking preferred speed (m/min)								
	Cardiorespiratory training (end of intervention)	12	588		4.47 (2.07 to 6.87)	0%	0.00		High
	Cardiorespiratory training (end of FU)	3	176		1.67 (-3.27 to 6.62)	0%	0.51		NR
	Resistance training (end of intervention)	5	203		2.15 (-3.57 to 7.87)	76%	0.46		oderate
	Mixed training (end of intervention)	10	738		4.71 (1.32 to 8.10)	76%	0.01		Moderate
	Mixed training (end of FU)	5	542		2.54 (-3.65 to 8.72)	77%	0.42		NR
	Walking capacity (m/min)								
	Cardiorespiratory training (end of intervention)	3	154		8.87 (1.35 to 16.40	42%	0.02		NR
	Cardiorespiratory training (end of FU)	5	312		6.71 (2.40 to 11.02)	0%	0.00		NR
	Resistance training (end of intervention)	7	274		2.83 (-0.49 to 6.14)	54%	0.1		NR
	Resistance training (end of FU)	2	117		7.80 (-3.32 to 18.91)	0%	0.17		NR

	Mixed training (end of intervention)	3	168		8.48 (1.76 to 15.20)	0%	0.01		NR
	Community walk (min)								
	Cardiorespiratory training (end of intervention)	2	47		-10.54 (-14.11 to 6.98)	0%	<0.0001		NR
	Community ambulation speed (>0.8 m/sec, OR)								
	Mixed training (end of intervention)	3	232		1.38 (0.78 to 2.42)	0%	0.26		NR
	Mixed training (end of FU)	3	217		1.33 (0.70 to 2.53)	15%	0.38		NR
	Timed up-and-go (sec)								
	Cardiorespiratory training (end of intervention)	5	223		-3.42 (-4.78 to -2.05)	0%	<0.0001		Moderate
	Resistance training (end of intervention)	5	224		-3.46 (-6.94 to 0.02)	89%	0.05		Low
	Resistance (end of FU)	2	117		-2.64 (-9.24 to 3.95)	0%	0.43		NR
	Mixed training (end of intervention)	7	586		-2.21 (-4.43 to 0.02)	45%	0.05		Low
	Mixed training (end of FU)	5	510		-1.41 (-3.74 to 0.92)	47%	0.24		NR

*'favours exercise': exercise better than control (P≤0.05); neutral: 'no difference' between exercise and control (P>0.05); 'favours control': control better than exercise (P≤0.05). †GRADE rating as reported in SR

MD: mean difference; SMD: standardised mean difference; CI: confidence interval; NR: not reported; FU: follow-up

15. Supplementary Figure 4 – Forest plot showing meta-analysis results for 6MWT (m).



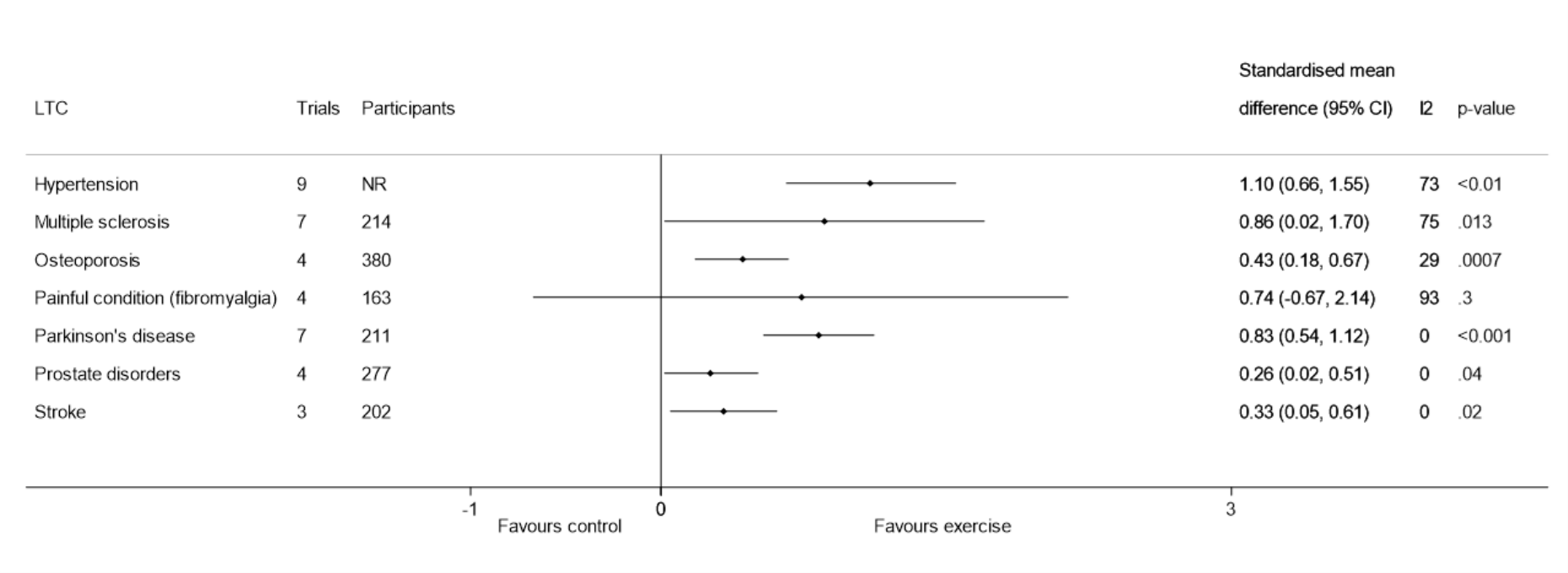
16. Supplementary Table 9 – Summary of exercise-based intervention vs control for strength outcomes by LTC

LTC	Unit of analysis	N trials	N participants	Exercise vs control effect SMD (95% CI)	Exercise vs control effect MD (95% CI)	I^2	p-value	Vote counting* or qualitative statement by authors	GRADE rating†
Anorexia	Strength (narrative, peak torque of knee extensors, knee and elbow flexors)	1	NR	-	-	NA	NA	3/3 results favour exercise	NR
Asthma	Muscular fitness	3	-	-	-	-	-	2/3 trials favour exercise 1/3 neutral	NR
Bronchiectasis	Quadriceps muscle strength	1	NR	-	-	-	-	1/1 trial neutral	NR
Cancer (solid tumour)	Kg (1 rep max): Bench press Leg press Left handgrip Right handgrip	 3 3 3 5	 NR NR NR NR	-	 6 (4 to 8) 19 (9 to 28) 4.3 (-1.5 to 10.2) 3.5 (0.3 to 6.7)	 54% 71% 71% 56%	 <0.01 <0.01 0.15 0.03	-	 NR NR NR NR
Cancer (haem)	Strength change, muscle strength, bicep curl, knee extension, grip strength	4	NR	-	-	-	-	4/6 results favour exercise 2/6 (43%) neutral	NR
Dementia	30s sit-to-stand (repetitions) Other types of sit-to-stand test Upper limb strength	4 4 4	278 NR NR	-	2.1 (0.3 to 3.9) - -	82%	0.02	 4/4 trials favour exercise 1/4 (25%) trials favour exercise 3/4 (75%) neutral	Moderate
Hypertension	Muscle strength (SMD)	9	NR	1.10 (0.66 to 1.55)	-	73%	<0.01	-	NR
Long-COVID	30s sit-to-stand Static quat test at the wall (post-intervention) Static quat test at the wall (FU)	1 1 1	196 120 120	-	-	-	-	1/1 trial favour exercise 1/1 trial favour exercise 1/1 trial favour exercise	NR
Multiple Sclerosis	Muscle strength (resistance trials only)	7	214	0.86 (0.02 to 1.70)	-	75%	0.013	-	NR

Osteoporosis	Leg strength Trunk strength Grip strength	6 2 4	349 48 380	2.02 (0.71 to 3.33) 0.60 (0.01 to 1.18) 0.43 (0.18 to 0.67)	-	95% 0% 29%	0.002 0.04 0.0007	-	NR NR NR
Painful condition (fibromyalgia)	Muscle strength	4	163	0.74 (-0.67 to 2.14)	-	93%	0.3	-	NR
Parkinson's disease	Muscle strength	7	211	0.83 (0.54 to 1.12)	-	0%	<0.001	-	NR
Prostate disorders	Upper body Lower body	4 6	277 245	0.26 (0.02 to 0.51) 0.29 (0.07 to 0.50)	-	0% 0%	0.04 0.01	-	NR NR
Psychoactive substance abuse	Strength	2	-	-	-	-	-	"As assessments and interventions varied greatly between each study, it is not possible to observe any trends in results"	NR
Stroke/TIA	**Composite measure of muscle strength** Resistance training (end of intervention) **Paretic knee flexion** Resistance training (end of intervention) **Paretic knee extension** Resistance training (end of intervention) Mixed training (end of intervention) **Ankle dorsiflexion** Mixed training (end of intervention) **Grip strength** Mixed training (end of intervention)	 2 3 3 3 2 3	 60 93 93 202 148 147	 0.58 (0.06 to 1.10) 0.72 (0.10 to 1.34) 1.09 (-0.23 to 2.41) 0.33 (0.05 to 0.61) 0.80 (-0.82 to 2.41) 0.32 (-0.88 to 1.52)		 0% 47% 87% 0% 94% 0%	 0.03 0.02 0.10 0.02 0.33 0.60	-	 Low Moderate Low Low Very low Low
Viral hepatitis	Grip strength 5 times sit-to-stand test	1 1	22 22	-	-	-	-	1/1 trial favour exercise 1/1 trial favour exercise	NR

*'favours exercise': exercise better than control (P≤0.05); neutral: 'no difference' between exercise and control (P>0.05); 'favours control': control better than exercise (P≤0.05). †GRADE rating as reported in SR
MD: mean difference; SMD: standardised mean difference; CI: confidence interval; NR: not reported; FU: follow-up

17. Supplementary Figure 5 – Forest plot showing meta-analysis results for strength (standardised mean difference).



18. Supplementary Table 10 – Summary of exercise-based intervention vs control for disability outcomes by LTC

LTC	Questionnaire	N trials	N participants	Exercise vs control effect SMD (95% CI)	Exercise vs control effect MD (95% CI)	I^2	p-value	Vote counting*	GRADE rating†
Arthritis (osteo-hip)	WOMAC/GARS Physical function				-			-	
	post intervention	9	521	0.30 (-0.54 to -0.05)		41%	0.02		High
	3-6 month FU	5	365	-0.37 (-0.57 to -0.16)		0%	0.0006		High
Arthritis (osteo-, knee)	WOMAC/VAS Physical function post treatment	44	3913	-0.52 (-0.64 to -0.39)	-	68%	<0.00001	-	Moderate
	2-6 month FU	10	1468	-0.15 (-0.26 to -0.04)		0%	<0.01		NR
	>6 month FU	8	1266	-0.57 (-1.05 to -0.1)		90%	<0.02		NR
Arthritis (rheumatoid)	HAQ	13	745	-	-0.10 (-0.26 to 0.06)	84%	<0.001	-	NR
COPD	MRC dyspnoea scale	11	NR	-	-0.59 (-0.81 to -0.37)	77%	<0.001	-	NR
Dementia	Barthel Index Score	4	237	-	10 (3 to 16)	89%	0.004	-	NR
Migraine	6-item headache impact test; pain disability index	2	NR	-	-	-	-	2/2 trials favour exercise	NR
Painful condition (chronic back pain)	Functional limitations – Roland-Morris Disability Questionnaire or Oswestry Disability Index			-				-	
	Overall – earliest FU	38	2942		-6.8 (-8.3 to -5.3)	38%	<0.00001		Moderate
	Short-term FU (3-months)	30	2555		-7.4 (-9.2 to -5.6)	43%	<0.00001		NR
	Medium-term FU (6 months)	22	1831		-6.6 (-8.3 to -4.8)	21%	<0.00001		NR
	Long-term FU (12 months)	6	550		-4.4 (-7.3 to -1.5)	0%	0.003		NR
Painful condition (fibromyalgia)	FIQ – physical function short-term FU	9	477	-	-10.99 (-14.8 to -7.18)	12%	<0.0001	-	NR
	Long-term FU (13-26 weeks)	3	179		-8.13 (-18.24 to 1.97)	63%	0.11		NR
Parkinson's disease	UPDRS III 'On-medication state'	6	277	-0.15 (-0.38 to 0.09)	-2.33 (-5.16 to 0.49)	0%	0.23	-	NR
	'Off-medication state'	4	320	-0.19 (-0.41 to 0.04)	-2.62 (-5.64 to 0.41)	0%	0.10		NR

Schizophrenia	Global functioning	10	NR	0.35 (0.16 to 0.54)	-	38%	<0.001	-	NR
Stroke/TIA	**Functional independence measure**							-	
	Cardiorespiratory training (end of intervention)	3	162	0.21 (-0.10 to 0.52)		0%	0.18		NR
	Barthel index								
	Cardiorespiratory training (end of intervention)	3	243		6.65 (-0.67 to 13.98)	94%	0.08		NR
	Mixed training (end of intervention)	6	256		2.84 (-0.48 to 6.17)	2	0.09		NR
	Mixed training (end of FU)	2	103		1.82 (-13.69 to 17.33)	68%	0.82		NR
	Rivermead mobility index								
	Cardiorespiratory training (end of intervention)	3	146		1.56 (0.20 to 2.92)	43%	0.02		NR
	Mixed training (end of intervention)	3	348		0.41 (-0.02 to 0.84)	23%	0.06		NR
	Mixed training (end of FU)	3	349		0.35 (0.02 to 0.69)	0%	0.04		NR
	Combined disability scales								
	Cardiorespiratory training (end of intervention)	8	462	0.52 (0.19 to 0.84)		61%	0.00		Moderate
	Cardiorespiratory training (end of FU)	3	220	0.20 (-0.07 to 0.46)		0%	0.14		NR
	Mixed training (end of intervention)	9	604	0.23 (0.03 to 0.42)		21%	0.02		Low
	Mixed training (end of FU)	5	452	0.10 (-0.17 to 0.37)		40%	0.45		NR
	Lawton IADL								
	Mixed training (end of intervention)	2	113		0.83 (-0.51 to 2.17)	0%	0.22		NR

	Nottingham Extended ADL Mixed training (end of FU)	2	106		3.10 (-5.20 to 11.40)	60%	0.46		NR

*'favours exercise': exercise better than control (P≤0.05); neutral: 'no difference' between exercise and control (P>0.05); 'favours control': control better than exercise (P≤0.05). †GRADE rating as reported in SR

MD: mean difference; SMD: standardised mean difference; CI: confidence interval; NR: not reported; FU: follow-up

19. Supplementary Table 11 – Summary of exercise-based intervention vs control for disease specific HRQoL outcomes by LTC

LTC	Questionnaire	N trials	N participants	Exercise vs control effect SMD (95% CI)	Exercise vs control effect MD (95% CI)	I^2	p-value	Vote counting*	GRADE rating†
Anaemia	**FACT-An**	1	55	-	-3.2 (-16.7 to 10.4)	NA	0.637	-	NR
Bronchiectasis	**SGRQ**	2	91	-	-4.65 (-6.70 to -2.60)	34%	<0.00001	-	NR
	LCQ	2	103		1.27 (-0.89 to 3.42)	77%	0.25		NR
Cancer (solid tumour)	**EORTC:**			-				-	NR
	Physical function	2	NR		-1.2 (-5.1 to 2.6)	0%	0.54		
	Emotional function	3	NR		1.5 (-9.8 to 12.7)	77%	0.80		NR
	Total	3	NR		3.7 (-5.2 to 12.6)	70%	0.41		NR
	FACT:								
	Physical wellbeing	6	NR		1.4 (-1.7 to 4.5)	92%	0.39		NR
	Emotional wellbeing	6	NR		0.7 (-0.6 to 1.9)	61%	0.31		NR
	Social/family wellbeing	6	NR		0.7 (-0.2 to 1.6)	15%	0.14		NR
	Functional wellbeing	6	NR		1.9 (-1.9 to 5.8)	93%	0.33		NR
	Breast	4	NR		1.9 (-1.6 to 5.4)	78%	0.28		NR
	Breast total	10	NR		7.6 (0.6 to 14.5)	86%	0.03		NR
	Colorectal total	3	NR		-1.6 (-6.2 to 2.9)	0%	0.48		NR
	General total	7	NR		4.2 (-3.1 to 11.5)	92%	0.26		NR
Chronic kidney disease	**KDQOL-SF 1.3**	3	NR	-	-	-	-	3/3 (100%) in favour of exercise	NR
Chronic liver disease	**CLDQ**	3	81	-	0.11 (-0.44 to 0.67)	33%	0.69	-	Low
COPD	**SGRQ**	25	NR	-	-6.66 (-8.38 to -4.94)	78%	<0.001	-	NR
Connective tissue disease	**SGRQ**			-				-	
	symptoms score (post-intervention)	7	312		-15.58 (-19.54 to -11.62)	52%	<0.00001		NR
	activity score (post-intervention)	7	312		-2.47 (-4.11 to -0.83)	54%	0.003		NR
	impact score (post-intervention)	7	312		-8.81 (-11.17 to -6.46)	0%	<0.00001		NR
	total score	11	478		-9.29 (-11.06 to -7.52)	27%	<0.00001		Moderate

	(post-intervention) symptoms score (long-term FU) activity score (long-term FU) impact score (long-term FU) total score (long-term FU)	 4 4 4 4	 240 240 240 240		 -11.31 (-16.58 to -6.03) -1.54 (-3.11 to 0.02) -4.73 (-7.76 to -1.69) -4.93 (-7.81 to -2.06)	 0% 56% 60% 63%	 <0.0001 0.05 0.002 0.0008		 NR NR NR Low
Endometriosis	**EHP-30**	1	NR	-	-	-	-	1/1 trial favours exercise	NR
Glaucoma	**Visual quality of life**	1	NR	-	-	-	-	1/1 trial favours exercise	NR
Heart failure	**MLWHFQ** 6-12 month FU >12 month FU	 17 3	 1995 329	-	 -7.11 (-10.49 to -3.73) -9.49 (-17.48 to -1.50)	 82% 73%	 <0.0001 <0.02	-	 Low Low
Inflammatory bowel disease	**IBDQ**	6	NR	-	-	-	-	5/6 trials favour exercise 1/6 neutral	NR
Irritable bowel syndrome	**IBS-QOL**	4	NR	-	-	-	-	3/4 trials favour exercise 1/4 neutral	NR
Migraine	**Migraine specific QoL questionnaire**	1	NR	-	-	-	-	1/1 trial neutral	NR
Painful condition (fibromyalgia)	**FIQ** short-term FU long-term FU (13-26 weeks) long-term FU (27-52 weeks)	 13 4 2	 610 224 146	-	 -6.95 (-10.51 to -3.38) -8.44 (-15.22 to -1.66) -5.29 (-11.42 to 0.84)	 51% 56% 0%	 0.00 0.01 0.09	-	 Moderate NR NR
Parkinson's disease	**PDQ-39** Resistance studies only	5	165	-0.41 (-0.72 to -0.09)	-5.4 (-10.5 to -0.3)	0%	<0.01	-	NR
Prostate disorders	Cancer-specific QoL	7	912	0.13 (-0.08 to 0.34)	-	46%	0.23	-	NR
Psychoactive substance abuse	**QOL DA**	1	NR	-	-	-	-	2/5 results favour exercise 3/5 neutral	NR

Viral hepatitis	**CLDQ**	1	40	-	-	-	-	1/7 results favour exercise 6/7 neutral	NR

*'favours exercise': exercise better than control (P≤0.05); neutral: 'no difference' between exercise and control (P>0.05); 'favours control': control better than exercise (P≤0.05). †GRADE rating as reported in SR

MD: mean difference; SMD: standardised mean difference; CI: confidence interval; NR: not reported; FU: follow-up

CLDQ = chronic liver disease questionnaire; EHP-30 = Endometriosis health profile-30; EORTC = European Organisation for Research and Treatment of Cancer; FACT = functional assessment of cancer therapy; FIQ = fibromyalgia impairment questionnaire; IBDQ = Inflammatory bowel disease questionnaire; IBS-QOL = irritable bowel syndrome quality of life; KDQOL-SF = kidney disease quality of life short form; MLWHFQ = Minnesota Living with Heart Failure Questionnaire; PDQ-39 = Parkinson's disease questionnaire; QOL DA = quality of life scale for drug addiction; SGRQ = St George Respiratory Questionnaire;

20. Supplementary Table 12 – Summary of exercise-based intervention vs control for generic HRQoL outcomes by LTC

LTC	Questionnaire Subscale	N trials	N participants	Exercise vs control effect SMD (95% CI)	Exercise vs control effect MD (95% CI)	I^2	p-value	Vote counting*	GRADE rating†
Arthritis (osteo-, hip)	SF-36/VAS - SMD	3	183	0.10 (-0.23 to 0.36)	-	0%	0.66	-	Low
Arthritis (osteo-, knee)	SMD (mix of generic and disease-specific questionnaires)	13	1073	0.28 (0.15 to 0.40)	-	0%	<0.00001	-	High
Atrial fibrillation	**SF-36:**				-			-	NR
	physical functioning	8	632	0.63 (0.18 to 1.09)		85.6%	<0.001		
	general health	8	632	0.64 (0.35 to 0.93)		66.2%	0.004		
	vitality	8	632	0.51 (0.31 to 0.71)		32%	0.172		
Cancer (solid tumour)	**SF-36:**			-				-	
	Physical function	2	NR		3.0 (0.7 to 5.3)	0%	0.01		NR
	Role physical	2	NR		6.1 (-4.1 to 16.2)	56%	0.24		NR
	Bodily pain	2	NR		4.3 (-0.6 to 9.2)	54%	0.08		NR
	General Health	2	NR		5.8 (-1.2 to 13.0)	76%	0.12		NR
	Vitality	2	NR		2.1 (-0.4 to 4.5)	0%	0.10		NR
	Social function	2	NR		3.4 (0.4 to 6.4)	0%	0.03		NR
	Role emotion	2	NR		-0.01 (-3.7 to 3.6)	0%	1.00		NR
	Mental Health	2	NR		2.4 (0.7 to 4.1)	0%	0.01		NR
	Physical component scale	4	NR		1.2 (-1.9 to 4.4)	55%	0.44		NR
	Mental component scale	4	NR		0.4 (-2.3 to 3.2)	39%	0.76		NR
Cancer (haem)	**Not reported**				-			-	
	overall	8	1259	0.11 (-0.03 to 0.24)		26%	0.14		Low
	physical functioning	8	1329	0.15 (-0.01 to 0.32)		48%	0.06		Low
	depression	6	445	0.19 (0.0 to 0.38)		0%	0.05		Low
	anxiety	6	445	0.03 (-0.30 to 0.36)		63%	0.85		Very low
Cancer (advanced metastatic)	**Not reported**				-			-	
	overall	8	564	0.22 (0.06 to 0.38)		21%	0.009		NR
	physical functioning	8	564	0.22 (0.05 to 0.38)		24%	0.009		NR

	social functioning	8	564	0.18 (0.02 to 0.34)		0%	0.03		NR
	Emotional function	7	500	0.18 (-0.00 to 0.35)		0%	0.05		NR
	Role function	7	510	0.13 (-0.04 to 0.30)		0%	0.13		NR
	Cognitive function	5	456	0.00 (-0.32 to 0.33)		56%	0.99		NR
Chronic fatigue syndrome	**SF-36** physical functioning (end of treatment)	5	725	-	-13.10 (-24.22 to -1.98)	89%	0.02	-	Low
	physical functioning (52-70 weeks)	3	621		-16.33 (-36.74 to 4.08)	96%	0.12		Very low
Chronic kidney disease	**SF-36**	5	NR	-	-	-	-	2/5 trials favour exercise 3/5 neutral	
Chronic liver disease	**EuroQol-VAS**	2	56	-	3.11 (-24.03 to 30.24)	88%	0.82	-	NR
	SF-36 mental component summary	2	51		2.26 (-3.84 to 8.37)	0%	0.47		NR
Coronary heart disease	**SF-36:** Physical component score	6	1741	-	1.70 (-0.08 to 3.47)	73%	0.06	-	NR
	Mental component score	6	1741		2.14 (1.07 to 3.22)	21%	<0.0001		NR
	Physical functioning	8	2756		8.47 (3.69 to 13.24)	92%	0.0005		NR
	Physical performance	8	2756		8.08 (2.89 to 13.27)	87%	0.002		NR
	Bodily pain	8	2756		-0.06 (-8.97 to 8.84)	97%	0.99		NR
	General health	8	2756		5.66 (2.08 to 9.25)	84%	0.002		NR
	Vitality	7	2638		5.78 (1.89 to 9.67)	85%	0.004		NR
	Social functioning	8	2756		1.98 (0.26 to 3.70)	20%	0.02		NR
	Emotional performance	7	2638		0.69 (-1.33 to 2.71)	18%	0.50		NR
	Mental health	8	2756		5.60 (1.21 to 9.98)	93%	0.01		NR
	EQ-5D	3	476		0.05 (-0.01 to 0.10)	69%	0.08		NR
Dementia	Not reported	8	Not reported	-	-	-	-	1/8 trials favour exercise 7/8 neutral	Moderate
Depression	**Not reported**				-			-	

	Overall QoL	3	104	0.39 (0.05 to 0.74)		0%	0.002		NR
	Physical domain	5	Not reported	0.53 (0.22 to 0.84)		0%	<0.001		NR
	Psychological domain	5	Not reported	0.53 (0.22 to 0.85)		5%	<0.001		NR
	Social domain	3	Not reported	0.28 (-0.13 to 0.71)		13%	0.18		NR
	Environment domain	3	Not reported	0.36 (-0.12 to 0.85)		31%	0.14		NR
Diabetes mellitus	**Not reported**	1	Not reported	-	-	-	-	1/1 trial neutral	NR
Epilepsy	**SWLS**	1	Not reported	-	-	-	-	1/1 trial neutral	NR
	WHOQOL-BREF	1	Not reported					1/1 trial neutral	
Heart failure	all HRQoL measures (SMD)	26	3833	-0.60 (-0.82 to -0.39)	-	87%	<0.0001	-	Low
Inflammatory bowel disease	**SF-36**	1	-	-	-	-	-	1/1 trial favour exercise	NR
Irritable bowel syndrome	**SF-36**	2	-	-	-	-	-	4/5 results favour exercise 1/5 neutral	NR
Long-COVID	**SF-12**	1	120	-	-	-	-	1/4 results favour exercise 3/4 neutral	NR
Migraine	**Profile of quality of life in the chronically ill**	1	Not reported	-	-	-	-	1/1 trial favour exercise	NR
Osteoporosis	Self-reported functioning	22	1254	-0.64 (-0.89 to -0.40)	-	75%	<0.00001	-	NR
Parkinson's disease	Quality of life (Not reported)				-			-	NR
	Aerobic only	4	230	-0.09 (-0.51 to 0.33)		51%	0.67		
Peripheral vascular disease	**SF-36**			-				-	
	3 month								
	Physical function	2	82		6.60 (2.37 to 10.83)	74%	0.00		NR
	Bodily pain	2	82		3.89 (-1.91 to 9.68)	0%	0.19		NR
	General health	2	82		4.52 (-0.01 to 9.04)	70%	0.05		NR
	Mental health	2	82		1.44 (-0.93 to 3.81)	0%	0.23		NR
	Role emotional	2	82		1.26 (-4.84 to 7.36)	0%	0.69		NR
	Social function	2	82		1.49 (-4.16 to 7.14)	0%	0.61		NR
	Vitality	2	82		5.55 (1.54 to 9.56)	0%	0.01		NR

	Role physical	2	82		10.31 (3.64 to 16.98)	90%	0.00		NR
	6 month Physical function	2	85		9.78 (0.82 to 18.74)	0%	0.03		NR
	Bodily pain	2	85		4.85 (-3.79 to 13.50)	0%	0.27		NR
	General health	2	85		10.19 (1.83 to 18.55)	0%	0.02		NR
	Mental health	2	85		1.82 (-5.28 to 8.92)	0%	0.62		NR
	Role emotional	2	85		4.90 (-7.15 to 16.94)	0%	0.43		NR
	Social function	2	85		3.48 (-6.74 to 13.71)	77%	0.50		NR
	Vitality	2	85		5.32 (-2.57 to 13.22)	0%	0.19		NR
	Role physical	2	85		8.55 (-2.69 to 19.79)	73%	0.14		NR
	Physical summary score	5	429		2.15 (1.26 to 3.04)	66%	<0.00001		Moderate
	Mental summary score	4	343		3.76 (2.70 to 4.82)	87%	<0.00001		Moderate
Polycystic ovarian syndrome	**SF-36** Physical functioning	3	84	-	11.81 (2.36 to 21.25)	74%	0.01	-	NR
	Role physical	3	84		5.33 (-13.70 to 24.37)	73%	0.58		NR
	Role emotional	3	84		7.46 (-8.78 to 23.69)	56%	0.37		NR
	Bodily pain	3	84		-2.21 (-9.56 to 5.13)	0%	0.56		NR
	General health	3	84		10.05 (3.89 to 16.20)	0%	0.001		NR
	Energy/vitality	3	84		6.43 (-0.82 to 13.67)	5%	0.08		NR
	Social functioning	3	84		11.75 (2.56 to 20.95)	6%	0.01		NR
	Mental health	3	84		11.70 (1.27 to 22.13)	47%	0.03		NR
Psychoactive substance abuse	**SF-36, WHOQOL-BREF**	7	Not reported	-	-	-	-	19/44 results favour exercise 25/44 neutral	NR
Schizophrenia	SMD - QLES, WHOQOL, SF-36, EQ-5D, MANSA Overall	10	Not reported	0.30 (0.02 to 0.57)	-	64%	0.03	-	NR
	Physical	14	Not reported	0.60 (0.32 to 0.87)		74%	<0.001		NR

	Mental	12	Not reported	0.37 (0.13 to 0.61)		65%	0.003		NR
	Social	8	Not reported	0.65 (0.22 to 1.08)		82%	0.003		NR
	Environmental	4	Not reported	0.17 (-0.01 to 0.36)		0%	0.07		NR
Stroke/TIA	**SF-36/SF-12 Physical health component**								
	Cardiorespiratory training (end of intervention)	2	164	0.51 (-5.02 to -2.13)		0%	0.00		NR
	SF-36/SF-12 Mental health component								
	Cardiorespiratory training (end of intervention)	2	164	0.58 (-0.52 to 1.68)		87%	0.3		NR
	EQ-5D								
	Cardiorespiratory training (end of intervention)	2	158		6.55 (-1.36 to 14.47)	48%	0.1		NR
	Cardiorespiratory training (end of FU)	2	150		-4.25 (-8.00 to 1.49)	0%	0.15		NR
	SF-36 physical functioning								
	Resistance training (end of intervention)	3	70		5.72 (-5.26 to 16.70)	80%	0.31		NR
	Mixed training (end of intervention)	2	112			0%	0.01		NR
	Mixed training (end of FU)	2	146	0.48 (0.10 to 0.85)	2.46 (-7.20 to 12.11)	57%	0.62		NR
	SF-36 mental health								
	Resistance training (end of intervention)	3	70		7.69 (1.56 to 13.83)	38%	0.01		NR
	SF-36 physical role functioning								
	Mixed training (end of intervention)	3	178			0%	0.00		NR
	Mixed training (end of FU)	2	146	0.56 (0.26 to 0.86)	11.61 (2.38 to 20.84)	0%	0.01		NR
	SF-36 social role functioning								
	Mixed training (end of intervention)	2	112	0.48 (-0.22 to 1.17)		54%	0.18		NR

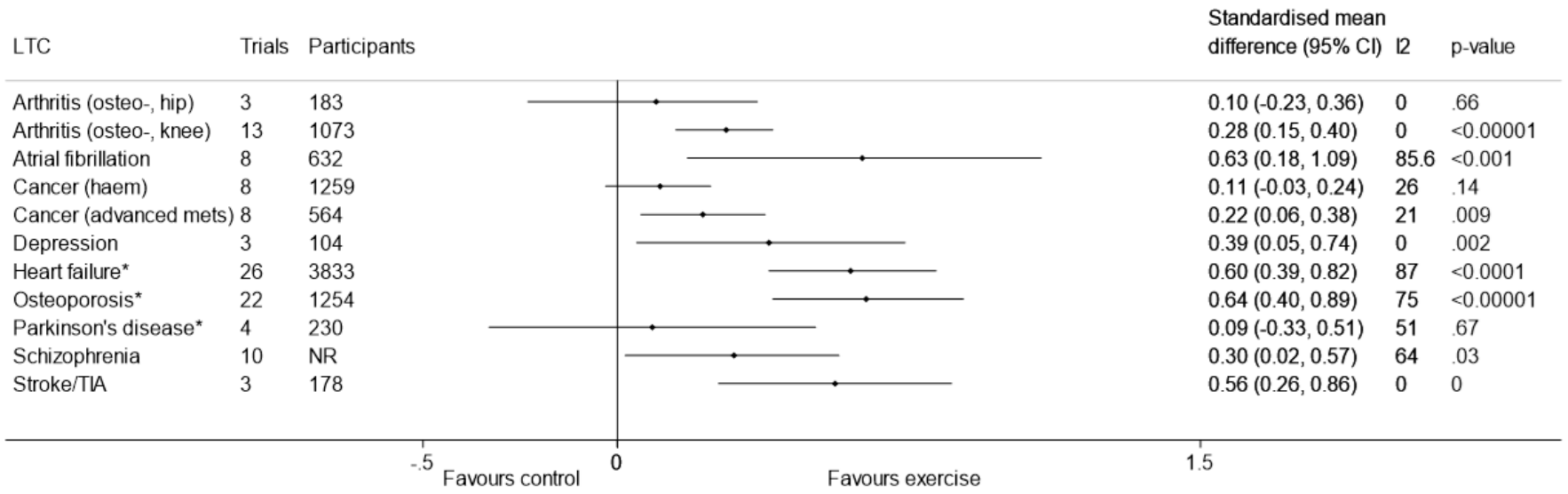
Treated constipation	**SF-36**, others Not reported	3	NR	-	-	-	-	8/8 results favour exercise	NR
Viral hepatitis	**SF-36**	1	22	-	-	-	-	1/19 results favour exercise 18/19 neutral	NR

*'favours exercise': exercise better than control (P≤0.05); neutral: 'no difference' between exercise and control (P>0.05); 'favours control': control better than exercise (P≤0.05). †GRADE rating as reported in SR

MD: mean difference; SMD: standardised mean difference; CI: confidence interval; NR: not reported; FU: follow-up

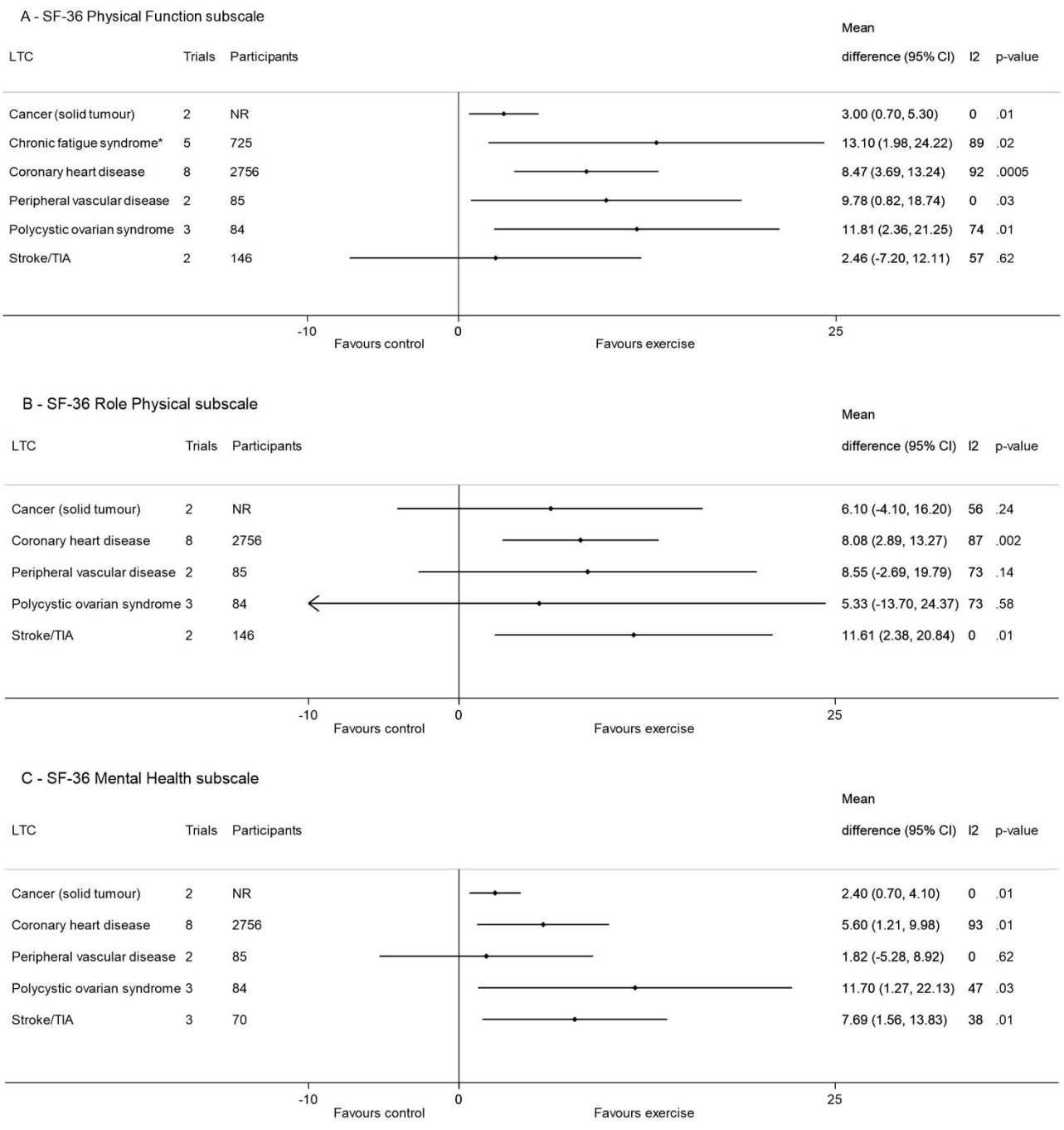
EuroQoL = European Quality of Life; EQ-5D = European Quality of Life 5 Dimensions; MANSA = Manchester Short Assessment of Quality of Life; QLES = QoL Enjoyment and Satisfaction scale; SF-36/12 = Short Form 36/12 Health Survey; SWLS = Satisfaction with Life Scale; VAS = visual analogue scale; WHOQOL-BREF = World Health Organization Quality of Life-BREF.

21. Supplementary Figure 6 – Forest plot for generic HRQoL for exercise-based intervention vs control across LTCs – standardized mean difference scale.
* Direction of HRQoL effect reversed so higher follow up outcome score indicates exercise intervention as beneficial.



22. Supplementary Figure 7 – Forest plot for HRQoL for exercise-based intervention vs control measured using three different SF-36 domains.

Results are presented as mean difference on 0-100 scale. Panel A shows the physical function subscale, panel B the role physical subscale, and panel C the mental health subscale. * Direction of HRQoL effect reversed so higher follow up outcome score indicates exercise intervention as beneficial.



23. Supplementary Table 13 – Summary of exercise-based intervention vs control for physical activity outcomes by LTC

LTC	Measurement method	N trials/ comparisons in MA	N participants in MA	Effect SMD (95% CI)	I^2	P-value	Vote counting
Dementia	Not reported	5	NR	-	-	-	1/4 results favour exercise 3/4 neutral
Long COVID	Steps/day (mobile app)	1	196	-	-	-	1/1 trials favour exercise
Psychoactive substance abuse	Moderate and Vigorous physical activity (days, mins; IPAQ)	1	NR	-	-	-	3/4 results favour exercise 1/4 neutral
Schizophrenia	Self-reported physical activity	4	NR	0.04 (-0.22 to 0.29)	35%	0.204	-
Stroke/TIA	Diary & accelerometer (total, light, moderate, vigorous at end of intervention or end of follow up)	1	NR	-	-	-	8/8 results neutral

*'favours exercise': exercise better than control (P≤0.05); neutral: 'no difference' between exercise and control (P>0.05); 'favours control': control better than exercise (P≤0.05). NR: not reported in SR; IPAQ: International Physical Activity Questionnaire