**Exercise 1**

**Read the following Abstract:**

**BACKGROUND:**

Exercise or physical activity is recommended for improving pain and functional status in people with knee or hip osteoarthritis. These are complex interventions whose effectiveness depends on one or more components that are often poorly identified. It has been suggested that health benefits may be greater with high-intensity rather than low-intensity exercise or physical activity.

**SEARCH METHODS:**

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; issue 06, 2014), MEDLINE (194 8 to June 2014), EMBASE (198 0 to June 2014), CINAHL (1982 to June 2014), PEDro (1929 to June 2014), SCOPUS (to June 2014) and the World Health Organization (WHO) International Clinical Registry Platform (to June 2014) for articles, without a language restriction. We also hand-searched relevant conference proceedings, trials, and reference lists and contacted researchers and experts in the ﬁeld to identify additional studies.

**SELECTION CRITERIA:**

We included randomized controlled trials of people with knee or hip osteoarthritis that compared high- versus low-intensity physical activity or exercise programs between the experimental and control group. High-intensity physical activity or exercise programs training had to refer to an increase in the overall amount of training time (frequency, duration, number of sessions) or the amount of work (strength, number of repetitions) or effort/energy expenditure (exertion, heart rate, effort).

**DATA COLLECTION AND ANALYSIS:**

Two review authors independently assessed study eligibility and extracted data on trial details. We contacted authors for additional information if necessary. We assessed the quality of the body of evidence for these outcomes using the GRADE approach.

**MAIN RESULTS:**

We included reports for six studies of 656 participants that compared high- and low-intensity exercise programs; five studies exclusively recruited people with symptomatic knee osteoarthritis (620 participants), and one study exclusively recruited people with hip or knee osteoarthritis (36 participants). The majority of the participants were females (70%). No studies evaluated physical activity programs. We found the overall quality of evidence to be low to very low due to concerns about study limitations and imprecision (small number of studies, large confidence intervals) for the major outcomes using the GRADE approach. Most of the studies had an unclear or high risk of bias for several domains, and we judged five of the six studies to be at high risk for performance, detection, and attrition bias. Low-quality evidence indicated reduced pain on a 20-point Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain scale (mean difference (MD) -0.84, 95% confidence interval (CI) -1.63 to -0.04; 4% absolute reduction, 95% CI -8% to 0%; number needed to treat for an additional beneficial outcome (NNTB) 11, 95% CI 14 to 22) and improved physical function on the 68-point WOMAC disability subscale (MD -2.65, 95% CI -5.29 to -0.01; 4% absolute reduction; NNTB 10, 95% CI 8 to 13) immediately at the end of the exercise programs (from 8 to 24 weeks). However, these results are unlikely to be of clinical importance. These small improvements did not continue at longer-term follow-up (up to 40 weeks after the end of the intervention). We are uncertain of the effect on quality of life, as only one study reported this outcome (0 to 200 scale; MD 4.3, 95% CI -6.5 to 15.2; 2% absolute reduction; very low level of evidence).Our subgroup analyses provided uncertain evidence as to whether increased exercise time (duration, number of sessions) and level of resistance (strength or effort) have an impact on the exercise program effects.Three studies reported withdrawals due to adverse events. The number of dropouts was small. Only one study systematically monitored adverse effects, but four studies reported some adverse effects related to knee pain associated with an exercise program. We are uncertain as to whether high intensity increases the number of adverse effects (Peto odds ratio 1.72, 95% CI 0.51 to 5.81; - 2% absolute risk reduction; very low level of evidence). None of the included studies reported serious adverse events.

Identify the population, participants, problem, …etc. (P)?

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What intervention or exposure, therapy, treatment, test, or issue of interest should be considered (I)?

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What will the comparison be - if anything (C)?

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What outcome is important? (O)?

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The study design is:

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The clinical research question is:

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**Exercise 2**

**Read the following Abstract:**

**BACKGROUND:**

Epidemiological studies have examined the association between the use of non-steroidal anti-inflammatory drugs (NSAIDs) and the risk of Alzheimer's disease (AD). Recently, a variety of experimental studies indicates that a subset of NSAIDs, such as ibuprofen or flurbiprofen, also have Abeta-lowering properties in both AD transgenic mice and cell cultures of peripheral, glial and neuronal origin.

**METHODS:**

Participants with mild-moderate AD (Mini-Mental State Examination score >15, <26; Clinical Dementia Rating= 0.5-1), 65 years or older, with reliable caregivers, were recruited between April 2003 and September 2004. Seven AD Outpatient Treatment Centers screened 530 patients, 132 of whom were enrolled. Intervention consisted of 400 mg ibuprofen twice a day or placebo, together with 20 mg once a day of esomeprazol, or placebo. The primary measure was any one-year change in the Alzheimer Disease Assessment Scale- Cognitive (ADAS-Cog) subscale score. Secondary measures included changes in MMSE, CDR, Basic and Instrumental Activities of Daily Living scales, and Neuropsychiatric Inventory (NPI).

**RESULTS:**

Fifty-one patients (77%) in the ibuprofen vs 46 (70%) in the placebo group completed the protocol (p>0.20). In intention-to- treat analysis, ADAS-Cog score worsening was similar in the two groups (p=0.951, treatment difference= 0.1, CI -2.7; 2.9). No differences were found for any secondary outcomes. In a subsample of genotyped patients, ApoE epsilon4 carriers treated with ibuprofen (n=27) were the only group without significant cognitive decline.

Identify the population, participants, problem, …etc. (P)?

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What intervention or exposure, therapy, treatment, test, or issue of interest should be considered (I)?

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What will the comparison be - if anything (C)?

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What outcome is important? (O)?

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The study design is:

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The clinical research question is:

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**Exercise 3**

**Read the following Abstract:**

**Setting:** Aberdeen.

**Subjects:** All 2792 children in Aberdeen born in 1921 and attending school on 1 June 1932 who sat a mental ability test as part of the Scottish mental survey 1932.

**Main outcome measure:** Survival at 1 January 1997.

**Results:** 79.9% (2230) of the sample was traced. Childhood mental ability was positively related to survival to age 76 years in women (P<0.0001) and men (P<0.0001). A 15 point disadvantage in mental ability at age 11 conferred a relative risk of 0.79 of being alive 65 years later (95% confidence interval 0.75 to 0.84); a 30 point disadvantage reduced this to 0.63 (0.56 to 0.71). However, men who died during active service in the second world war had a relatively high IQ. Overcrowding in the school catchment area was weakly related to death. Controlling for this factor did not alter the association between mental ability and mortality.

Identify the population, participants, problem, …etc. (P)?

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What intervention or exposure, therapy, treatment, test, or issue of interest should be considered (I)?

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What will the comparison be - if anything (C)?

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What outcome is important? (O)?

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The study design is:

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The clinical research question is:

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**Exercise 4**

**Read the following Abstract:**

**BACKGROUND:**

Allotments in the UK are popular and waiting lists are long. There is, however, little evidence on the health benefits of allotment gardening.

**METHODS:**

Self-esteem, mood and general health were measured in 136 allotment gardeners pre- and post- an allotment session, and 133 non-gardener controls. Allotment gardeners also detailed the time spent on their allotment in the current session and previous 7 days, and their length of tenure.

**RESULTS:**

Paired t-tests revealed a significant improvement in self-esteem (P < 0.05) and mood (P < 0.001) as a result of one allotment session. Linear regression revealed that neither the time spent on the allotment in the current session, the previous 7 days or the length of tenure affected the impacts on self-esteem and mood (P > 0.05). One-way ANCOVA revealed that allotment gardeners had a significantly better self-esteem, total mood disturbance and general health (P < 0.001), experiencing less depression and fatigue and more vigour (P < 0.0083).

Identify the population, participants, problem, …etc. (P)?

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What intervention or exposure, therapy, treatment, test, or issue of interest should be considered (I)?

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What will the comparison be - if anything (C)?

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What outcome is important? (O)?

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The study design is:

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The clinical research question is:

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**Exercise 5**

**Read the following Abstract:**

**Background**

Human papillomavirus (HPV) vaccination programmes were first implemented in several countries worldwide in 2007. We assessed the population-level consequences and herd effects after female HPV vaccination programmes, to verify whether or not the high efficacy reported in randomised controlled clinical trials are materialising in real-world situations.

**Methods**

We searched the Medline and Embase databases (between Jan 1, 2007 and Feb 28, 2014) and conference abstracts for time-trend studies that analysed changes, between the pre-vaccination and post-vaccination periods, in the incidence or prevalence of at least one HPV-related endpoint: HPV infection, anogenital warts, and high-grade cervical lesions. We used random-effects models to derive pooled relative risk (RR) estimates. We stratified all analyses by age and sex. We did subgroup analyses by comparing studies according to vaccine type, vaccination coverage, and years since implementation of the vaccination programme. We assessed heterogeneity across studies using *I*2 and χ2 statistics and we did trends analysis to examine the dose–response association between HPV vaccination coverage and each study effect measure.

**Findings**

We identified 20 eligible studies, which were all undertaken in nine high-income countries and represent more than 140 million person-years of follow-up. In countries with female vaccination coverage of at least 50%, HPV type 16 and 18 infections decreased significantly between the pre-vaccination and post-vaccination periods by 68% (RR 0·32, 95% CI 0·19–0·52) and anogenital warts decreased significantly by 61% (0·39, 0·22–0·71) in girls 13–19 years of age. Significant reductions were also recorded in HPV types 31, 33, and 45 in this age group of girls (RR 0·72, 95% CI 0·54–0·96), which suggests cross-protection. Additionally, significant reductions in anogenital warts were also reported in boys younger than 20 years of age (0·66 [95% CI 0·47–0·91]) and in women 20–39 years of age (0·68 [95% CI 0·51–0·89]), which suggests herd effects. In countries with female vaccination coverage lower than 50%, significant reductions in HPV types 16 and 18 infection (RR 0·50, 95% CI 0·34–0·74]) and in anogenital warts (0·86 [95% CI 0·79–0·94]) occurred in girls younger than 20 years of age, with no indication of cross-protection or herd effects.

Identify the population, participants, problem, …etc. (P)?

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What intervention or exposure, therapy, treatment, test, or issue of interest should be considered (I)?

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What will the comparison be - if anything (C)?

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What outcome is important? (O)?

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The study design is:

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The clinical research question is:

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