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The Effects of Exercise Interventions on Quality of Life in Clinical and Well Populations; a Meta-Analysis.

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Abstract

The aim of the study was to provide an overview of the effect of exercise interventions on subjective quality of life (QoL) across adult clinical populations and well people, and to systematically investigate the impact of the exercise setting, intensity and type on these outcomes. From a systematic search of six electronic databases, 56 original studies were extracted, reporting on 7937 sick and well people. A meta-analysis was conducted on change in QoL from pre- to post-intervention compared with outcomes from a no-exercise control group, using weighted (by the study's sample size) pooled mean effect sizes and a fixed-effects model. Significant differences in outcome were found when treatment purpose was compared; prevention/promotion (well populations), rehabilitation, or disease management. Three to six months post-baseline, a moderate positive effect of exercise interventions was found for overall QoL in rehabilitation patients (effect size [ES] = 0.55), but no significant effect for well or disease management groups (ES = 0.11 and ES = -0.00 respectively). However, physical and psychological QoL domains improved significantly relative to controls in well participants (ES = 0.22 and ES = 0.21 respectively). Psychological QoL was significantly poorer relative to controls in the disease management group (ES = -0.26). This pattern of results persisted over one year. With some exceptions, better overall QoL was reported for light intensity exercise undertaken in group settings, with greater improvement in physical QoL following moderate intensity exercise. The implications for future practice and research are discussed.

Introduction

There is considerable and growing evidence that physical activity and/or exercise behaviour plays a role in a person's perception of their quality of life (QoL) (Rejeski, Brawley, & Shumaker, 1996; Wolin, Glynn, Colditz, Lee, & Kawachi, 2007). Additional to links reported in naturalistic settings, studies measuring QoL before and after an exercise intervention can provide clear evidence of a causal pathway that is necessary before promoting exercise as a means of improving QoL[1]. Systematic reviews (SR) and meta-analyses (MA) have quantified the outcomes of exercise interventions for specific population sub-groups such as cancer patients (Oldervoll, Kaasa, Hjermstad, Lund, & Loge, 2004), frail older adults (Schechtman & Ory, 2001), and mental health service users (Lawlor & Hopker, 2001). However, no review was found that compared the outcomes of exercise across disease groups. Furthermore, as QoL is often applied as a secondary rather than primary outcome measure in exercise trials, many such reviews only report on a small group of studies (e.g., Jolly, Taylor, Lip, & Stevens, 2006; Oldervoll et al., 2004). Furthermore, the mechanisms by which the physical activity/exercise-QoL relationship functions are still the subject of investigation.

Using the search terms listed in the methods section of the present paper, eight meta-analyses reporting on the impact of exercise on QoL published between 2001 and 2007 were retrieved. Five of these only conducted within-group analyses, without comparison with a control group; three of these reported no beneficial effect of physical activity on QoL (Jolly et al., 2006; Schmitz, Holtzman, Courneya, Masse, Duval, & Kane, 2005; Spronk, Bosch, Veen, den Hoed, & Hunink, 2005), and two a positive effect (Oldervoll et al., 2004; van Tol, Huijsmans, Kroon, Schothorst, & Kwakkel, 2006). However, accounting for variation in QoL over time in control populations is particularly important; in clinical populations, perceptions of health and well-being may not be stable, as change in QoL resulting from significant illness or disability may be affected by factors other than the intervention itself. An example is adjustment to diagnosis or response shift (Schwartz & Sprangers, 2000). Of the three remaining MAs that did calculate pooled effect sizes controlling for the degree of change in no-exercise control groups, one reported no effect (Lawlor & Hopker, 2001), and two a positive effect (Netz, Wu, Becker, & Tenenbaum, 2005; Schechtman & Ory, 2001). However, a lack of standardisation of the nature of the exercise activity intervention (e.g., exercise intensity and setting), and the type of QoL measures used, compromises the comparability of studies within meta-analyses, and consequently the reliability of their findings (Oldervoll et al., 2004).

The aim of the present review was to conduct a meta-analysis to assess the efficacy of exercise interventions across clinical and well populations. It also aimed to explore whether characteristics of either the exercise intervention, or the domain of QoL measured, can account for heterogeneity in outcomes across studies. Consistent with previous work it was hypothesised that there would be an improvement in QoL across studies of a small effect size. In addition, six *a priori* hypotheses were specified to test the potential moderating role of exercise purpose, QoL domain, exercise intensity, and exercise type, on the effect of exercise on QoL. Each of the hypotheses is addressed in turn.

Intervention purpose. The first aim of the present review was to compare the outcome of exercise interventions between well and clinical populations, and to assess the consistency of the QoL response across disease groups according to intervention purpose. As interventions conducted with well populations typically involve adults with existing health risk-factors, and thus participants with an initially low level of fitness, we expected there to be similar responses for both well and clinical samples. However, we expected variation in the responses of clinical populations to be further differentiated by illness severity and the intended goals of treatment. To conduct this comparison, studies were classified into one of three groups according to the following criteria (in brackets); (1) health promotion/prevention (an intervention delivered to a non-clinical population), (2) rehabilitation (an intervention delivered following a health threat, but patients are expected to recover full or near-full functioning), and (3) disease management (an intervention delivered as part of a treatment regimen, for symptom management, or to prevent deterioration where increased function is not expected).

We predicted that greater improvement in QoL would be reported by those who could expect to discern benefits from exercise than those exercising to maintain current levels of functioning. Thus, it was predicted that rehabilitation studies (Group 2) would report the greatest gains in QoL. Furthermore, we compared the degree of heterogeneity between studies that could be explained through this method of categorisation than by splitting groups into clinical versus well populations.

Variation across QoL domain. Research suggests that the impact of exercise on QoL outcomes may differ between domains (Taylor, Cable, Faulkner, Hillsdon, Narici, & Van der Bij, 2004). Six QoL domains have been identified as universally important to both sick and well people: *physical health, psychological state, level of independence, social relationships, environment,* and *spirituality, religiousness and personal beliefs* (The WHOQOL Group, 1998). However, different health-related measures of QoL are constructed with diverse conceptual emphases. Some largely assess the psychological domain (e.g., The General Well-Being Scale; Dupuy, 1984); many address physical functioning and/or independence (e.g., SF-36, Ware & Sherbourne, 1992), and many others report only an overall QoL evaluation without differentiating between domains. Although interpretation is more complex, retaining a multi-dimensional profile for comparison purposes allows for greater specificity, enabling detection of an important range of QoL changes associated with exercise. Pragmatically, it also allows for better targeting of poor QoL (Skevington & O'Connell, 2004). Previous MAs have reported the greatest benefits to exercise be in the psychological rather than the physical domain, for example in self-efficacy (Netz et al., 2005), emotions (Schechtman & Ory, 2001), and self-esteem (Oldervoll et al., 2004). No change or even deterioration along physical dimensions has been reported with clinical populations (e.g., Schechtman & Ory, 2001).

Thus, a second hypothesis stipulated that the greatest gains in QoL would be observed in the psychological, as opposed to the physical domain.

Exercise type and intensity. Interventions expose participants to a range of different acute exercise bouts, including intensive aerobic exercise training that results in notable gains in fitness (e.g., using cycle ergometers), low intensity walking programmes, and passive physiotherapy exercises. Drawing from research in acute exercise settings, it would be expected that psychological outcomes, particularly positive mood, may differ as a result of exercise intensity. For example, lower intensity exercise is associated with greater enjoyment and persistence than high intensity, aerobic exercise is more beneficial to mood than resistance (isometric) exercise, and fitter individuals report more positive psychological responses to higher intensity exercise (e.g., Ekkekakis & Petruzzello, 1999). Some previous SRs have assessed QoL outcomes in response to variation in exercise intensity, for example Netz et al. (2005) reported better QoL in response to moderate intensity exercise over light or strenuous intensity in older adults (d =.34). However, in clinical populations, the majority of MAs have either not tested this, or have retrieved insufficient numbers of studies to statistically evaluate differences in outcome according to exercise intensity (Oldervoll et al., 2004; Schmitz et al., 2005; Spronk et al., 2005).

Exercise intensity may be particularly pertinent for clinical populations for whom poor physical condition may influence how exercise is experienced. For instance, exercise of the same objective intensity has been associated with greater perceived effort and lesser enjoyment in obese participants than non-obese samples (Ekkekakis & Lind, 2006). This suggests a moderating role for health state or physical condition. Similarly, in a study involving survivors of childhood leukaemia, former patients reported experiencing moderate intensity exercise to be more strenuous than did a healthy control group, even after recovery from cancer (Bell, Warner, Evans, Webb, Mullen, & Gregory, 2006). Further investigation from a wider range of studies across health states is therefore warranted in investigating the importance of exercise intensity on QoL outcomes.

The present review aimed to examine whether physical health moderates the effect of exercise on QoL. Specifically, we tested the hypothesis that greater gains in QoL would be reported for interventions involving light, rather than moderate or strenuous intensity exercise for patients with a chronic physical illness (Hypothesis 3), whereas greater gains in QoL will be reported for moderate, rather than light intensity exercise in well populations (Hypothesis 4).

The type of exercise undertaken has also been considered as a moderator in the exercise-QoL relationship; however, evidence in support of this is variable. In a healthy but elderly sample, Netz et al. (2005) found better QoL for aerobic over resistance training in promoting QoL; in cancer patients, resistance training (isometric exercise) resulted in a better QoL response (Segal, Reid, Courneya, Malone, Parliament, Scott et al., 2003), and for depressed patients, exercise type had no differential effect on QoL (Lawlor & Hopker, 2001). Exercise type when crudely differentiated between aerobic or resistance training is not independent of exercise intensity (i.e, resistance training is classified as light intensity exercise), however the two are not synonymous (e.g., walking is light intensity, but is also aerobic). Therefore a fifth hypothesis was tested that predicted better QoL outcomes from interventions incorporating aerobic exercise than resistance training alone.

Across studies, exercise is reported to take place in a variety of settings; whether in groups or alone, supervised or unsupervised, and in or out of the home (Netz et al., 2005). In hypothesis 6 we predicted that greater improvement in the social domain of QoL would result from group-based, rather than individual- or home-based interventions.

The purpose of establishing a firmer basis for our understanding of a potential causal link between exercise interventions and QoL is to assist in the identification of necessary and sufficient factors of either the exercise, or participant group, in order to experience beneficial effects. It is important from an ethical basis to ensure that patients who are already experiencing health problems are not asked to change their lifestyle in ways that they may find difficult or uncomfortable, unless there is a clear evidence base for this. Furthermore, better understanding of likely outcomes of intervention may enable greater cost efficacy through more efficient targeting of resources.

Method

Inclusion criteria:

Papers were allocated to the following inclusion criteria:

1. randomised controlled trials
2. intervention incorporating an active exercise component
3. pre- and post-test ratings of QoL for both intervention and control groups
4. adult populations (i.e., over 18)
5. available in English

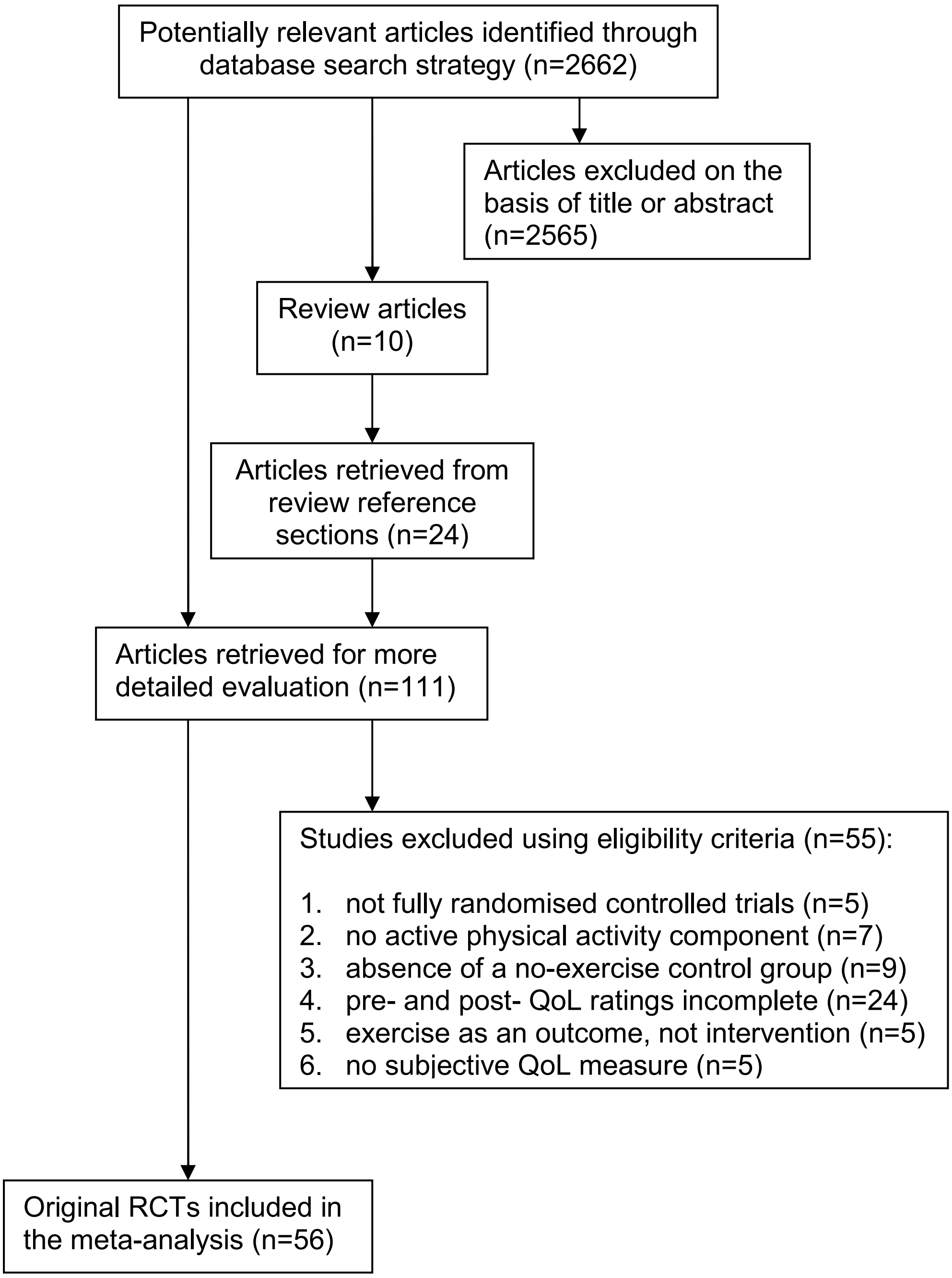
Exclusion criteria:

1. passive receipt of physiotherapy exercise (this served the purpose of restricting the review to a more homogenous set of interventions)
2. absence of a no-exercise control group

Search strategy:

This systematic review was conducted using the keywords: ‘quality of life’, ‘well-being or wellbeing’, ‘exercise(s)’, ‘physical activity/ies’, ’randomis(z)ed control(l)ed trial(s)’ ’RCT’. Six electronic data bases were searched from their first year of operation until September 2007: Pub Med (1966), EMBASE (1974), Cochrane Library, SCOPUS (1960), Psych INFO (1967), Web of Science (1970). Figure 1 displays the process of article selection. An initial pool of 2662 articles was generated, and these were scrutinised for eligibility from the title and abstract. Clearly ineligible studies were removed i.e., those that were not original research, interventions, randomised controlled

Figure 1: Article selection process



trials, or that did not use exercise as an intervention. A total of 111 studies were then retrieved in their entirety.

Two authors independently assessed whether each study matched the inclusion criteria; a third author arbitrated on disagreements. The final sample consisted of 56 RCTs. To facilitate comparisons across QoL instruments, results were extracted separately for each domains or facet (i.e., sub-domains) of QoL reported in each study. These were then clustered into the higher order framework set out by the WHOQOL Group (WHOQOL, 1995). Where results for more than one facet within a domain were reported, the mean of facet scores was calculated to indicate a domain effect. The WHOQOL framework was selected as the most appropriate structure to apply, as it is a comprehensive instrument generated by international experts through extensive consultation with patients and communities across 15 countries. However, so as not to exclude the 27 studies that reported only overall QoL, results for QoL as a whole are also reported.

Analysis

Mean change scores for each study were obtained by subtracting pre- from post-intervention scores, and the pooled standard deviation of change was calculated. Where full information was unavailable, the corresponding author was requested to supply the remaining data. The effect size for each study (calculated separately for each time point provided) was calculated as the standardized mean difference between the change in the experimental and control groups, using Hedges bias correction for small or uneven sample sizes (i.e., pooled standard deviation, equation 1; Hedges & Olkin, 1985). Although effect sizes provide standardized scores, those for larger studies provide more accurate estimates of the true statistic. To account for this, effect size statistics were further weighted by the inverse of the sampling error variance (equation 2; Hedges & Olkin, 1985). In line with recommendations, outliers (≥2 SD) were recoded to an effect size of two standard deviations above/below the population mean, to avoid their having a disproportionate effect on the final estimate (Lipsey & Wilson, 2002). A final estimate of effect for the entire sample of studies was then computed through calculating a mean of the weighted effect sizes using a fixed effects model (equation 3; Lipsey & Wilson, 2002).

Equation 1a (biased effect size):

$$ES_{sm} = \left(X_{G1} - X_{G2}\right) / s_p$$

Equation 1b (unbiased effect size):-

$$ES'_{sm} = \left[1 - \frac{3}{4N - 9}\right] ES_{sm}$$

Equation 2 (inverse sampling error variance):

$$w_{sm} = \frac{1}{SE^2_{sm}} \quad \text{where, } SE_{sm} = \sqrt{\frac{n_{G1} + n_{G2}}{n_{G1} n_{G2}} + \frac{\left(ES'_{sm}\right)^2}{2(n_{G1} + n_{G2})}}$$

Equation 3 (weighted mean effect size):

$$\overline{ES} = \frac{\sum\left(w_i ES_i\right)}{\sum w_i}$$

Notes: s_p = pooled standard deviation of control and experimental group outcomes; N = total number of control and experimental group participants; w_{sm} = inverse sampling error variance; SE_{sm} = standard error of the standardised mean; n_{G1} (n_{G2}) = sample size of experimental (control) group; w_i = inverse variance weight for effect size of study i, and i is equal to 1 to k, with k being the number of effect sizes.

Effect sizes were interpreted through applying Cohen's criteria i.e., small (0.2), medium (0.5), and large (0.8). In line with *a priori* hypotheses that sample and intervention characteristics would influence effect sizes, the homogeneity of estimates was assessed through a Q test (Lipsey & Wilson, 2002). The Q statistic is calculated from the sum of weighted square differences from the group mean, and is distributed as a χ^2 distribution. A significant Q test indicated a lack of homogeneity, and indicated a systematic variation in outcomes according to study characteristics. An analogue to ANOVA was then applied to partition the variance between and within groups, to establish whether homogeneity is improved (i.e., value of Q reduced) by accounting for *a priori* grouping characteristics.

Results

The 56 studies in the final sample varied in size from 9 to 264 participants, including patients from seven broad disease categories and well people. They totalled 7937 participants and provided follow-up data at points from one to 26 months following an intervention. Full characteristics of studies according to the proposed moderating factors are shown in Table 1, and summarised in Table 2.

To enable comparisons to be made at similar time points across studies, the main analyses were conducted on the outcomes reported at 3-6 months post intervention, which was available for 47 of the 56 studies. We took the statistic for the follow-up closest to, but not exceeding 6 months as the primary outcome (minimum = 2.5 months, maximum = 6 months), and included only one time point for each study to ensure independence of data. Only 10 studies provided follow-up data at 12 months or more, and assessment of these long-term outcomes is presented after the main analyses. Table 3 shows the change in QoL score following intervention relative to change in control groups for clinical and well populations. There was a small but significant advantage to overall QoL for clinical populations (ES=0.27), but no significant effects for individual domains. In well participants, there was no significant change in overall QoL; however significant improvements were specifically reported in psychological and physical QoL domains (ES=0.21, and ES=0.22 respectively). In both clinical and well samples, there was significant heterogeneity between study effects for overall, physical and psychological QoL, providing justification for the testing of the six *a priori* hypotheses.

Table 1: Characteristics of studies included in the meta-analysis

Study ID	First Author (year)	N IV/ control	Population characteristics				Physical activity characteristics			Purpose of intervention	QoL measure
			age range	disease type	severity	sex	intensity	type	setting		
1	Burnham (2002)	12/6	*M* > 50	Cancer	mild	both	light	mixed	supervised	rehabilitation	QoL index for cancer patients
2	Courneya (2003a)	62/31	*M* > 60	Cancer	chronic stable	both	moderate	free choice	home	rehabilitation	FACT
3	Courneya (2003b)	45/51	*M* > 50	Cancer	mild	both	moderate	walking	home	rehabilitation	FACT
4	Courneya (2003c)	24/28	*M* > 50	Cancer	mild	female	moderate	aerobic	supervised	rehabilitation	FACT
5	Mutrie (2007)	101/102	*M* > 50	Cancer	mild	female	moderate	aerobic	supervised	rehabilitation	FACT
6	Segal (2001)	40/42	*M* > 50	Cancer	older adults	female	light	walking	supervised	disease management	SF36
7	Segal (2003)	82/73	*M* > 60	Cancer	chronic stable	male	moderate	resistance	supervised	disease management	FACT
8	Segal (1997)	33/34	*M* > 50	Cancer	mild	female	light	walking	supervised	disease management	SF36
9	Thorsen (2005)	59/52	*M* > 50	Cancer	chronic stable	both	mod/vig	walking	home	rehabilitation	EORTC QLQ C30
10	Belardinelli (1999)[a]	50/49	*M* > 50	CVD	chronic stable	both	light	mixed	supervised	disease management	MHLWHF
11	Belardinelli (1999)	50/49	*M* > 50	CVD	chronic stable	both	light	aerobic	supervised	disease management	MHLWHF
12	Berg-Emons (2004)	18/16	*M* > 50	CVD	chronic stable	both	light	aerobic	supervised	disease management	MHLWHF

Study ID	First Author (year)	N IV/ control	Population characteristics				Physical activity characteristics			Purpose of intervention	QoL measure
			age range	disease type	severity	sex	intensity	type	setting		
13	Collins (2004)	12/15	*M* > 60	CVD	mild	male	moderate	walking	supervised	disease management	SF36
14	de Mello Franco (2006)	17/12	*M* > 50	CVD	moderate	female	moderate	aerobic	supervised	disease management	MHLWHF
15	Dugmore (1999)	62/62	*M* > 50	CVD	chronic stable	both	light	aerobic	home	rehabilitation	HRQOL visual analogue
16	Focht (2004)	40/37	*M* > 50	CVD	moderate	female	moderate	walking	supervised	rehabilitation	SF36
17	Gardner (2001)	31/30	*M* > 60	CVD	mild	both	light	walking	supervised	disease management	SF36
18	Gary (2004)	16/16	*M* > 50	CVD	mild	female	light	walking	home	disease management	MHLWHF
19	Higgins (2001)	54/51	*M* > 50	CVD	mild	both	moderate	walking	home	rehabilitation	PAIS-SR
20	Keteyan (1999)	26/25	*M* > 50	CVD	moderate	male	light	aerobic	supervised	disease management	MHLWHF
21	Koukouvou (2004)	16/10	*M* > 50	CVD	mild	male	light	aerobic	supervised	disease management	MHLWHF, QLI
22	Oka (2000)	12/12	*M* > 50	CVD	moderate	both	moderate	walking	home	disease management	Chronic Heart Failure Questionnaire
23	Taft (2001)	57/61	*M* > 60	CVD	chronic stable	both	-	aerobic	supervised	disease management	EORTC QLQ C30
24	Tsai (2004)	52/50	*M* > 50	CVD	-	both	mod/vig	aerobic	supervised	preventive/health promotion	SF36

Study ID	First Author (year)	N IV/ control	Population characteristics				Physical activity characteristics			Purpose of intervention	QoL measure
			age range	disease type	severity	sex	intensity	type	setting		
25	Tyni-Lenne (2001)	16/8	*M* > 60	CVD	chronic stable	both	light	stretching	supervised	disease management	MHLWHF
26	Wielenga (1998)	35/32	*M* > 60	CVD	mild	male	light	aerobic	supervised	disease management	SIP
27	Worcester (1993)	108/116	*M* > 50	CVD	chronic stable	male	light	aerobic	supervised	rehabilitation	HRQOL visual analogue
28	Yu (2003)	71/40	*M* > 60	CVD	chronic stable	both	moderate	aerobic	supervised	rehabilitation	SF36
29	Anderson (2005)	130/134	*M* > 50	Well	-	male	mod/vig	free choice	home	preventive/health promotion	PQOL
30	Atlantis (2004)	36/37	-	Well	-	both	mod/vig	aerobic	home	preventive/health promotion	SF36
31	Perrig-Chiello (1998)	23/23	Cut-off > 60	Well	Frail	both	light	resistance	supervised	preventive/health promotion	other
32	Brand (2006)	88/89	*M* < 50	Well	-	both	light	mixed	supervised	preventive/health promotion	WHOQOL
33	Brox (2005)	45/49	*M* < 50	Well	-	both	light	aerobic	supervised	preventive/health promotion	COOP
34	Chin (2002)	67/72	*M* > 60	Well	Frail	both	mod/vig	walking	supervised	preventive/health promotion	Subjective Well-Being for Older Persons Scale
35	Cramer (1991)	18/17	*M* < 50	Well	-	female	moderate	walking	supervised	preventive/health promotion	General Well Being scale (GWB)
36	Li (2001)	53/45	Cut-off > 60	Well	Frail	both	light	other	supervised	preventive/health promotion	SWLS, CESD, SEES

Study ID	First Author (year)	N IV/ control	Population characteristics				Physical activity characteristics			Purpose of intervention	QoL measure
			age range	disease type	severity	sex	intensity	type	setting		
37	Lindh-Astrand (2004)	15/15	*M* < 50	Well	-	female	moderate	aerobic	supervised	preventive/health promotion	other
38	Ornes (2005)	9/9	*M* < 50	Well	-	female	light	flexibility	home	preventive/health promotion	POMS
39	Partonen (1998)	70/28	*M* < 50	Well	-	both	vig	-	supervised	preventive/health promotion	SF36
40	Rejescki (2002)	80/78	Cut-off > 60	Well	moderate	both	moderate	mixed	supervised	disease management	SF36
41	Sorensen (1999)	54/43	*M* < 50	Well	moderate	both	light	resistance	supervised	preventive/health promotion	SF36
42	Stoll (2002)	50/29	*M* > 50	Well	older adults	both	light	mixed	supervised	preventive/health promotion	Trait anxiety and somatic complaints
43	Beaupre (2004)	65/66	*M* < 50	Musculo-skeletal	moderate	both	light	resistance	supervised	rehabilitation	SF36
44	Papaioannou (2003)	37/37	Cut-off > 60	Musculo-skeletal	Frail	female	light	stretching	home	disease management	Osteoporosis QoL Questionnaire
45	Ashburn (2007)	70/71	*M* > 60	Neurological	Frail	both	light	resistance	home	disease management	Euro QoL EQ 5D
46	Martin-Ginis (2003)	21/13	*M* < 50	Neurological	moderate	both	moderate	aerobic	supervised	disease management	PQOL
47	Hicks (2003)	21/13	*M* < 50	Neurological	moderate	both	moderate	aerobic		disease management	PQOL
48	Kuhl (2005)	26/27	*M* > 50	Neurological	moderate	both	-	-	home	disease management	SF36

Study ID	First Author (year)	N IV/ control	Population characteristics				Physical activity characteristics			Purpose of intervention	QoL measure
			age range	disease type	severity	sex	intensity	type	setting		
49	Romberg (2005)	47/78	*M* < 50	Neurological	chronic stable	both	light	mixed	home	disease management	MSQOL-54
50	Bendstrup (1997)	20/22	*M* > 60	Pulmonary	moderate	both	light	mixed	supervised	disease management	YQOLQ
51	Cambach (1997)	36/28	*M* < 50	Pulmonary	mild	both	mod/vig	aerobic	supervised	disease management	QWB, QLI
52	Manzetti (1994)	4/5	*M* < 50	Pulmonary	severe	both	light	aerobic	supervised	rehabilitation	CRDQ
53	Fitts (1999)	9/9	*M* < 50	Renal disease	chronic stable	both	light	stretching	home	rehabilitation	SIP
54	Parsons (2004)	6/7	*M* > 50[b]	Renal disease	End stage	both	light	aerobic	supervised	disease management	SF36
55	Da-jian (2005)	85/41	*M* < 50	Rheumatoid arthritis	mild	both	moderate	walking	supervised	disease management	QoL for Rheumatoid Arthritis
56	Zijlstra (2005)	58/76	*M* < 50	Fibromyalgia	moderate	both	light	aerobic	supervised	disease management	SF36

Notes: IV – intervention group, CVD – cardio-vascular disease, mod/vig – moderate to vigorous intensity; PAIS-SR – psychological adjustment to illness scale, PQOL – Perceived Quality of Life scale, SF36, EORTC QLQ C30 – European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire, MHLWHF – Minnesota Living with Heart Failure Questionnaire, FACT - Functional Assessment of Cancer Therapy, MSQOL-54 – Multiple Sclerosis Quality of Life Questionnaire, YQOLQ – York Quality of Life Questionnaire, CRDQ – Chronic Respiratory Disease Questionnaire, QWB – Quality of Well-Being, QLI – Quality of Life Index, SWLS – life satisfaction, CESD – Centre for Epidemiological studies Depression scale, SEES – Subjective exercise experience scale; [a]results assessed separately for two different conditions, vs control group; [b]control group *M* age = 49 ±25, IV *M* age = 60 ±17.

Table 2: Distribution of studies across classification variables

Moderating variable	Classification	N studies
Disease group		
	cardiovascular diseases	19
	neurological diseases	5
	respiratory diseases	3
	cancer	9
	musculoskeletal conditions	3
	renal disease	2
	arthritis	1
	no diagnosed disease (well)	14
Sample characteristics		
	Mean age <50	25
	Mean age >50 & <60	15
	Mean age >60	15
	Male only*	7
	Female only	13
	Mixed sex	40
Purpose of intervention**		
	rehabilitation	12
	prevention or health promotion	11
	chronic disease management/ treatment	24
Exercise intensity**		
	Light	32
	Moderate	22
Exercise type**		
	Aerobic (of which walking)	34 (13)
	resistance	5
	Other (stretching, flexibility, free choice)	5
	combined	7
Social exercise environment**		
	Home based	18
	Supervised, individual	17
	Supervised, group	18

* N>56 as 2 studies reported outcomes for male and females separately.
** where N<56, this is due to missing information from original studies.

Table 3 ES of change in QoL outcome compared with control groups by domain using a fixed effects model

Domain	Clinical population				Well population			
	N	Mean ES (95% CI) [a]	SE	Q[b]	N	Mean ES (95% CI) [a]	SE	Q[b]
Overall QoL	21	0.27** (0.17, 0.38)	0.05	175.89**	7	0.11 (-0.03, 0.24)	0.07	28.09**
Physical Health	18	0.04 (-0.06, 0.15)	0.05	12.72**	6	0.22* (0.07, 0.37)	0.08	19.66*
Psychological Wellbeing	17	0.05 (-0.06, 0.16)	0.06	20.08	6	0.21* (0.06, 0.36)	0.08	16.91*
Level of Independence	12	-0.02 (-0.15, 0.12)	0.07	16.48	3	-0.06 (-0.31, 0.17)	0.12	1.41
Social Relationships	10	0.05 (-.09, 0.19)	0.07	3.82	5	0.00 (-0.16, 0.17)	0.08	8.09

Notes: [a] test represents significance of difference from zero; **p* <.01, ***p* <.001; [b]significant Q statistic indicates heterogeneity within the sample; [c]insufficient numbers to analyse; N relates to number of studies in the analysis; all statistics related to a single measurement per trial (that closest to 6 months)

Hypothesis 1: The pool of studies providing data at the three to six month time-point included 12 rehabilitation studies, 11 disease prevention studies (well participants), and 24 studies aimed at symptom control, or preventing the deterioration of a condition i.e., the disease management group (Table 4). The degree of heterogeneity explained by the reason for intervention ($Q(2,25) = 31.88$, $p<.001$) was significantly greater than that explained by splitting well from clinical populations ($Q(1,26) = 3.79$, $p = 0.05$).

The first hypothesis was supported for overall QoL, in that rehabilitation interventions reported better gains in QoL than well participants, or patients exercising for disease management (ES rehabilitation [ESr] = 0.55 vs ES prevention [ESp] = 0.11 vs ES treatment [ESt] = -0.001). Splitting the interventions involving clinical groups according to intervention purpose explained some, but not all of the heterogeneity in overall QoL response; while still significant within each sub-group, the value of the Q statistic reduced significantly for both rehabilitation ($\Delta\chi^2(13) = 54.85$, $p<0.001$) and disease management groups ($\Delta\chi^2(8) = 149.13$, $p<0.001$). However, greater improvements in the psychological domain were reported for preventative initiatives (i.e., well population; ESp = 0.21 vs ESr = 0.11), with the poorest effects reported by the disease management group (ESt = -0.26) (see Table 4). There were no significant differences between groups in the other domains. As heterogeneity was at least partially explained by intervention purpose, the subsequent results are presented separately for each subgroup.

Hypothesis 2: The hypothesis that better gains in QoL would be detected for the psychological than for the physical health domain was not supported. For well participants, both psychological and physical QoL showed a similar degree of significant improvement relative to no-exercise controls (ES = -0.21, $p<.01$ [N = 6] and ES = 0.22, $p<.01$ [N = 6] respectively). Patients undertaking exercise for rehabilitation purposes also reported a small, but non-significant positive effect for both domains (psychological QoL ES = 0.12, [N = 4]; physical QoL ES = 0.09, [N = 5]). However, patients exercising for disease management reported a significant deterioration in psychological QoL (ES = -0.26, *p*<.001 [N = 13]), despite a small but significant improvement in physical QoL (ES = 0.19, *p*<.01 [N = 13]).

Table 4: Estimated weighted mean effect size of intervention group response compared with control group by purpose of intervention under a fixed-effects model

	Q_B		Rehabilitation ES (SE)	Prevention ES (SE)	Treatment ES (SE)
Overall QoL	31.88***		0.55*** (0.07)	0.11 (0.07)	-0.001 (0.07)
		CI:	0.41, 0.69	-0.03, 0.24	-0.14, 0.14
Physical Health	1.20		0.09 (0.09)	0.22** (0.08)	0.19 (0.06)
		CI:	-0.09, 0.27	0.07, 0.37	0.06, 0.32
Psychological well-being	22.82***		0.12 (0.10)	0.21** (0.08)	-0.26*** (0.07)
		CI:	-0.09, 0.32	0.05, 0.36	-0.39, -0.13
Level of independence	0.91		0.04 (0.10)	-0.07 (0.12)	-0.09 (0.10)
		CI:	-0.16, 0.24	-0.30, 0.17	-0.28, 0.10
Social relationships	0.36		-0.03 (0.10)	0.00 (0.08)	0.06 (0.11)
		CI:	-0.23, 0.17	-0.16, 0.17	-0.16, 0.27

Notes: ES = pooled weighted mean effect size; SE = standard error; Q_B = between group variance; CI = 95% confidence interval; **p* <0.05, ***p* <0.01, ****p* <0.001,

Hypothesis 3: For overall QoL, the hypothesis that exercise intensity would explain a significant part of the heterogeneity in overall QoL was supported for rehabilitation patients ($\Delta\chi^2(1) = 70.05$, $p<0.001$), but not for those exercising for disease management ($\Delta\chi^2(1) = 1.31$, $p>.05$). Due to small numbers of studies involving vigorous intensity exercise, the moderate and vigorous exercise groups were collapsed for analysis. As predicted, rehabilitation patients, reported greater gains in QoL for light intensity exercise than for moderate intensity (ES = 1.30 vs ES = 0.05). In the disease management group, although psychological QoL was significantly poorer post-intervention for moderate intensity exercise (moderate intensity; ES = -0.69 vs light intensity; ES = -0.01), this was as a result of a significant QoL decrease of a moderate effect size in response to moderate intensity exercise, rather than a positive QOL outcome for light intensity exercise. However, physical QoL improved significantly more for moderate exercise than light intensity (ES = 0.57 vs ES = -0.03 respectively) in the disease management group.

Hypothesis 4: There was a significant advantage for light over moderate intensity exercise in the well group, for overall QoL (Q (1, 5) = 15.95, $p<0.001$; low intensity ES = 0.63 [CI = 0.34, 0.92], $p<0.001$, moderate intensity ES = -0.04 [CI = -0.19, 0.11], $p = 0.64$) and in the psychological domain (Q(1,4) = 20.14, $p<0.001$; ES = 0.16, vs. ES = -0.54). However, moderate intensity exercise resulted in better gains in QoL in the physical health domain (Q (1,4) = 4.62, $p<0.05$; ES = 0.63, vs. ES = 0.29). Domain specific analyses were not possible for the independence and social domains due to insufficient studies. Thus, hypothesis 4 was supported for the physical QoL, but rejected for overall QoL, and psychological QoL.

Hypothesis 5: Exercise type was differentiated into three variants; structured aerobic exercise (i.e., using gym based equipment or exercise classes [N = 15]), walking (N = 8), and resistance/ stretching (N = 5). However, the number of studies within each intervention purpose subgroup was too small for analysis.

Hypothesis 6: The number of studies reporting on social QoL was small (N= 5 well studies, N = 4 rehabilitation studies, N = 5 disease management studies) and therefore the number of possible analyses were limited. However, exercise setting explained a significant amount of variance between studies in the social domain for well populations (Q(1,3) = 6.82, $p<.01$), showing better QoL outcomes for well participants exercising in individual (ES = 0.34) rather than group settings (ES = -0.14). There were no significant differences in rehabilitation studies (Q(1, 2) = 0.14), or the disease management group (Q(1,3) = 0.27).

However, the social setting in which exercise took place did influence overall QoL. Well participants reported greater improvements to QoL when exercising individually than as a group, for both the psychological domain (ES = 0.54 vs. ES = 0.09; Q(1,3)=5.97, $p<0.05$), and physical domain (ES = 0.52 vs. ES = 0.10; Q(1,3)=5.06, $p<0.05$). However, in contrast to the outcomes for individual domains, overall QoL improved when exercising in groups rather than individually for all subgroups of participants (well participants; ES (group) = 0.29 vs. ES (individual) = -0.01; rehabilitation ES = 0.83 vs. ES = 0.29; disease management ES = 0.35 vs. ES = -0.02).

After one year, rehabilitation studies reported a moderate significant improvement in overall QoL (N = 4, ES = 0.42, $p<.001$), although there was still significant heterogeneity between studies (Q = 25.16, $p<.001$). However, there was a deterioration across all studies in the independence QoL domain (ES = -0.26, $p<.05$). Disease management groups reported a small but negative change in overall QoL, although this was not significant (N = 3, ES = -0.22, $p = 0.06$). Insufficient studies for analysis reported one year outcomes on specific domains in disease management studies or well populations.

Discussion

The results of this comprehensive meta-analysis suggest that over the short term of three to six months, a small but meaningful improvement in QoL can be brought about by exercise interventions in well populations, and in patients exercising as part of their rehabilitation from a health event. However, there was a small deterioration in overall and psychological QoL for patients involved in exercise interventions as part of the treatment or management of chronic conditions (e.g., people diagnosed with chronic obstructive pulmonary disease or multiple sclerosis). The results reflect outcomes compared with similar patients in a no-exercise control group, and persisted over one year. The findings indicate that disease severity and the reason for exercise i.e., to achieve an improvement in condition rather than maintenance of a poor health state, should be considered carefully when recommending exercise interventions for clinical populations. Although patients exercising for the management of their health conditions did report a small improvement in their perceptions of their physical QoL, their psychological and overall QoL improved significantly less than for patients in the no-exercise condition over the same period of time.

Greater specificity was gained by assessing individual domains in addition to overall QoL. This was particularly evident in studies involving well populations, where a null result for change in overall QoL masked significantly better outcomes for both the psychological and physical health domains. Furthermore, greater improvements were reported for psychological QoL in response to light rather than moderate intensity exercise, although the opposite effect was reported for the physical domain where greater improvements in physical QoL were associated with moderate intensity exercise. Thus, contrary to the hypotheses, overall and psychological QoL were improved more following light intensity, as opposed to moderate intensity exercise. This finding may be unsurprising given that studies typically recruited unfit or inactive adults who are identified as being at high risk for future health problems. Fitness has been previously identified as a moderating factor in the enjoyment of higher exercise intensities (Ekkekakis & Petruzzello, 1999), and the finding that barriers to the uptake of exercise are far from unique to chronically ill populations has been reported elsewhere recently (Ofir, Laveneziana, Webb, Lam, &

O'Donnell, 2008). Furthermore, light intensity exercise has been reported as having a more positive effect in frail elderly populations (e.g., Netz et al., 2005), of which there were five in the present review.

Variation in outcomes across QoL domains were also reported in the disease management group. Here the null finding of an effect for overall QoL masked a significant decrease in psychological QoL, relative to a small improvement in physical QoL. Furthermore, as for healthy exercisers, moderate to high intensity exercise was associated with a significant improvement in QoL in the physical domain, but was associated with a significant reduction in psychological QoL in the disease management group. Given that patients perceived a positive impact on their physical QoL following moderate intensity exercise, the relative negative response for overall and psychological QoL was surprising. An explanation for this finding may result from the inability of the concrete fitness outcomes of exercise interventions to match up to patients' unrealistically high expectations which can stem from optimism generated by the novelty of being offered a potentially effective treatment (e.g., Shim, Russ, & Kaufman, 2007). While meeting ones' expectations is reported to be a significant positive predictor of future adherence (Brassington, Atienza, Perczek, DiLorenzo, & King, 2002), failure to do so may compromise self-efficacy and self-worth, resulting in a negative impact on mood and emotions.

Unexpected results were also found for exercise setting, in that well participants reported better improvements in social QoL for individual rather than group-based settings. No difference was reported for either clinical population group. This finding suggests that the contact made with others in the single context of exercise classes may not have a meaningful impact on broader social support and concerns. An individual's most important determinants of social QoL may continue to be their close friends and family, leaving the benefits of group exercise settings to be transmitted through self-efficacy and enjoyment, as suggested by the improvements found in the psychological domain. Further investigation of whether the quality and quantity of social contacts moderates the effect of group exercise on the social QoL domain would be useful in evaluating this possibility.

While the final hypothesis was not supported for the social domain, group settings were found to promote better overall QoL across the three participant groups. Prior research suggests better outcomes result from group interventions as they promote adherence, and thereby provide greater exercise exposure or dose (Hong, Hughes, & Prohaska, 2008). Increased adherence in chronically ill populations may also result from the facilitated social support from exercising with others diagnosed with a similar condition (Duncan & McAuley, 1993), and a reduction in the barriers to physical activity perceived to exercising in mainstream settings (Emslie, Whyte, Campbell, Mutrie, Lee, Ritchie et al., 2007). Few studies reported the level of adherence of participants to exercise interventions, which further restricts the ability of MAs such as this to determine the impact of attendance or exercise dose on QoL outcomes.

Limitations

While an effort was made in the analysis to cluster results of studies using different measures into similar domains, no two measures are directly comparable. As such, the accuracy with which we can conclude the findings in relation to each of the specific domains listed, is limited by the degree to which designers of different QoL instruments interpret and reflect these. Similarly, although it is useful to present an overall QoL score for comparison purposes, many measures do not cover a comprehensive range of important QoL issues, so may still reflect somewhat different constructs. Consequently some measures may miss crucial subjective changes.

A further limitation is that a relatively large number of statistical analyses were employed. An attempt was made to reduce the likelihood of Type I error through specifying *a priori* hypothesis tests rather than conducting *post hoc* exploratory analyses. However, we considered that this approach was justified, given the opportunity of a review of this size to explore the effects of a wide range of possible moderators of the effects of exercise on QoL. To retain as many studies as possible in the analysis, the quality of interventions was also not included as an inclusion/exclusion criterion beyond the basic requirements that only randomized trials were included, and those that provided sufficient pre- and post-test data for both intervention and control groups for the calculation of effect sizes. Greater specificity of exercise effects may be possible through restriction of consideration to only the highest quality studies. However, this too has potential disadvantages, for example as a result of bias through lack of inclusion of all available data.

Conclusions and practical implications

The present study extended previous disease-specific MAs by analysing the outcomes of exercise on patients from a range of disease groups. Greater explanatory power was obtained by differentiating between populations according to the purpose of the intervention than by splitting studies into clinical versus well populations alone. It is likely that this finding stems from the greater information contained within the purpose of the intervention than by disease state alone, for instance, disease severity, physical condition (i.e., strength or fitness), and a persons' potential for improvement. As the detail necessary to extract these individual factors from original studies is not routinely available, categorisation by intervention purpose may represent a more accessible proxy than other features, as a basis for considering the appropriateness of interventions for particular populations. Not all previous SRs have reported improvements in QoL following exercise interventions (Lawlor & Hopker 2001; Jolly et al., 2006), and it may be that the nature of the populations and intended uses for the interventions included in their samples may provide some explanation of the heterogeneity of meta-analytical results.

Although there is a tendency in health care to conclude that because physical health has not improved an intervention has not worked, psychological and other dimensions of change are also important. Psychological factors give some insight into why improvements in physical health may not be occurring. For example, lack of change on QoL measures may indicate that patients do not perceive the benefits of exercise interventions to be meaningful, which may serve to explain their poor adherence to treatment, but may also provide a starting point for opening further patient-professional discussions. Furthermore, it seems likely that poor emotional functioning may significantly inhibit the perception of physical benefits. Previous research on QoL shows how the presence of intense negative feelings like moderate depression, has a widespread effect on all important dimensions of QoL, so that they are perceived through this negative filter as poorer (Skevington & Wright, 2001). If we can identify what types of intervention are associated with better gains in QoL, we can then at least start to build interventions that have a greater chance of adoption and success in physical terms.

The finding of a poor response in overall and psychological QoL in patients recommended to exercise in the management of their chronic disease, has implications for the timing of exercise interventions. The results suggest that this period in the 'natural history' of a chronic illness may not be optimal for introducing a physical exercise intervention. Participants may be less receptive to behaviour change as their mood becomes more negative, and if it is at its poorest at the point that they leave the programme there may be damaging consequences to any resolve towards maintenance or adherence in the longer term. As such, it would be beneficial to consistently monitor patients' psychological responses simultaneously with their physical responses to exercise, to ensure that the benefits truly outweigh the costs for vulnerable patient groups. Similarly, it is understood that there may be a reciprocal relationship between QoL and exercise behaviour, such that rather than exercise behaviour determining QoL outcomes, having better QoL may increase one's ability to engage in exercise behaviour. Identifying whether patients have a sufficiently positive level of QoL at the outset of an intervention to be able to bring to it the energy and commitment it needs, may increase the efficiency and acceptability of interventions and could help to avoid inappropriate referrals.

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Footnotes:

1 The term *exercise* is often used interchangeably with *physical activity*, however, the two are conceptually distinct. Exercise is a sub-type of physical activity which is planned, structured, repetitive, and purposeful (Caspersen, Powell, & Christenson, 1985). As the interventions that are the subject of this paper seek to increase purposeful behaviour, the term *exercise* is adopted throughout.