



**How to narrow the gap in disability free life expectancy between rich and poor, with a focus on long-term conditions: a rapid evidence synthesis**

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**Final Report**

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## Main messages

### What is the problem?

- Socioeconomic inequalities in disability free life expectancy (DFLE) are a major and growing public health concern.
- People living in the least deprived areas of England can expect to live longer in good health than their peers in the most deprived areas.
- Long-term conditions are a key driver of disability, and many have a differential impact on people who are more disadvantaged.
- Intervening to prevent / optimise the management of long-term conditions offers potential to reduce disability and extend disability free life expectancy. Targeting disadvantaged populations may help to narrow the gap in DFLE
- National Institute for Health and Care Excellence (NICE) has produced guidelines on effective interventions for key long-term conditions
- Questions remain over which interventions are effective at preventing/tackling long-term conditions for people who are disadvantaged.

### What did we do?

We selected three long-term conditions to study (depression, osteoarthritis (OA) and type 2 diabetes (T2D)), as major sources of morbidity and mortality. For each condition:

- NICE guidelines were searched to identify recommended, evidence-based interventions.
- In the evidence that supports NICE recommendations, we looked for variation in outcomes by social disadvantage.
- We updated and extended the NICE evidence reviews to include a wider range of study designs beyond randomised controlled trials.
- Evidence was synthesised using standard rapid review methods.

### What did we find?

Research evidence underpinning NICE recommendations for intervening in T2D, OA and depression offered no robust information on how outcomes may vary with social disadvantage.

In our wider searches, we found limited evidence for social patterning in outcomes of interventions for two of the exemplar conditions (depression and OA), and no evidence for T2D.

The limited evidence of social patterning was heterogeneous (in study design, populations, comparable measures of SES, outcomes) and tended to show better outcomes for less disadvantaged people.

NICE guidance aims to improve consistency in the delivery of effective treatments and clinical outcomes at a population level. However, a lack of consideration of SES within the evidence base generates uncertainty about the impact of the recommended interventions for disadvantaged populations.

### What does it mean?

This study has identified an important gap in the evidence needed to inform policy on improving the gap in DFLE between rich and poor. There is a dearth of research on how the impacts of LTC interventions vary for people living in different socioeconomic circumstances. Routine inclusion of measures of socioeconomic status/social disadvantage in intervention studies could be considered to develop the evidence base at minimal cost and inconvenience.

# Executive summary

## Context:

Socioeconomic inequalities in disability free life expectancy (DFLE) are a major and growing public health concern. People living in the least deprived areas of England can expect to live longer in good health than their peers living in the most deprived areas. Action is required to close this gap and achieve five extra years of life in good health across the population. Long-term health conditions are a key driver of disability. Therefore, intervening to reduce the impact of common long-term health conditions on the most disadvantaged in society has potential to narrow the gap in DFLE.

This report aims to summarise high-level evidence on how best to increase DFLE through intervening in long-term health conditions, and which approaches work best for the most disadvantaged populations. A focus on three common, exemplar conditions is used to address the following questions:

- Which interventions are effective at the prevention<sup>1</sup> of disability associated with common, specified long-term conditions (LTCs)?
- What is the size of the impact of effective interventions and how does this vary by socioeconomic status?

## Method:

This study focuses on depression, osteoarthritis (OA), and type 2 diabetes (T2D), three LTCs that are a major source of morbidity and mortality. Evidence on effective interventions for these conditions has already been reviewed and distilled into recommendations by the UK National Institute for Health and Care Excellence (NICE)<sup>2</sup>. We took the NICE evidence reviews as our start point, to identify information on differential impact of interventions by socioeconomic status.

For each condition, we followed a four-step process:

- NICE guidelines were searched to identify recommended interventions.
- Evidence cited in support of these NICE interventions was examined to identify any variation in outcomes by socioeconomic status.
- We updated the reviews of evidence to support the NICE guidance for each condition: July 2008 (depression); January 2016 (OA); and July 2012 (T2D).
- Where we found no data on outcomes by socioeconomic status in the evidence supporting NICE recommendations, we extended our search. Key bibliographic databases were used to identify observational studies (which are not included in NICE reviews), and to update NICE searches for randomised controlled trials.

Where NICE guidance included a large range of interventions, we focussed on the most commonly implemented or clinically important, based on expert recommendations. Our approach to evidence for diabetes was modified to consider only systematic reviews. This

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<sup>1</sup> Secondary prevention refers to identification of disease in its early stages, before the onset of signs and symptoms. Tertiary prevention aims to reduce the impact of established disease, through treatment and rehabilitation.

<sup>2</sup> NICE guidance is based on expert evaluation of research evidence and is in widespread use in the NHS.

reflects the size of the evidence base and recent work by the Cochrane group to identify evidence of social patterning in diabetes outcomes.

## **Results:**

None of the evidence to support interventions in NICE guidance for depression, OA, and T2D reported outcomes for people of different socioeconomic status. We identified additional evidence about the effectiveness of interventions by SES in seven systematic reviews for depression and 12 primary studies (2 randomised controlled trials and 10 prospective cohort studies) for OA. A full text assessment of 164 systematic reviews was conducted for T2D, but no studies met our criteria.

## **Depression**

Evidence focused on the effectiveness of cognitive behaviour therapy (CBT) by employment (three reviews), educational level (two reviews), and socioeconomic status (two reviews). Educational level and employment status did not moderate outcomes following CBT or iCBT. There was no evidence that CBT produces different outcomes by SES for depression in primary school children. In secondary school settings, CBT interventions appeared to be less effective for people of lower socioeconomic status. In adults, we found that there was no evidence to support that iCBT offers different outcomes based on an individual's SES, specifically, level of education. Although guided and unguided iCBT did not offer different outcomes between patients who were unemployed, we found that guided iCBT was associated with poor outcomes when compared to usual care.

## **Osteoarthritis**

Six studies focused on effectiveness of surgical interventions, five on education and self-management and one on pharmacological management. Findings were inconsistent. Five studies reported no difference in effectiveness by level of education, five reported that the interventions favoured people with higher educational levels. Education and self-management programmes reduced pain amongst the employed at three months. By 12 months no one reported any benefit. Single studies have reported total knee arthroplasty (TKA) improved clinical outcomes best in high income groups and no relationship between outcomes and rural/urban living.

## **Type II Diabetes**

No studies assessing the impact of T2D interventions by SES status were identified. Ten Cochrane reviews of T2D interventions planned to report outcomes by SES, but this was not possible due to the lack of data in the primary studies.

## **Conclusion:**

This study has identified an important gap in the evidence needed to inform policy on narrowing the gap in DFLE between the rich and poor. There is a dearth of research on how the impacts of interventions for long-term conditions vary for people living in different socioeconomic circumstances. In order to target interventions or evaluate the impact of policies and interventions on disadvantaged groups, measurement of socioeconomic status has to become the norm. More widespread capture of data on socioeconomic circumstances in intervention studies and routine health and social care should be considered to fill this gap.

## Context

Inequalities in disability-free life expectancy (DFLE) by socioeconomic status (SES) continue to grow.<sup>1</sup> Men and women living in the least deprived areas of England can expect to live over 18 years longer in good health than people living in the most deprived areas.<sup>2</sup> DFLE is influenced by the prevalence of disability as well as mortality rates. People with a disability experience poor health outcomes, have worse access to education and work opportunities, and are more likely to live in poverty than those without a disability.<sup>3</sup>

Long-term health conditions are one of the key drivers of disability.<sup>4</sup> Currently, around 26 million people in England live with at least one LTC,<sup>5</sup> and the prevalence is increasing. The burden of LTCs falls on more disadvantaged groups, who experience earlier onset of single and multiple LTCs, and greater disease severity.<sup>6</sup> Evidence to guide the management of LTCs is extensive, but our understanding of the impact on the development of disability is more limited. However, a forthcoming review of evidence by Jagger and colleagues identified and ranked 22 long-term conditions<sup>3</sup> that impact on disability-free (and total) life expectancy. They include some of the greatest contributors to mortality and morbidity, including osteoarthritis, diabetes and depression.

Interventions that enhance the prevention and management of LTCs have potential to impact on the development of disability in later life and play a key role in DFLE. To narrow the gap in DFLE, interventions would need to be effective (or disproportionately effective) in the high risk (disadvantaged) groups, and/or able to raise average population health. In contrast, interventions that are equally effective across socioeconomic groups, or which produce better outcomes in more advantaged populations, will do little to close the gap in DFLE.

This study aims to address a gap in our understanding of what works to narrow the gap in DFLE between different SES groups. To complete this work within available resources, we focus on a) three conditions that have a significant impact on population health (See Appendix 1), and b) secondary and tertiary (but not primary) prevention.

### Research objective

This report aims to summarise evidence on how best to increase DFLE through intervening in long-term health conditions, and which approaches work best for the most disadvantaged populations.

This research addresses the following objectives:

- (i) To identify effective interventions that prevent or postpone the development of disability associated with common, specified long-term conditions (depression, OA and T2D)
- (ii) To describe how the impact of interventions varies by socio-economic status, and which interventions are effective for people of lower socio-economic status.

In the following sections, we present three evidence syntheses, reporting on the most effective interventions for each LTC, including an analysis of how these vary by SES group.

## Box 1 Key terms

**A long-term condition (LTC)** is defined as a disease that cannot be cured but can be managed or controlled with medication and/or therapy.<sup>7</sup>

**Socioeconomic status (SES)** is a complex multi-factor construct which measures an individual's combined wealth and social status, often commonly defined by factors such as income, level of education, and social class.<sup>8</sup>

**Disability:** The World Health Organisation describes disability as a condition that causes:

- a) Impairment – a deterioration of the functioning of the body;
- b) Activity limitation – difficulty in performing basic activities necessary for independent living at home such as bathing, dressing, cooking, eating or walking;
- c) Restrictions in participating in social activities or activities that are not required daily such as managing personal finances.<sup>9</sup>

**Disability free life expectancy (DFLE)** is a measure of the number of years that a person is expected to continue to live in a healthy condition.<sup>10</sup>

### **Prevention:**

**Primary prevention** - prevention of disease or injury before it occurs.

**Secondary prevention** - measures that lead to early detection/diagnosis & prompt treatment of illness.

**Tertiary prevention** - measures aimed at rehabilitation following significant illness/reducing the consequences of disease.<sup>11</sup>

## Scoping of the evidence

Initial scoping work confirmed the breadth of evidence in this area. To ensure the work could be completed in a reasonable timescale, we narrowed our focus in three ways. First, we selected three of the 22 LTCs identified by Jagger and colleagues to use as exemplar conditions (depression, OA and T2D). These are common and known to make a significant contribution to population level morbidity, disability and mortality. Second, we focused on interventions recommended in National Institute for Health and Care Excellence (NICE) guidance. NICE recommendations are based on robust and transparent evaluation of research evidence, and are used to guide practice in the NHS.<sup>12</sup> Third, we have focussed on secondary and tertiary prevention.

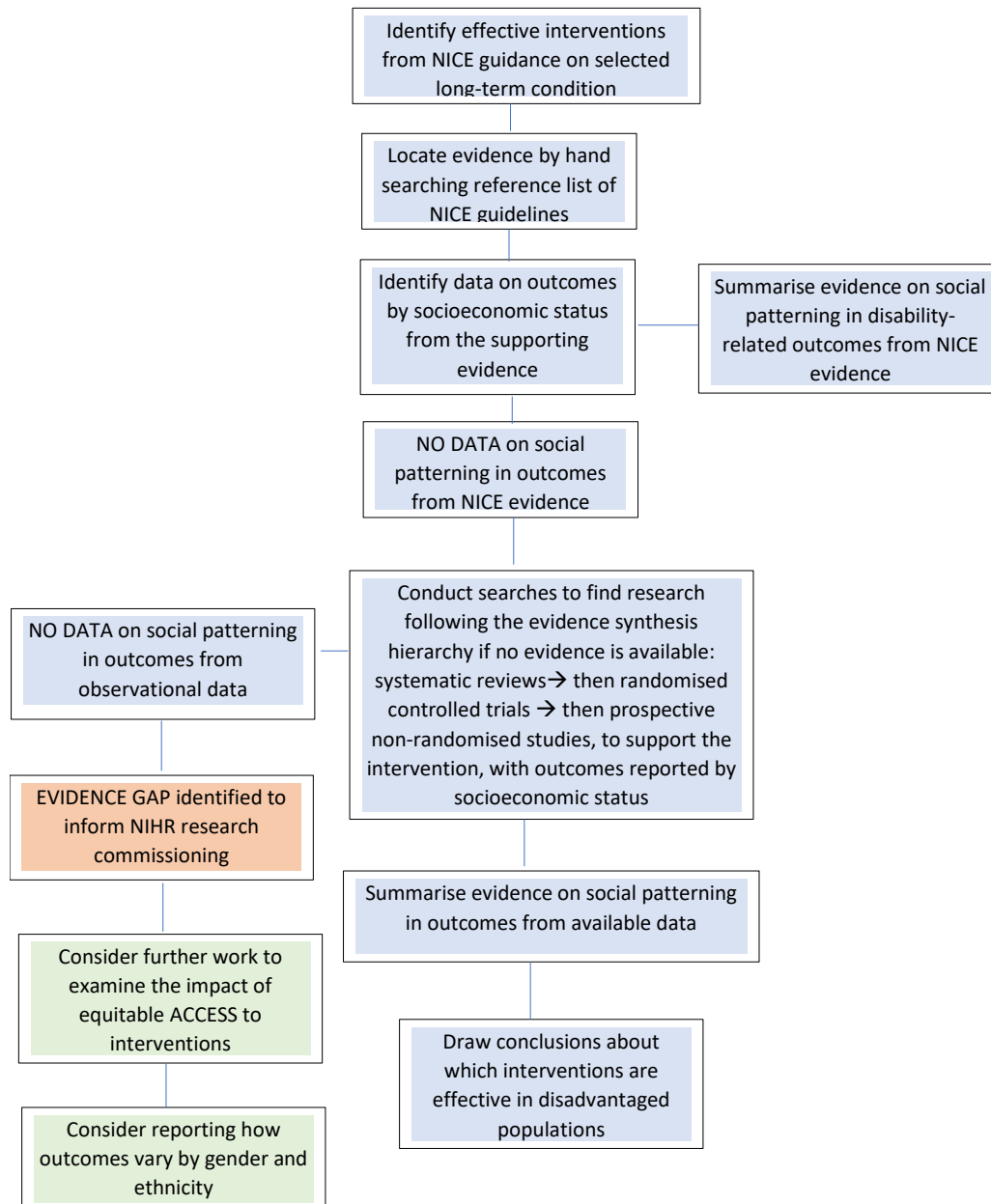
## Methods

For all three conditions, we adopted the following process (shown in Figure 1), to identify the highest quality evidence used to support NICE recommendations on interventions and



identify data on variation in outcomes by SES. We employed rapid evidence ‘review of reviews’ methodology,<sup>13</sup> A rapid review is a type of systematic review done in a shortened timeframe in order to provide more timely evidence for stakeholders and decision-makers.<sup>14</sup> This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>15</sup> A protocol for the whole project of which this review is part of, is published on the Policy Research Unit Older People and Frailty website.<sup>16</sup>

**Fig 1. Evidence Synthesis Plan**



### Search strategy

Step 1: Relevant guidelines were retrieved from the NICE website and appropriate references checked.

Step 2: Search strategies were designed by an experienced information specialist in collaboration with the project team, based on the scoping searches previously run. A separate search was designed for each condition, using the following concepts:

Condition AND the most commonly used/prominent interventions identified in the relevant NICE guidance AND terms relating to socioeconomic status, adapted from the Prady inequalities filter.<sup>17</sup>

For depression and diabetes, a systematic review filter<sup>18</sup> was used to restrict to a manageable number of references. For OA, the search was restricted to RCTs published since the date of searching for the appropriate NICE guideline (July 2008 for depression, January 2016 for OA, and July 2015 for T2D). Subsequently the original OA search was extended to observational studies. MEDLINE strategies can be found in Appendix 2 for depression, Appendix 3 for OA, and Appendix 4 for T2D.

### Inclusion and exclusion criteria

The eligibility criteria were based on the patient, intervention, comparator and outcome (PICO) formula and defined as follows:

#### Inclusion criteria

*Population:* People reporting symptoms of, or diagnosed with, depression, type 2 diabetes or osteoarthritis; and no age restrictions.

*Intervention:* Individual or population level intervention, recommended by NICE guidelines that impacts on the development of disability, (including education and self-management, non-pharmacological, pharmacological, or surgical intervention).

*Outcome measures:* We included all reported clinical outcomes and sought to include studies where outcomes were stratified by a measure of SES and included a measure of the effect size.

*Study design:* Where available we included relevant systematic reviews of preventative interventions. Systematic reviews were included if they met at least four of the five mandatory criteria of Database of Abstracts of Reviews of Effects (DARE): (i) inclusion/exclusion criteria were reported relating to the primary studies which addressed the review question; (ii) a search strategy was included that showed evidence of searching in relevant databases and grey literature; (iii) the validity of included studies was adequately assessed; (iv) sufficient detail of the individual studies was presented, and (iv) primary studies were summarised appropriately.<sup>19</sup> In the absence of eligible reviews, we first considered randomised trials of (secondary and tertiary) preventive interventions, then non-randomised prospective studies and finally prospective cohort studies.

#### Exclusion criteria

- Studies that reported access to services and interventions (i.e., differential levels of service utilisation between socioeconomic groups) as an outcome measure
- Abstracts and studies where full texts were not available
- Retrospective cohort studies
- Case studies, case series

## Data collection

### Selection of studies

For each condition, a two-stage approach was employed to select eligible studies. Firstly, titles and abstracts of the studies were screened by two reviewers in Rayyan.<sup>20</sup> Secondly, the full texts of the relevant studies were retrieved for further evaluation in Endnote X9.<sup>21</sup> In both stages, discrepancies were resolved by consensus.

### Data extraction

Data extraction forms were developed, piloted, and refined as necessary prior to full data extraction in an excel spreadsheet. Data extraction was conducted by one researcher and checked for accuracy by a second. For the included systematic reviews, where they reported multiple interventions, we extracted the data for populations who received the interventions relevant to our study. To avoid an overlap, or double counting findings from reviews that reported the same primary studies, we used the overall findings and conclusions of the reviews as our main data. We did not extract data from the primary studies included in the reviews. The following domains were extracted: population, number of primary studies with relevant interventions, type of intervention, outcomes, SES parameters, and review author's interpretation of findings. Citation matrices showing the degree of overlap in the primary studies included in the reviews were created where applicable (Appendix 5). For the primary studies included in our analysis, the following domains were extracted from the included primary studies: study setting, sample characteristics, condition under investigation, objectives, design, intervention types, outcomes, SES parameters and conclusions.

### Data analysis

Heterogeneity in study populations, interventions, control groups, follow-up periods, SES outcomes and measurement tools, precluded us from pooling the findings for differential effects across all the studies. The extracted data were tabulated and grouped by the type of intervention and a narrative report produced. To assess whether SES factors influence or moderate intervention outcomes, where possible, we extracted the reported effect sizes, associated confidence intervals, and significance levels. Where information was reported at different time points, both the short-term and long-term effectiveness of the intervention were examined. There are two broad approaches to understanding the effectiveness of interventions across groups:

1. Moderation analysis – the extent to which socioeconomic status moderates the relationship between an intervention and an outcome (applied within models as an interaction between SES and the intervention).<sup>22</sup>
2. Stratification of sample: the effectiveness of an intervention is analysed separately for each sub-group of socioeconomic status.<sup>23</sup>

Both approaches were eligible for this review. Where reported in reviews, the approach to analysing the role of socioeconomic status was noted.

The association of SES factors with an outcome were classified as follows:

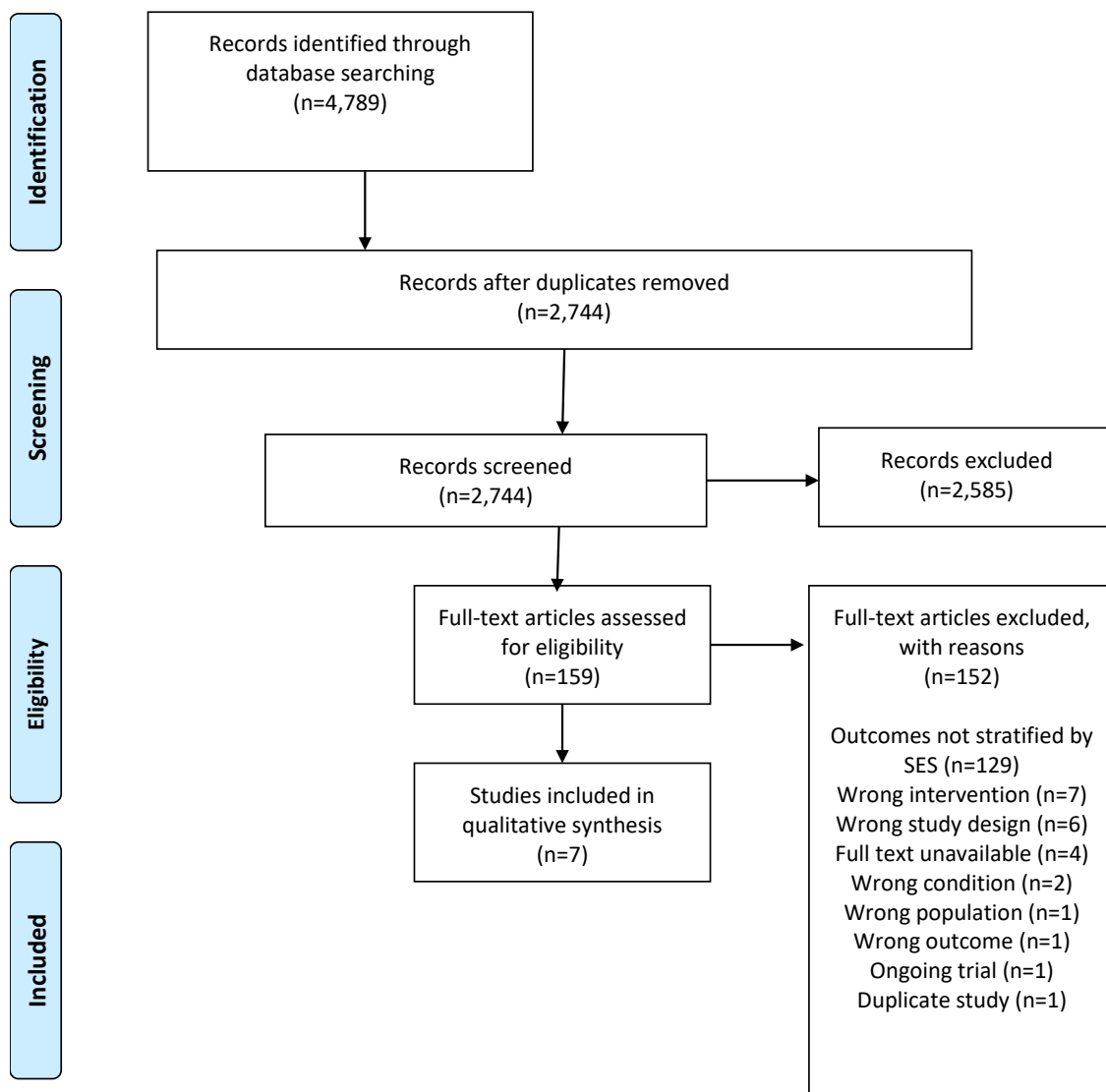
- Favours disadvantaged populations – the intervention favoured or improved outcomes for those in the lower SES group
- Favours advantaged populations – the intervention favoured or improved outcomes for those in the higher SES group
- No evidence of differential impact – the intervention had no difference in effectiveness by level of SES

# Results

## Depression

Our search identified 4,789 results from five databases, and following deduplication, a total of 2,744 unique articles were screened at title and abstract stage. From this, 159 full texts were assessed for eligibility and 7 reviews,<sup>24-30</sup> reporting on 85 unique primary studies, were included for synthesis. The inclusion and exclusion process are presented in the PRISMA chart in Fig. 2.

Fig 2. PRISMA flowchart – Depression



## Characteristics of included reviews

A summary of the descriptive characteristics of the included reviews is available in Appendix 6. The reviews were published between 2009 and 2021, in Canada,<sup>30</sup> the Netherlands,<sup>27</sup> United Kingdom,<sup>24, 25, 28, 29</sup> and the United States of America.<sup>26</sup> The reviews were reported as Systematic Review (SR) and Meta-analyses (MA),<sup>24, 25, 28</sup> MA of Individual Patient Data (IPD),<sup>27, 29</sup> SR of IPD and Network MA (NMA),<sup>26</sup> and an Equity-focused SR.<sup>30</sup> All studies within the reviews were randomised controlled trials. Follow-up periods were reported in five reviews and ranged from four weeks<sup>28</sup> to 24 months.<sup>24</sup> Outcomes were stratified by low vs. middle vs. high SES in two reviews,<sup>24, 28</sup> educational level in four reviews,<sup>25, 27, 29, 30</sup> and employment status in two reviews.<sup>26, 27</sup> One review included patients diagnosed with major depression,<sup>29</sup> another with elevated symptoms of depression,<sup>27</sup> and another with post-partum depression.<sup>30</sup> The remaining four studies,<sup>24-26, 28</sup> included participants based on any diagnosis or any self-report scale of depression or both.

## Overview of evidence

A summary of the identified evidence, presented according to the type of intervention, the reported outcomes, the measure of SES available, and the direction of association of these factors is available in Appendix 7. All reviews focused on the effectiveness of Cognitive Behavioural Therapy (CBT) interventions, including: school-based CBT, community based CBT, guided internet CBT, self-guided CBT, mindfulness CBT, and mobile CBT. We found no reviews that reported the effectiveness of pharmacological interventions (selective serotonin reuptake inhibitors, and third-generation antidepressants) by a measure of SES. Reported outcomes included self-reported depression,<sup>24</sup> reduction in depressive symptoms,<sup>28</sup> severity of depressive symptoms, depressive symptom response, treatment response, and relapse to depression.

### **Key highlights from evidence for interventions for depression:**

- Community-based, mindfulness and mobile CBT produced similar outcomes across socioeconomic groups.
- School-based CBT may favour children from middle and higher SES backgrounds, although there was contrasting evidence in a review of studies with greater risk of bias.
- Two reviews offered contrasting evidence about the effectiveness of self-guided CBT across socioeconomic groups.
- Internet-guided CBT may offer worse outcomes for unemployed people, compared to usual care.

A detailed overview of evidence for each intervention is provided below.

### *School-based CBT*

Two reviews reported the effects of school-based CBT,<sup>24, 28</sup> an intervention usually directed at students and most often delivered by school staff and school psychologists. There was some overlap in the studies, with thirteen studies included in both reviews, however, as previously reported, we report the overall findings from the individual reviews.

One review reported the findings of a network meta-analysis of 19 randomised trials relating to school-based CBT versus usual curriculum (UC) to prevent depression in children and young people aged 4–18 years. The review assessed the effects of the intervention on

health inequalities by SES. Descriptions of SES were varied across the included studies and were broadly defined as low versus high SES households by review authors.<sup>24</sup> The outcome assessed was post-intervention self-reported depression measured by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). (Standard mean differences (SMD) were reported to summarise intervention effects, with SMD 0.2-0.5 considered small, 0.5-0.8 medium, and > 0.8 large.)<sup>31</sup> Overall, after 13 to 24 months, there was no evidence to conclude that school based CBT was effective in preventing depression in children and young people. There were no differences in the effect of school-based CBT vs UC on depression symptoms between children from high and low SES households (high SES SMD -0.05, 95% CI: -0.55 to 0.45, low SES SMD -0.23, 95% CI: -0.60 to 1.13). The risk of bias for most studies in this review was unclear, suggesting uncertainty in these findings.<sup>24</sup>

The second review reported the findings of a meta-analysis of six randomised trials (n=2,343) analysing the effects of a whole population (universal intervention) school-based CBT in reducing depressive symptoms in young people aged 11–19, from low, medium and high SES populations.<sup>28</sup> None of the included studies compared the intervention with an active control. The outcome assessed was reduction in depressive symptoms post intervention, measured by the Children's Depression Inventory, and Beck Depression Inventory (BDI).<sup>28</sup> Overall results from this study suggest that school-based CBT can help reduce symptoms of depression. After 4 weeks, subgroup analyses suggest that school-based CBT may be more effective for young people from families of middle (SMD: -0.28, 95% CI: -0.44 to -0.11; two studies; n=2,003) to high SES (SMD: -0.31, 95% CI: -0.54 to -0.07; two studies; n=283) compared to families of low SES (SMD: 0.44, 95% CI: -0.09 to 0.97; two studies; n=57).<sup>28</sup> Studies in this review were of high quality.

#### *Community-based online CBT*

One review reported the findings from a single high quality randomised trial that assessed factors that moderate response to CBT in depression.<sup>25</sup> Online CBT was delivered to 210 patients from community general practices compared to waiting list.<sup>25</sup> No relationship was found between level of education (more or less than Advanced level) and treatment outcomes (severity of depressive symptoms measured by the BDI-II) following CBT ( $p = 0.372$ ).<sup>25</sup> The risk of bias for this study was low.

#### *Guided internet-based CBT*

One review reported the findings from an IPD NMA (Individual patient data network meta-analysis) of 39 randomised clinical trials (n=9,751), analysing the effect modification by employment status, of guided and unguided (self-guided)-internet-based CBT (iCBT) against each other or against treatment as usual (TAU) in the presence of other modifiers.<sup>26</sup> Guided iCBT was delivered via the internet and involved therapeutic support, either synchronous or asynchronous, delivered by a professional or a paraprofessional. Unguided or self-guided iCBT was delivered via the internet where automated and technical support was permitted, but not support related to the therapeutic content.<sup>26</sup> The outcome of interest was the severity of depressive symptoms, post intervention, measured by Patient Health Questionnaire–9 (PHQ-9) scores. Standard deviations (SD), and their corresponding credible intervals were reported to summarise the moderating effects. Overall, not being employed was associated with poor outcomes when guided iCBT was compared to TAU at six months (SD: 0.041; 95% CrI, -0.119 to 0.043) and at 12 months (SD: 0.046; 95% CrI: -0.087 to 0.094).<sup>26</sup> Post treatment effects between guided and unguided iCBT did not differ between patients who were unemployed at six months (SD: 0.044; 95% CrI: -0.116 to 0.058) and at 12 months (SD: 0.043; 95% CrI: -0.081 to 0.089). Risk of bias for all studies in this review was low.<sup>26</sup>

### *Self-guided iCBT*

Two reviews published by the same author examined the effectiveness of unguided or self-guided iCBT.<sup>26, 27</sup> There was some overlap in the studies, with thirteen studies included in both reviews, however, as previously reported, we report the overall findings from the individual reviews.

In the review by Karyotaki and colleagues, published in 2017, authors identified 10 randomised trials (n=2,538) and conducted an IPD MA to explore whether level of education and employment status moderated the effect of self-guided iCBT in depression outcomes in the presence of other covariates.<sup>27</sup> Outcomes assessed were depressive symptom severity, and treatment response post-intervention, both measured by composite scores of the BDI; PHQ-9 scores; and the Center for Epidemiological Studies–Depression Scale, transformed into z scores.<sup>27</sup> Level of education was found to have no effect on depressive symptom severity ( $p = 0.21$ ); tertiary vs primary ( $\beta = 0.03$ ;  $p = 0.79$ ), and treatment response [secondary vs. primary ( $\beta = -0.40$ ;  $p = 0.31$ ); tertiary vs primary ( $\beta = -0.16$ ;  $p = 0.68$ ).<sup>27</sup> Similarly, employment status was found to be not associated with depressive symptoms severity ( $\beta = 0.12$ ;  $p = 0.11$ ), and treatment response ( $\beta = -0.34$ ;  $p = 0.12$ ). Risk of bias for all studies in this review was low.<sup>27</sup>

As previously reported, the review Karyotaki and colleagues, published in 2021, conducted an IPD MA and estimated the distribution of possible effect modifiers for self-guided iCBT compared to guided iCBT, and TAU, on depressive symptom response by employment status.<sup>26</sup> The outcome was measured by PHQ-9 scores and reported by SD and found that not being employed was associated with poor depressive symptom response at 6 months (SD: 0.03; 95% CrI: -0.068 to 0.05) and at 12 months (SD: 0.032; 95% CrI: -0.066 to 0.059).<sup>26</sup> Risk of bias for all studies in this review was low.<sup>26</sup>

### *Mindfulness-based CBT*

One review reported the findings from an IPD MA of nine randomised trials (n=1,258) examining the efficacy of mindfulness-based CBT for recurrent depression compared to usual care and other active treatments including antidepressants. The authors looked at whether educational level was associated with depressive relapse in the presence of other covariates.<sup>29</sup> The intervention was a combination of systematic mindfulness training with elements from cognitive therapy.<sup>29</sup> The outcome of interest was relapse to depression post-intervention. Within 60 weeks of follow-up, although the review reported positive outcomes, there was no evidence to support differential effects based on an individual's level of education (no qualifications, qualifications below degree level, and degree or higher).<sup>29</sup> Risk of bias for all studies in this review was low.<sup>29</sup>

### *Mobile CBT*

One review reported the findings from a single randomised trial (n=78) relevant to our review.<sup>30</sup> The review assessed the effectiveness of a mobile CBT intervention in postpartum depression, by educational level.<sup>30</sup> The intervention was described as a smartphone application which provided women with CBT in the form of 8 lessons that read like a story. The outcome assessed was severity of postpartum depression post-intervention, measured by the Edinburgh Postnatal Depression Scale (EPDS)-Persian version.<sup>30</sup> Review authors reported that within three months of follow-up, there was no evidence to support differential effects based on an individual's level of education, with post-intervention correlation reported as  $p = 0.44$  and  $p = 0.89$  for the intervention and control groups, respectively.<sup>30</sup> However, this study was reported to have a high risk of bias, therefore results should be considered with caution.

## Osteoarthritis

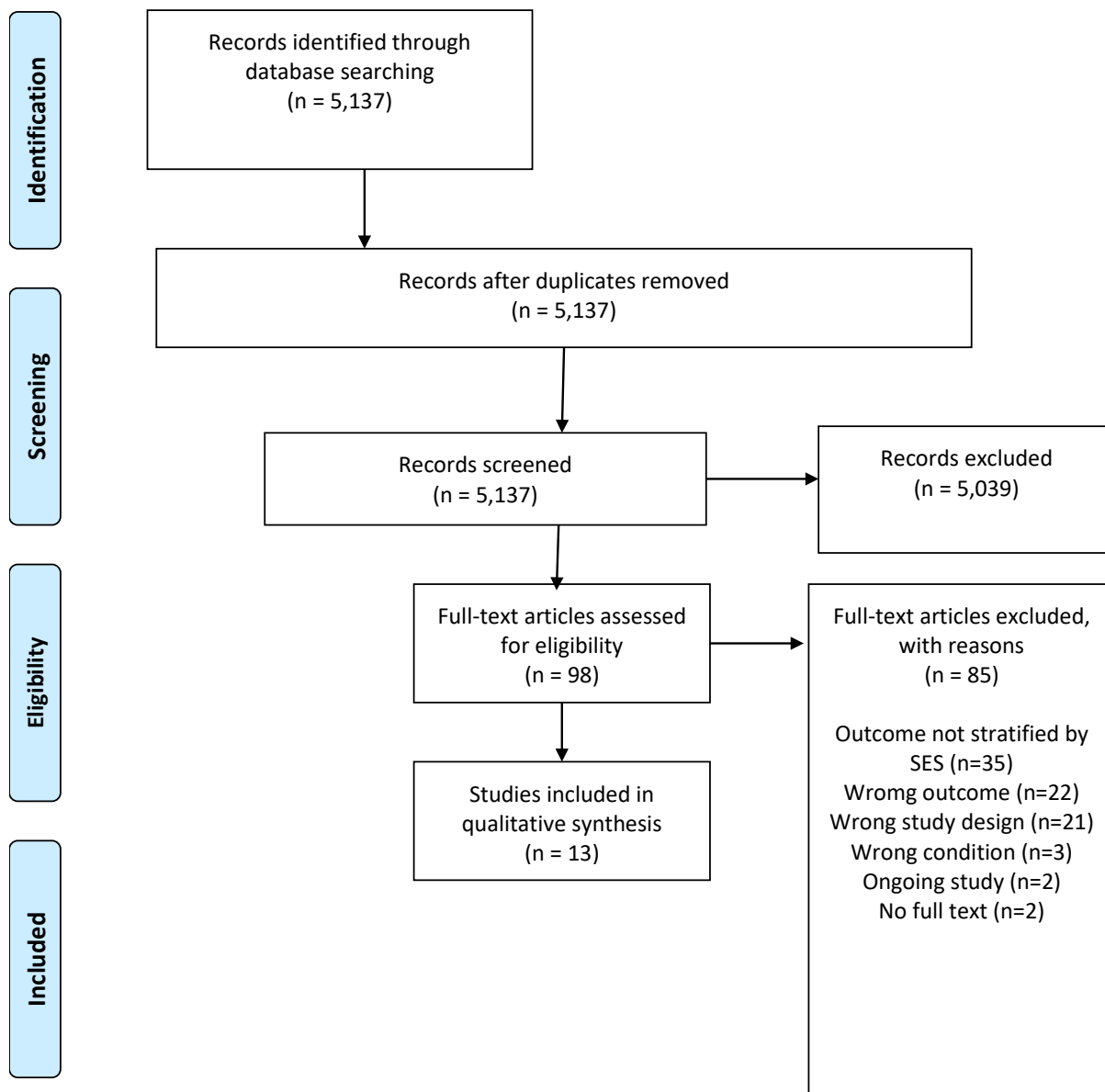
Database searches retrieved 8,300 records. After de-duplication, 5,137 unique records were identified and following a brief screening of the titles and abstracts, 98 full-text potentially relevant articles were retrieved for thorough examination. The PRISMA flow diagram outlines the study selection process and the reasons for exclusion (Fig 3). A total of 12 published papers were judged to meet the full inclusion criteria of this review.<sup>32-43</sup>

### Characteristics of included studies

Descriptive information on each individual study is presented in Appendix 8. Studies were conducted in the USA,<sup>35, 38</sup> Sweden,<sup>34, 43</sup> Denmark,<sup>37, 41</sup> Canada,<sup>33</sup> Turkey,<sup>32</sup> Australia,<sup>39</sup> Lithuania,<sup>42</sup> Belgium,<sup>40</sup> and Pakistan.<sup>36</sup> Two of the studies were RCTs,<sup>35, 39</sup> and the rest were prospective cohort studies.<sup>32-34, 36-38, 40-43</sup> Study sample sizes varied between 70<sup>32</sup> and 35,496.<sup>41</sup> Studies included participants who were predominantly female, and one study recruited only female participants.<sup>36</sup> The average ages varied from 60.8 years<sup>39</sup> to 70.9 years,<sup>42</sup> however, one study only reported the age range as 30 to 80 years,<sup>36</sup> and another did not report the age of the participants.<sup>38</sup> Outcome measures included pain, physical function, quality of life (QoL), change in frequency in engagement in life activities, physical and mental health. Eleven studies<sup>32-35, 37-43</sup> described participants' level of education and most of these reported that participants had some tertiary level of education (usually greater than high school),<sup>33, 35, 37, 39-43</sup> Five studies<sup>32, 35, 37, 39, 41</sup> reported the employment status of participants, unemployed,<sup>32, 35</sup> employed,<sup>39, 41</sup> or retired.<sup>37</sup> Two studies reported the birthplace of participants as a majority from Denmark,<sup>41</sup> and Sweden.<sup>43</sup> Place of residence was reported in one study, with most participants recorded as living in a rural area.<sup>32</sup> Only one study reported the income status of participants, of which the majority were from middle income households or higher.<sup>35</sup>



Fig 3. PRISMA flowchart – Osteoarthritis



### Overview of evidence

A summary of the identified evidence, presented according to the type of intervention as recommended by NICE, the reported outcomes, the measure of SES available, and the direction of association of these factors is available in Appendix 9. Most of the evidence (six studies) focused on effectiveness of surgical interventions, five focused on education and self-management and one on pharmacological management.

### Key highlights from the evidence on interventions for osteoarthritis:

- Surgical, education and exercise interventions produced equivalent outcomes across socioeconomic groups or favoured more advantaged populations.
- Self-management interventions favoured more advantaged populations.
- Limited evidence on pharmacological interventions suggested that outcomes were similar across socioeconomic groups, but the study data were not formally analysed

A detailed overview of evidence for each intervention is provided below.

#### Education and self-management

Five studies reported using education and self-management interventions.<sup>34, 37, 39, 41, 43</sup>

##### *Education and exercise*

Three studies examined education and exercise programs.<sup>37, 39, 41</sup> Two of these studies<sup>37, 41</sup> assessed the effectiveness of the Good Life with OA in Denmark (GLA:D) education and exercise program, a treatment plan for OA which included patient education and neuromuscular exercises. Both studies were prospective cohort studies of knee and hip OA patients aged 60 years and over, in Denmark. The studies assessed the differential intervention effects in pain improvement by educational level and employment status.

Johnsen and colleagues assessed the impact of employment status and level of education on change in pain intensity in 22,588 patients, measured by a Visual Analogues Scale (VAS). The pain VAS is a unidimensional measure of pain intensity with a score determined by measuring the distance (mm) on a 10cm line, ranging from 0 (no pain) to 100 (greater pain intensity). According to employment status, employed patients or students had greater improvement in pain after treatment (-2.2mm; 95% CI: -2.9 to -1.5) and at 12 months (-1.3mm; 95% CI: -2.1 to -0.5) compared with retired patients (reference). The study reported that patients with long-term education had less improvement after treatment (2.0 mm; 95% CI: 0.8 to 3.1) and at 12 months (2.0 mm; 95% CI: 0.6 to 3.4) compared with primary school only.<sup>37</sup> In comparison, according to the forest plots produced by Pihl and colleagues, there were no significant differences in pain improvement by educational level at 8 weeks (n=19,927).<sup>41</sup> It is important to note that the clinical significance of these changes in VAS is unclear.

Pihl and colleagues also assessed the improvements in QoL after supervised exercise therapy and education in patients with knee and hip OA and found no statistically significant differential effect by educational level at 8 weeks.<sup>41</sup>

Lawford and colleagues examined demographic and clinical moderators of the effect of an internet-delivered exercise, education, and pain coping skills training intervention on changes in pain and physical function in people with knee osteoarthritis.<sup>39</sup> The study was a RCT of 148 knee OA patients with an average age of 60.8 years, conducted in Australia. The intervention group received educational material about exercise and physical activity, an

online pain coping skills training (PCST) program, and seven online physical therapist consultations over 12 weeks. The control group received all the above, except for the automated PCST. There was no statistically significant change (moderation effect) in walking pain scores at 3 months (mean difference=1.87, 95% CI: 1.10 to 2.64,  $p = 0.22$ ), and at 9 months (1.08; 95% CI: 0.18 to 1.97,  $p = 0.58$ ) between those educated at tertiary level in the intervention group compared to similar participants in the control group. A significant reduction in walking pain was observed in employed patients in the intervention group compared to similar participants in the control group at 3 months; (mean difference=2.38; 95% CI: 1.52 to 3.23,  $p = 0.02$ ), however this was not observed at 9 months (mean difference=1.20; 95% CI: 0.17 to 2.22,  $p = 0.86$ ). The study also found that there was no evidence that the level of education moderated the effects of the intervention on changes in physical function at 3 months ( $p = 0.22$ ) and at 9 months ( $p = 0.25$ ).

### *Self-management*

Two prospective cohort studies examined the effects of the Better Management of Patients with OA (BOA) self-management programme.<sup>34, 43</sup> BOA is a Swedish based, national register, that evaluates patient-reported outcomes following a Supported OA Self-Management Programme.<sup>44</sup> The intervention group received at least “2 theoretical group sessions led by a physical therapist focusing on the disease pathophysiology and on the benefit of exercise, including self-management advice and strategy to incorporate exercise into daily life.”<sup>34</sup>

The study by Dell Isola and colleagues included 16,547 knee OA patients with an average age of 66.3 years, and 6,762 hip OA patients with an average age of 67.1 years.<sup>34</sup> The study did not compare the intervention with an active control. The study assessed whether there were educational level differences in pain reduction.<sup>34</sup> Linear regression models were used to assess the association of educational level and other independent variables with the change in pain from baseline to 3 and 12 months. Results were reported as unstandardized regression coefficients (B) and are accompanied by their 95% CI, and negative results indicate a reduction in pain. The study found that higher levels of education (> 14 years) were associated with decreased pain in the knee OA patients at 3 months (B = -0.12; 95% CI: -0.19 to -0.05) and 12 months (B = -0.24; 95% CI: -0.32 to -0.16). Similarly, higher levels of education were associated with decreased pain in the hip OA patients at 3 months (B = -0.13; 95% CI: -0.23 to -0.02) and 12 months (B = -0.16; 95% CI: -0.28 to -0.38).<sup>34</sup>

The study by Unevik and colleagues included 22,741 OA patients with an average age of 66.3 years.<sup>43</sup> Associations between the exposure to educational level or domestic/foreign country of birth and the BOA self-management program outcomes, in relation to walking difficulties, joint impairment, health-related quality of life (HRQoL), and joint related pain were assessed using multivariate analyses. The study did not compare the intervention with an active control.<sup>43</sup> Results for continuous outcomes were reported as adjusted means with 95% CI. Dichotomous outcomes were reported as adjusted odds ratio (OR) with 95% CI, where an exposure is either associated with higher odds of an outcome (OR > 1), or lower odds of an outcome (OR < 1), exposure does not affect odds of an outcome (OR = 1).<sup>45</sup>

Authors reported that patients with lower levels of education were more likely than those with a university education to report difficulties with walking, at 3 months: [Compulsory only: (OR=1.12; 95% CI: 1.03 to 1.20); Upper secondary: (OR=1.02; 95% CI: 0.95 to 1.10)], and at 1 year: [Compulsory only: (OR=1.16; 95% CI: 1.03 to 1.20); Upper secondary: (OR=1.06;

95% CI: 0.99 to 1.14)]. Foreign born patients were more likely than domestic born patients to report difficulties with walking at 3 months (OR=1.14; 95% CI: 1.02 to 1.27), and at 1 year (OR=1.16; 95% CI: 1.04 to 1.30).<sup>43</sup>

They also found that patients with lower levels of education were more likely than those with a university education to suffer enough joint impairment to consider surgery at 3 months: [Compulsory only: (OR=1.36; 95% CI: 1.21 to 1.52); Upper secondary: (OR=1.20; 95% CI: 1.07 to 1.35)] and at 1 year: [Compulsory only: (OR=1.23; 95% CI: 1.12 to 1.35); Upper secondary: (OR=1.12; 95% CI: 1.03 to 1.23)]. Foreign born patients were more likely than domestic born patients to suffer enough impairment to consider surgery at 3 months: [Foreign born: (OR=1.09; 95% CI: 0.93 to 1.27)] and at 1 year: [Foreign born: (OR=1.07; 95% CI: 0.94 to 1.22)].<sup>43</sup>

The authors reported that HRQoL was higher for those with higher levels of education at 3 months: [Compulsory only: (Mean=0.70; 95% CI: 0.70 to 0.70); Upper secondary: (Mean=0.71; 95% CI 0.71 to 0.71); University: (Mean= 0.72; 95% CI 0.71 to 0.72)], and at 1 year [Compulsory only: (Mean=0.67; 95% CI: 0.67 to 0.67); Upper secondary: (Mean=0.67; 95% CI: 0.67 to 0.68); University: (Mean= 0.68; 95% CI: 0.68 to 0.69)]. HRQoL scores were also found to be slightly higher for domestic born patients compared to foreign born patients at 3 months: [Domestic born: (Mean= 0.71; 95% CI: 0.71 to 0.71); Foreign born: (Mean=0.69; 95% CI: 0.69 to 0.70)], and at 1 year: [Domestic born: (Mean=0.68; 95% CI: 0.68 to 0.68) vs. Foreign born: (Mean= 0.66; 95% CI: 0.65 to 0.66)].<sup>43</sup>

The study also found that higher educational levels were associated with decreased pain at 3 months: [Compulsory only: (Mean=4.0; 95% CI: 4.0 to 4.1); Upper secondary: (Mean=4.0; 95% CI: 3.9 to 4.0); University: (Mean= 3.8; 95% CI: 3.8 to 3.8)], and 12 months [Compulsory only: (Mean=4.5; 95% CI: 4.4 to 4.5); Upper secondary: (Mean=4.3; 95% CI: 4.3 to 4.4); University: (Mean=4.1; 95% CI: 4.1 to 4.2)]. Additionally, the study found that pain scores were slightly lower for domestic born patients at 3 months: [Domestic born: (Mean= 3.9; 95% CI: 3.9 to 4.0); Foreign born: (Mean=4.0; 95% CI: 3.9 to 4.1)], and at 12 months: [Domestic born: (Mean=4.3; 95% CI: 4.3 to 4.3); Foreign born: (Mean=4.5; 95% CI: 4.4 to 4.6)].<sup>43</sup>

### *Pharmacological management*

One study reported outcomes following pharmacological management of OA using intra-articular corticosteroid injections.<sup>36</sup> The study was a prospective cohort study of 124 knee joint OA patients with an age range of 30 to 80 years, conducted in Pakistan. The study assessed whether there are any SES (defined as upper, middle, and lower class) related differences in the McMaster University Osteoarthritis Index (WOMAC) pain and function. The authors reported that a relationship could not be established between SES and outcome,<sup>36</sup> however, no test statistics were reported.

### *Surgical interventions*

Six studies reported the association of a variety of SES parameters with clinical outcomes following surgical intervention. Of these, five investigated total knee arthroplasties (TKA),<sup>32, 33, 35, 40, 42</sup> and one study examined the effects following anterior cruciate ligament (ACL) reconstruction.<sup>38</sup> TKA is a surgical procedure to resurface or replace damaged, worn or a diseased knee.<sup>46</sup> ACL reconstruction is a surgical procedure to replace a torn ACL, which is a major ligament in the knee.<sup>47</sup>

#### *TKA*

A small prospective study in Turkey recruited 70 adults aged 65+ from hospital rehabilitation settings following TKA for OA.<sup>32</sup> At 6 months, there was no relationship between functional improvement and place of residence ( $p = 0.881$ ), employment status ( $p = 0.521$ ), or level of

education ( $p = 0.521$ ).<sup>32</sup> They also reported no relationship between QoL and place of residence ( $p = 0.112$ ), and employment status ( $p = 0.341$ ). However, higher educational level was an influential factor in improving QoL ( $p = 0.028$ ).<sup>32</sup>

In Canada, a prospective cohort study of 418 patients with OA recruited from tertiary care centres, assessed the effects of TKA on change in frequency in engagement in life activities, measured by the Late Life Disability Index (LLDI).<sup>33</sup> At 12 months, higher levels of education were not significantly associated with LLDI frequency [ $\beta = -0.81$ ; 95% CI -2.66 to 1.04;  $p = 0.4$ ].<sup>33</sup>

Two studies assessed the effects of TKA on pain intensity, measured by WOMAC post intervention.<sup>35, 42</sup> The RCT by Dumenci and colleagues included 384 knee OA patients from university-based sites in the US with an average age of 63 years.<sup>35</sup> They conducted a piecewise latent class growth analysis to estimate WOMAC pain and function trajectories, and the factors that influence these trajectories. At 12 months, the study found that lower income was associated with poor WOMAC pain scores (OR = 0.33; 95% CI 0.15 to 0.715;  $p = 0.004$ ).<sup>35</sup> In Lithuania, 294 adults aged 65+ with knee OA were recruited from a rehabilitation centre.<sup>42</sup> At 12 months following TKA, no significant differences ( $p = 0.168$ ) in pain scores were observed between patients educated at lower (secondary school or vocational training) or higher (University) levels.<sup>42</sup> Multiple regression models were used to estimate the influence of patient factors on WOMAC and SF-12 scores post intervention. At 12 months, there were no reported differences in post-operative outcomes between level of education and WOMAC pain ( $p = 0.168$ ), stiffness ( $p = 0.059$ ), and function ( $p = 0.225$ ), and SF-12 physical ( $p = 0.461$ ), and mental ( $p = 0.594$ ) scores.<sup>42</sup>

A third study assessed the effects of TKA on total WOMAC scores which covered pain, stiffness and physical function.<sup>40</sup> This was a prospective cohort of 626 knee and hip OA patients with a median age of 66, recruited from a university hospital in Belgium.<sup>40</sup> Multiple regression analyses were conducted to determine which factors had influence on total WOMAC scores post intervention. Results were reported as unstandardized regression coefficients (B) and are accompanied by their 95% CI. The authors reported that at 5 years, higher levels of education was significantly associated with better WOMAC total scores in pain, stiffness and physical function [ $B=7.33$  (1.99 to 12.38),  $p < 0.01$ ].<sup>40</sup>

#### *ACL reconstruction*

Only one of the included studies assessed the effects of ACL on patient reported outcome in post-traumatic OA by educational level.<sup>38</sup> The study was a prospective cohort of 1,512 US patients with an average age of 23 years.<sup>38</sup> Outcomes assessed were knee function measured by the international Knee Documentation Committee Subjective Knee Form (IKDC) scores, KOOS scores (symptom scores, pain, activities of daily living (ADL), QoL, sports or recreation activities, and Marx activity level scores. At 6 years, having less education was associated with worse patient reported outcomes for knee function (odds ratio (OR) = 1.35; 95% CI: 1.11 to 1.64), symptom scores (OR=1.48; 95% CI: 1.21 to 1.81); pain (OR=1.39; 95% CI: 1.14 to 1.70); ADL (OR= 1.57; 95% CI: 1.27 to 1.93); sports and recreation activities (OR= 1.42; 95% CI: 1.16 to 1.74); QoL (OR=1.30; 95% CI: 1.06 to 1.59); and Marx activity level scores (OR=1.22; 95% CI: 1.02 to 1.45).<sup>38</sup>

## Type 2 diabetes

### **Key highlights from the evidence on interventions for T2D:**

No relevant data were identified, on social patterning in outcomes for recommended interventions for T2D.

Our search strategy identified 786 records. After deduplication, 755 articles were evaluated, of which 164 articles were retrieved for full-text analysis (Fig 4). Interventions reported in these articles included:

- Patient education and information provision
- Telehealth monitoring of blood glucose/Haemoglobin A1c (HbA1c)
- Lifestyle interventions (weight management, diet)
- Diabetes Self-Management Education (DSME)
- Pharmacological treatments (insulin, metformin)
- Peer support

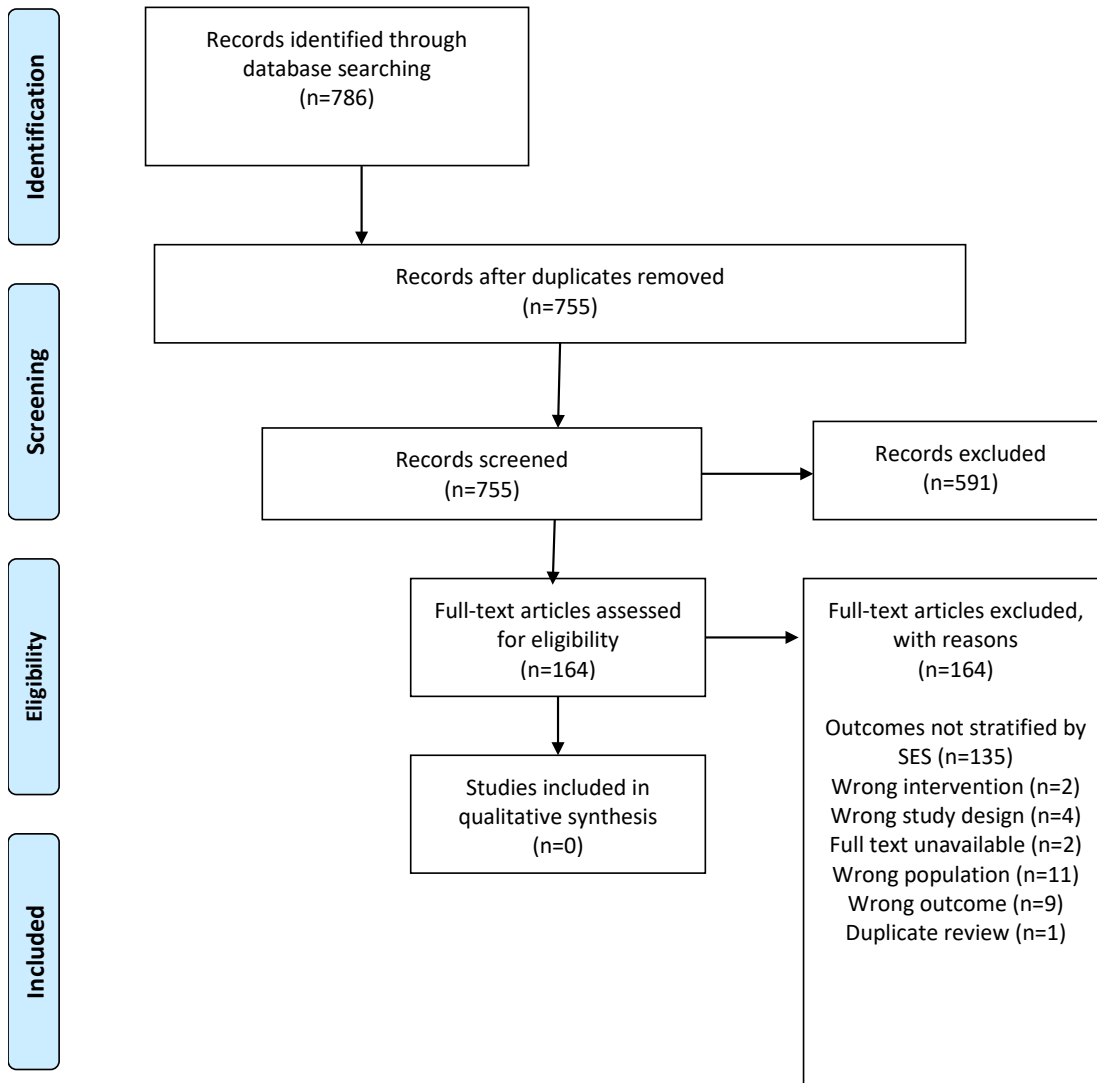
Outcomes assessed included improvements in:

- Blood glucose levels, measured by HbA1c<sup>48</sup> (average levels over time)
- Body mass index (BMI)
- QoL
- Body weight

However, all studies were excluded; none reported data about the effectiveness of interventions across socioeconomic groups. The absence of any data stratified or analysed by socioeconomic group was also noted in 10 Cochrane reviews that were assessed at the full text stage of screening. These reviews assessed the effects of rapid-acting insulin analogues for diabetic ketoacidosis;<sup>49</sup> psychological interventions for diabetes-related distress in adults with T2D;<sup>50</sup> sliding scale insulin for non-critically ill hospitalised adults with diabetes mellitus;<sup>51</sup> zinc supplementation for the prevention of T2D;<sup>52</sup> diet, physical activity or both on the prevention or delay of T2D;<sup>53</sup> non-nutritive sweeteners in people with diabetes mellitus;<sup>54</sup> metformin for the prevention or delay of T2D mellitus;<sup>55</sup> diabetes self-management interventions specifically tailored for people with T2D;<sup>56</sup> diet, physical activity and behavioural interventions (behaviour-changing interventions) for the treatment of overweight or obese children aged 6 to 11 years;<sup>57</sup> alpha-glucosidase inhibitors in people with impaired glucose tolerance, impaired fasting blood glucose, moderately elevated glycosylated HbA1c or any combination of these;<sup>58</sup> and preconception care in women with diabetes on health outcomes for mothers and their infants.<sup>59</sup>

In summary, we identified no relevant data on social patterning in outcomes for recommended interventions for T2D.

Fig 4. PRISMA flowchart – Type 2 Diabetes



## Discussion

### Summary of findings

We aimed to review the published evidence to identify interventions for depression, OA, or T2D that would be effective at narrowing the gap in DFLE. We focussed on secondary and tertiary (rather than primary) prevention, and analyses that explored the effectiveness across socioeconomic groups. Despite the vast literature that examines the effectiveness of interventions to improve outcomes for populations with depression, OA and T2D, very little of this evidence considers whether such interventions generate equitable outcomes. Overall, seven systematic reviews, reporting 85 unique randomised trials for depression, and twelve primary studies (2 RCTs and 10 prospective cohort studies) for OA were reported data relevant for this review. For T2D, no systematic reviews met our inclusion criteria. The included studies were heterogeneous and did not allow quantitative synthesis of findings. This is a critical finding and signals the need for future research to pay greater attention to the role of socioeconomic advantage in the success of interventions.<sup>60</sup>

### Implications for policy

Closing the gap in DFLE between the richest and poorest populations is a policy priority. Improving health outcomes for the most disadvantaged populations with long-term conditions may help achieve this goal. Yet our rapid synthesis suggests that evidence about NICE-recommended interventions for three long-term conditions - depression, OA and T2D – rarely considers socioeconomic inequalities in outcomes. The limited evidence we identified suggests that current NICE-recommended interventions either disproportionately benefit the more advantaged, or have little impact on improving the health of the poorest. Our remit in this review was focused on interventions for depression, OA and T2D, because these are three of the biggest drivers of later life disability. Beyond this focus, evidence about interventions for other conditions and health problems may offer different answers about approaches to improving health outcomes for the least advantaged populations. For example, an equity-focused systematic review published in 2017 explored the effectiveness of universal interventions on social inequalities in physical activity within older populations.<sup>60</sup> Findings from this review mirrored those reported here: very few studies considered the impact of interventions on socioeconomic health inequalities.

### Strengths and limitations

To the best of our knowledge, this is the first rapid synthesis of evidence about the effectiveness of depression, OA and T2D interventions across socioeconomic groups. Our use of standard systematic review approaches to searching, selection, and reporting ensured a robust synthesis. The focus on NICE-recommended interventions enabled a rapid review of evidence relevant to the UK health context. Similarly, by restricting to depression, OA and T2D, we prioritised evidence about conditions that make a substantial contribution to later life disability. Our conclusions are therefore limited to evidence about these conditions and interventions: a wider focus on interventions for other conditions may yield different answers. Finally, we included any clinical outcomes on the basis that an



improvement in depression, OA and T2D symptomology will delay the onset of disability linked to condition. This was a pragmatic decision in order to assess the potential of interventions to close the socioeconomic gap in DFLE. However, we recognise that wider social determinants of health also play a key role in shaping later life disability – beyond the contribution of illness alone.

## Conclusion

Limited evidence suggests that NICE-recommended interventions targeting depression, OA, or T2D offer little scope to reduce the socioeconomic gap in health. A g equity and/or inequity measures to be included in evaluation studies to strengthen evidence base.

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# Appendix 1: Background to depression, OA, and T2D

## Depression

Depression, also known as major depressive disorder or clinical depression, is a common mental disorder and the leading cause of disability in the world.<sup>61</sup> The worldwide prevalence of depression is estimated to be about 3.8%.<sup>61</sup> In the UK alone, approximately 1 in 5 (21%) adults aged 16 years and over experienced some form of depression in early 2021, an increase from 19% in November 2020, and it is more prominent in woman than men.<sup>62</sup> An analysis of the proportion of the British adult population with depression showed that over 4 in 10 women aged 16 to 29 years experienced depressive symptoms compared with 26% of men of the same age in 2021.<sup>62</sup> The condition can affect an individual's ability to perform day to day activities, by interfering with thoughts, feelings, behaviour, and physical health, leading to a range of psychological, physical, and social problems.<sup>61, 63</sup> Symptoms of depression include low mood, sadness, lack of energy and self-worth, appetite changes, and suicidal ideation, and is often accompanied by long-term dysphoria (severe unhappiness).<sup>64, 65</sup> The cause of depression is unknown, and it is understood to be a combination of factors.<sup>61</sup> Contributing factors include difficult experiences in childhood, stressful or traumatic life events, co-morbid mental health conditions, physical health problems, genetic inheritance, a result of medication or alcohol and drug abuse, and poor sleep, diet and exercise.<sup>63</sup> Most people who experience depression at some point in their life, are predicted to recover within one year, however, a small percentage of these may not recover and after five years or more will show no sign of remission.<sup>66, 67</sup> For patients with major depressive disorder, 30% may reach the treatment goal of remission, whilst the other 50% will either not respond at all or will respond without remission (20%).<sup>68</sup> For most people with depression, medication and psychotherapy are effective treatment options.<sup>68</sup> However, over-reliance on antidepressants is associated with high mortality and morbidity as medication is ineffective in some patients or is not being used by the correct patient group.<sup>69</sup> Furthermore, the response to treatment from psychological therapy and medication can be influenced by various sociodemographic factors regarding patient beliefs surrounding depression and treatment preference.<sup>70</sup> NICE, published best-practice guidance for managing symptoms of depression, with a range of interventions recommended. The most prominent interventions are high-intensity psychological interventions, specifically cognitive behavioural therapies (CBT); and pharmacological interventions (selective serotonin reuptake inhibitors, and third-generation antidepressants).<sup>71</sup>

## Type 2 diabetes

T2D is the most common type of diabetes.<sup>72</sup> It occurs when the production of, or response to insulin is inadequate. Insulin is an essential hormone that allows the glucose in the blood to enter blood cells and fuel the body.<sup>73</sup> For people with T2D, the body breaks down carbohydrates and turns it into glucose, and the pancreas responds by releasing insulin. However, because this insulin does not work properly, blood glucose keeps rising, causing more insulin to be released. Across the lifespan, T2D can develop at any age, even throughout childhood however it is more common in people who are: middle aged or older, of African or Caribbean descent, overweight or obese, physically inactive or genetically linked to the disease.<sup>74</sup> Approximately 4.9 million in the UK have diabetes, of which 90% have T2D.<sup>75</sup> Symptoms of T2D include increased thirst and urination, increased hunger, feeling tired, numbness or tingling in the feet or hands, blurred vision, unexplained weight loss, and sores that do not heal. One study suggests that symptoms of T2D in adults aged 60 and older contribute to a greater number of limitations for activities for daily living (ADL).<sup>76</sup>

NICE, published best-practice guidance for managing symptoms of T2D in 2015 and updated in 2020.<sup>77</sup> The guidance set key priorities for implementing individualised care that is personalised and tailored to the needs of an individual including:<sup>78</sup>

- Patient education – implementing patient-education programmes
- Dietary advice and bariatric surgery - ongoing dietary and nutritional advice and obesity treatment
- Blood glucose management – encouraging self-monitoring of blood glucose
- Drug treatment – e.g., metformin, a dipeptidyl peptidase-4 (DPP-4) inhibitor or pioglitazone

## **Osteoarthritis**

Osteoarthritis (OA) is a disease involving inflammation of the bone and joint cartilage. It is the main common type of arthritis in the UK.<sup>79</sup> A study of data from the UK Clinical Practice Research Datalink from 1997 to 2017 estimated that there were 494,716 incident OA cases for people aged  $\geq 20$  years.<sup>80</sup> The causes of OA are unknown; however, risk factors include genetic predisposition, increasing age, female sex, high or low bone density, joint injury and damage, joint laxity and reduced muscle strength, joint malalignment, exercise stresses, or occupational stresses.<sup>81, 82</sup> Main symptoms of OA include pain, stiffness and difficulty in movement, and can have a variety of physical, psychological and social impacts on ADL in older adults, most of which is reported as progressively worsening over time.<sup>83</sup> Current intervention options for managing chronic pain due to OA as recommended in the NICE clinical guideline published in 2014 and updated in 2020 include:<sup>84</sup>

- Provision of a holistic approach to osteoarthritis assessment and management – offering advice on core treatments
- Education and self-management – encouraging positive behavioural changes, such as exercise, weight loss, or use of suitable footwear
- Non-pharmacological management – exercise or manual therapy
- Pharmacological management - oral analgesics, topical treatments, non-steroidal anti-inflammatory drugs (NSAIDs), cyclo-oxygenase 2 (COX-2) inhibitors or opioids, or Intra-articular injections.
- Referral for joint surgery



## Appendix 2: Medline Search Strategy - Depression

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)** 1946 to December 01, 2021

Search Strategy:

#	Searches	Results
1	Depression/	135370
2	Depressive Disorder/	74390
3	Depression, Postpartum/	6491
4	Depressive Disorder, Major/	34006
5	Dysthymic Disorder/	1161
6	Mood Disorders/	15215
7	Seasonal Affective Disorder/	1243
8	(depress\$ or dysphori\$ or dysthym\$ or melanchol\$ or seasonal affective disorder\$.tw.	508088
9	or/1-8	559386
10	Cognitive Behavioral Therapy/	28132
11	"cognitive behavio?ral therap*".tw.	15180
12	(CBT or CCBT).tw.	12363
13	or/10-12	36898
14	Serotonin Uptake Inhibitors/	20312
15	(serotonin adj3 inhibitor*).tw.	18186
16	SSRI*.tw.	10469
17	Citalopram/	5122
18	Citalopram.tw.	5235
19	Escitalopram.tw.	2793
20	Fluoxetine/	9505
21	Fluoxetine.tw.	12846
22	Fluvoxamine/	1899
23	Fluvoxamine.tw.	2752

24	Paroxetine/	4052
25	Paroxetine.tw.	5721
26	Sertraline/	3233
27	Setraline.tw.	16
28	Duloxetine Hydrochloride/	1695
29	Duloxetine.tw.	2707
30	Mirtazapine/	1390
31	Mirtazapine.tw.	2267
32	Reboxetine/	611
33	Reboxetine.tw.	873
34	Venlafaxine Hydrochloride/	2703
35	Venlafaxine.tw.	4274
36	or/14-35	51834
37	9 and (13 or 36)	34538
38	exp Socioeconomic Factors/	481313
39	(socioeconomic* or socio-economic*).ti,ab,kw.	148848
40	exp Employment/	93781
41	employ*.ti,ab,kw.	662560
42	Unemployment/	7432
43	unemploy*.ti,ab,kw.	20458
44	exp Educational Status/	55968
45	educat*.ti,ab,kw.	671876
46	(education* adj2 level?).ti,ab,kw.	56576
47	((higher or better or worse or less) adj educated).ti,ab,kw.	6163
48	((higher or better or worse or less) adj level? of education).ti,ab,kw.	2576
49	Economic Status/	382
50	(household* adj3 income).ti,ab,kw.	13703
51	Poverty/	41295
52	poverty.ti,ab,kw.	29459

53	Healthcare Disparities/	20279
54	health status disparities/	18369
55	Health Equity/	2341
56	(health adj3 (disparit* or inequalit* or inequit* or equalit* or equit*)).ti,ab,kw.	35784
57	exp Social Class/	43588
58	"Social Determinants of Health"/	4977
59	exp sociological factors/	714343
60	(social* adj3 (class* or determinant* or status or position or background or circumstance*)).ti,ab,kw.	40554
61	(sociodemographic* or socio-demographic*).ti,ab,kw.	91599
62	ses.ti,ab,kw.	18405
63	"medically underserve".ti,ab,kw.	1673
64	depriv*.ti,ab,kw.	94480
65	exp Medical Assistance/	67541
66	(medicaid or medicare).ti,ab,kw.	66090
67	or/38-66	2292604
68	37 and 67	3662
69	meta-analysis.pt.	148119
70	meta-analysis/	148119
71	systematic review/	178116
72	Meta-Analysis as Topic/	20570
73	"Review Literature as Topic"/	8592
74	exp technology assessment, biomedical/	11697
75	(systematic* adj3 review*).ti,ab,kf,kw.	245766
76	(systematic* adj3 overview*).ti,ab,kf,kw.	2365
77	(methodologic* adj3 review*).ti,ab,kf,kw.	4008
78	(methodologic* adj3 overview*).ti,ab,kf,kw.	336
79	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf,kw.	13061

80	((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf,kw.	32590
81	(data synthes* or data extraction* or data abstraction*).ti,ab,kf,kw.	33001
82	(handsearch* or hand search*).ti,ab,kf,kw.	10188
83	(mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf,kw.	30609
84	(met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf,kw.	10641
85	(meta regression* or metaregression*).ti,ab,kf,kw.	11549
86	(meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.	380930
87	(medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.	275820
88	(cochrane or (health adj2 technology assessment) or evidence report).jw.	20503
89	(comparative adj3 (efficacy or effectiveness)).ti,ab,kf,kw.	15370
90	(outcomes research or relative effectiveness).ti,ab,kf,kw.	10327
91	((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab,kf,kw.	2498
92	or/69-91	570082
93	68 and 92	427

### Appendix 3: Medline Search Strategy - Osteoarthritis

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)** 1946 to July 27, 2021

Search Strategy:

#	Searches	Results
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1	exp Osteoarthritis/	67833
2	osteoarthritis.ti,ab,kw.	71861
3	or/1-2	96283
4	Patient Education as Topic/	87124
5	"patient education".ti,ab,kw.	20620
6	patient education handout/	5395
7	"patient information".ti,ab,kw.	8558
8	Self-Management/	3419
9	"self management".ti,ab,kw.	21723
10	Health Behavior/	53062
11	(health adj3 (behaviour or behavior or change*)).ti,ab,kw.	45797
12	exp Exercise/	213927
13	(exercise or "physical activit*").ti,ab,kw.	377153
14	Weight Loss/	38886
15	(weight adj3 (loss or lose)).ti,ab,kw.	100706
16	Shoes/	6558
17	(footwear or shoe*).ti,ab,kw.	12079
18	thermotherapy.ti,ab,kw.	2460
19	exp Musculoskeletal Manipulations/	17437
20	("manual therapy" or "musculoskeletal manipulation").ti,ab,kw.	2611
21	exp Physical Therapy Modalities/	162637
22	("physical therap*" or physiotherap*).ti,ab,kw.	54415
23	Exercise Therapy/	43789
24	electric stimulation therapy/ or transcutaneous electric nerve stimulation/	25357
25	(electrotherapy or (electric adj2 therap*) or "transcutaneous electrical nerve stimulation" or TENS).ti,ab,kw.	20304
26	Braces/	5715
27	Foot Orthoses/	1130
28	(bracing or brace or braces or "joint support" or insole*).ti,ab,kw.	11224

29	Self-Help Devices/	5229
30	Orthopedic Equipment/	3475
31	Occupational Therapy/	13704
32	"disability equipment assessment centre*".ti,ab,kw.	0
33	"occupational therap*".ti,ab,kw.	15829
34	("walking stick*" or cane or walker or "walking frame*" or "tap turner*" or "assistive device*").ti,ab,kw.	18456
35	Acetaminophen/	19031
36	(paracetamol or acetaminophen or tylenol).ti,ab,kw.	26927
37	Anti-Inflammatory Agents, Non-Steroidal/	69302
38	("Non-steroidal anti-inflammatory drug*" or NSAID*).ti,ab,kw.	34339
39	Capsaicin/	10673
40	(ibuprofen or advil or capsaicin).ti,ab,kw.	28587
41	Cyclooxygenase 2 Inhibitors/	9343
42	("Cyclooxygenase 2 Inhibitor*" or "COX-2 inhibitor*").ti,ab,kw.	9461
43	Analgesics, Opioid/	49310
44	opioid*.ti,ab,kw.	99751
45	Injections, Intra-Articular/	8396
46	((intra-articular or intraarticular) adj3 injection*).ti,ab,kw.	6614
47	exp Arthroplasty/	76570
48	(arthroplasty or "joint replacement*" or "joint surger*").ti,ab,kw.	76446
49	or/4-48	1311431
50	3 and 49	39511
51	exp Socioeconomic Factors/	471527
52	(socioeconomic* or socio-economic*).ti,ab,kw.	144080
53	exp Employment/	91367
54	employ*.ti,ab,kw.	644213
55	Unemployment/	7306
56	unemploy*.ti,ab,kw.	19785

57	exp Educational Status/	54443
58	educat*.ti,ab,kw.	653032
59	(education* adj2 level?).ti,ab,kw.	54628
60	((higher or better or worse or less) adj educated).ti,ab,kw.	6018
61	((higher or better or worse or less) adj level? of education).ti,ab,kw.	2507
62	Economic Status/	331
63	(household* adj3 income).ti,ab,kw.	13046
64	Poverty/	40237
65	poverty.ti,ab,kw.	28502
66	Healthcare Disparities/	19284
67	health status disparities/	17621
68	Health Equity/	1985
69	(health adj3 (disparit* or inequalit* or inequit* or equalit* or equit*)).ti,ab,kw.	33869
70	exp Social Class/	42820
71	"Social Determinants of Health"/	4445
72	exp sociological factors/	697158
73	(social* adj3 (class* or determinant* or status or position or background or circumstance*)).ti,ab,kw.	39127
74	(sociodemographic* or socio-demographic*).ti,ab,kw.	87320
75	ses.ti,ab,kw.	17802
76	"medically underserve*".ti,ab,kw.	1610
77	depriv*.ti,ab,kw.	92582
78	exp Medical Assistance/	65719
79	(medicaid or medicare).ti,ab,kw.	64683
80	or/51-79	2232649
81	50 and 80	2739
82	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.	631801
83	Randomized Controlled Trial/	538355
84	exp Randomized Controlled Trials as Topic/	150066

85	"Randomized Controlled Trial (topic)"/	0
86	Controlled Clinical Trial/	94308
87	exp Controlled Clinical Trials as Topic/	155631
88	"Controlled Clinical Trial (topic)"/	0
89	Randomization/	105654
90	Random Allocation/	105654
91	Double-Blind Method/	165998
92	Double Blind Procedure/	0
93	Double-Blind Studies/	165998
94	Single-Blind Method/	30598
95	Single Blind Procedure/	0
96	Single-Blind Studies/	30598
97	Placebos/	35585
98	Placebo/	0
99	Control Groups/	1758
100	Control Group/	1758
101	(random* or sham or placebo*).ti,ab,hw,kw.	1610695
102	((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kw.	248639
103	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kw.	1215
104	(control* adj3 (study or studies or trial* or group*)).ti,ab,kw.	1064980
105	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kw.	47861
106	allocated.ti,ab,hw.	72273
107	((open label or open-label) adj5 (study or studies or trial*)).ti,ab,hw,kw.	38181
108	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,hw,kw.	9639
109	(pragmatic study or pragmatic studies).ti,ab,hw,kw.	476
110	((pragmatic or practical) adj3 trial*).ti,ab,hw,kw.	6002
111	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,hw,kw.	9258



112	(phase adj3 (III or "3") adj3 (study or studies or trial*).ti,hw,kw.	30832
113	or/82-112	2312237
114	81 and 113	741

## Appendix 4: Medline Search Strategy – Type 2 diabetes

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)** 1946 to January 24, 2022

Search Strategy

#	Searches	Results
1	exp Diabetes Mellitus, Type 2/	151773
2	(Type* adj3 ("2" or "II" or two*) adj3 (diabete* or diabetic*).tw.	168022
3	((Maturit* or adult* or slow*) adj3 onset* adj3 (diabete* or diabetic*).tw.	3167
4	((Ketosis-resistant* or stable*) adj3 (diabete* or diabetic*).tw.	824
5	((Non-insulin* or Non insulin* or Noninsulin*) adj3 depend* adj3 (diabete* or diabetic*).tw.	11870
6	NIDDM.tw.	6949
7	or/1-6	219609
8	exp Socioeconomic Factors/	483828
9	(socioeconomic* or socio-economic*).ti,ab,kw.	150875
10	exp Employment/	94354
11	employ*.ti,ab,kw.	670565
12	Unemployment/	7482
13	unemploy*.ti,ab,kw.	20747
14	exp Educational Status/	56365
15	educat*.ti,ab,kw.	680110
16	(education* adj2 level?).ti,ab,kw.	57466
17	((higher or better or worse or less) adj educated).ti,ab,kw.	6249
18	((higher or better or worse or less) adj level? of education).ti,ab,kw.	2603
19	Economic Status/	398

20	(household* adj3 income).ti,ab,kw.	14013
21	Poverty/	41578
22	poverty.ti,ab,kw.	29821
23	Healthcare Disparities/	20590
24	health status disparities/	18603
25	Health Equity/	2443
26	(health adj3 (disparit* or inequalit* or inequit* or equalit* or equit*)).ti,ab,kw.	36625
27	exp Social Class/	43802
28	"Social Determinants of Health"/	5170
29	exp sociological factors/	718686
30	(social* adj3 (class* or determinant* or status or position or background or circumstance*)).ti,ab,kw.	41235
31	(sociodemographic* or socio-demographic*).ti,ab,kw.	93506
32	ses.ti,ab,kw.	18693
33	"medically underserve*".ti,ab,kw.	1696
34	depriv*.ti,ab,kw.	95296
35	exp Medical Assistance/	68056
36	(medicaid or medicare).ti,ab,kw.	66718
37	or/8-36	2316546
38	meta-analysis.pt.	151335
39	meta-analysis/	151335
40	systematic review/	183010
41	Meta-Analysis as Topic/	20710
42	"Review Literature as Topic"/	8644
43	exp technology assessment, biomedical/	11746
44	(systematic* adj3 review*).ti,ab,kf,kw.	252230
45	(systematic* adj3 overview*).ti,ab,kf,kw.	2416
46	(methodologic* adj3 review*).ti,ab,kf,kw.	4071
47	(methodologic* adj3 overview*).ti,ab,kf,kw.	338

48	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf,kw.	13278
49	((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf,kw.	33188
50	(data synthes* or data extraction* or data abstraction*).ti,ab,kf,kw.	33723
51	(handsearch* or hand search*).ti,ab,kf,kw.	10291
52	(mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf,kw.	31082
53	(met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf,kw.	10811
54	(meta regression* or metaregression*).ti,ab,kf,kw.	11840
55	(meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.	388963
56	(medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.	281936
57	(cochrane or (health adj2 technology assessment) or evidence report).jw.	20622
58	(comparative adj3 (efficacy or effectiveness)).ti,ab,kf,kw.	15549
59	(outcomes research or relative effectiveness).ti,ab,kf,kw.	10414
60	((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab,kf,kw.	2535
61	or/38-60	580790
62	7 and 37 and 61	1198
63	limit 62 to yr="2015 -Current"	749
64	"30204377".an.	1
65	"29553668".an.	1



## Appendix 5. Depression – Studies within reviews

Primary study	Type	Title	Review						
			Caldwell 2019 <sup>24</sup>	Finegan 2018 <sup>25</sup>	Kavanagh 2009 <sup>28</sup>	Karyotaki 2017 <sup>27</sup>	Karyotaki 2021 <sup>26</sup>	Kuyken 2016 <sup>29</sup>	Saad 2021 <sup>30</sup>
Lamb et al. 1998	RCT	School-based intervention to promote coping in rural teens' MCN: The American Journal of Maternal Child Nursing 23:187–194.			<input type="checkbox"/>				
Listung-Lunde 2005	RCT	A Cognitive-Behavioral Treatment for Depression in Native American Middle-School Students Unpublished doctoral thesis, University of North Dakota: United States of America.			<input type="checkbox"/>				
Lock and Barrett 2003	RCT	A longitudinal study of developmental differences in universal preventive intervention for child anxiety' Behaviour Change 20:183–199	<input type="checkbox"/>		<input type="checkbox"/>				
Spence et al. 2003	RCT	Preventing adolescent depression: An evaluation of the Problem Solving for Life program' Journal of Consulting and Clinical Psychology 71:3–13	<input type="checkbox"/>		<input type="checkbox"/>				
Chaplin et al. 2006	RCT	Depression prevention for early adolescent girls: A pilot study of all girls versus co-ed groups' The Journal of Early Adolescence 26:110–126	<input type="checkbox"/>		<input type="checkbox"/>				

Yu and Seligman 2002	RCT	Preventing depressive symptoms in Chinese children' Prevention and Treatment 5:1–39	<input type="checkbox"/>		<input type="checkbox"/>				
Button et al. 2012	RCT	Factors associated with differential response to online cognitive behavioural therapy. Social Psychiatry and Psychiatric Epidemiology, 47(5), 827–833.		<input type="checkbox"/>					
Teasdale et al. 2000	RCT	Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. J Consult Clin Psychol. 2000;68(4):615-623.						<input type="checkbox"/>	
Ma and Teasdale 2004	RCT	Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. J Consult Clin Psychol. 2004;72(1):31-40						<input type="checkbox"/>	
Kuyken et al. 2008	RCT	Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. J Consult Clin Psychol. 2008;76(6):966-978						<input type="checkbox"/>	
Bondolfi et al. 2010	RCT	Depression relapse prophylaxis with mindfulness-based cognitive therapy: replication and extension in the Swiss health care system. J Affect Disord. 2010;122(3):224-231						<input type="checkbox"/>	
Godfrin and van Heeringen 2010	RCT	The effects of mindfulness-based cognitive therapy on recurrence of depressive episodes, mental health and quality of life: a randomized controlled study. Behav Res Ther. 2010;48(8):738-746						<input type="checkbox"/>	

Segal et al. 2010	RCT	Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression. Arch Gen Psychiatry. 2010;67 (12):1256-1264							<input type="checkbox"/>	
Huijbers et al. 2012 and 2015	RCT	Adding mindfulness-based cognitive therapy to maintenance antidepressant medication for prevention of relapse/recurrence in major depressive disorder: randomised controlled trial. J Affect Disord. 2015;187:54-61							<input type="checkbox"/>	
Kuyken et al. 2015	RCT	Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. Lancet. 2015;386(9988):63-73							<input type="checkbox"/>	
Williams et al. 2014	RCT	Mindfulness-based cognitive therapy for preventing relapse in recurrent depression: a randomized dismantling trial. J Consult Clin Psychol. 2014;82(2):275-286							<input type="checkbox"/>	
Jannati et al. 2020	RCT	Effectiveness of an app-based cognitive behavioral therapy program for postpartum depression in primary care: a randomized controlled trial. Int J Med Inf 2020; 104145.								<input type="checkbox"/>
Araya 2013	Cluster RCT	School intervention to improve mental health of students in Santiago, Chile: a randomized clinical trial. Jama, Pediatr	<input type="checkbox"/>							

		2013; 167(11): 1004-10 mental health promotion 2013; 6(2): 93-121.							
Cardemil 2002	RCT	The prevention of depressive symptoms in low-income, minority children: two-year follow-up. Behav Res Ther 2007; 45(2): 313-27.	<input type="checkbox"/>						
Gillham 2007	RCT	School-based prevention of depressive symptoms: A randomized controlled study of the effectiveness and specificity of the Penn Resiliency Program. J Consult Clin Psychol 2007; 75(1): 9-19	<input type="checkbox"/>						
Kindt 2014	Cluster RCT	Evaluation of a school-based depression prevention program among adolescents from low-income areas: a randomized controlled effectiveness trial. Int J Environ Res Public Health 2014; 11(5): 5273-93.	<input type="checkbox"/>						
Pattison 2001	RCT	The prevention of depressive symptoms in children: The immediate and long-term outcomes of a school-based program. Behaviour change 2001; 18(2): 92-102	<input type="checkbox"/>						
Perry 2017	Cluster RCT	Preventing Depression in Final Year Secondary Students: School-Based Randomized Controlled Trial. J Med Internet Res 2017; 19(11): e369.	<input type="checkbox"/>						
Possel 2011	Cluster RCT	A randomized trial to evaluate the course of effects of a program to prevent adolescent	<input type="checkbox"/>						



		depressive symptoms over 12 months. Behav Res Ther 2011; 49(12): 838-51.							
Quayle 2001	RCT	The effect of an optimism and lifeskills program on depressive symptoms in preadolescence. Behaviour change 2001; 18(4): 194-203.	<input type="checkbox"/>						
Roberts 2003	Cluster RCT	The prevention of depressive symptoms in rural school children: a randomized controlled trial. J Consult Clin Psychol 2003; 71(3): 622-8	<input type="checkbox"/>						
Rooney 2006	Cluster RCT	The Prevention of Depression in 8- to 9-Year-Old Children: A Pilot Study. Australian journal of guidance and counselling 2006; 16(1): 76-90.	<input type="checkbox"/>						
Sawyer 2010	Cluster RCT	School-based prevention of depression: a randomised controlled study of the beyondblue schools research initiative. J Child Psychol Psychiatry 2010; 51(2): 199-209.	<input type="checkbox"/>						
Clarke 1995	RCT	Targeted prevention of unipolar depressive disorder in an at-risk sample of high school adolescents: a randomized trial of a group cognitive intervention. J Am Acad Child Adolesc Psychiatry 1995; 34(3): 312-21	<input type="checkbox"/>						
Congleton 1995	RCT	The effect of a cognitive-behavioral group intervention on the locus of control, attributional style, and depressive	<input type="checkbox"/>						

		symptoms of middle school students; 2019. Thesis. University of Kentucky, USA.							
Gaete 2016	RCT	Indicated school-based intervention to improve depressive symptoms among at risk Chilean adolescents: a randomized controlled trial. BMC Psychiatry 2016; 16: 276.	<input type="checkbox"/>						
Gillham 2012	RCT	Evaluation of a group cognitive-behavioral depression prevention program for young adolescents: a randomized effectiveness trial. J Clin Child Adolesc Psychol 2012; 41(5): 621-39	<input type="checkbox"/>						
Jaycox 1994	Cluster RCT	Prevention of depressive symptoms in school children. Behav Res Ther 1994; 32(8): 801-16.	<input type="checkbox"/>						
McCarty 2011	RCT	Feasibility of the positive thoughts and actions prevention program for middle schoolers at risk for depression. Depress Res Treat 2011; 2011: 241386.	<input type="checkbox"/>						
McCarty 2013	RCT	A randomized trial of the Positive Thoughts and Action program for depression among early adolescents. J Clin Child Adolesc Psychol 2013; 42(4): 554-63.	<input type="checkbox"/>						
McLaughlin 2011	RCT	Evaluating the effect of an empirically-supported group intervention for students at-risk for depression in a rural school district [thesis]. Dissertation abstracts	<input type="checkbox"/>						

		international: section b: the sciences and engineering 2011; 71(9-b): 5820							
Rhode 2014	RCT	Indicated cognitive behavioral group depression prevention compared to bibliotherapy and brochure control: acute effects of an effectiveness trial with adolescents. J Consult Clin Psychol 2014; 82(1): 65-74.	<input type="checkbox"/>						
Stice 2006	RCT	Randomized trial of a brief depression prevention program: an elusive search for a psychosocial placebo control condition. Behav Res Ther 2007; 45(5): 863-76.	<input type="checkbox"/>						
Stoppelbein 2003	Cluster RCT	An evaluation of a high-school based cognitive-behavioral program. Dissertation abstracts international: section b: the sciences and engineering 2004; 64(8-B): 4066.	<input type="checkbox"/>						
Woods 2011	RCT	Effectiveness of a school-based indicated early intervention program for Maori and Pacific adolescents. Journal of pacific rim psychology 2011; 5(1): 40-50	<input type="checkbox"/>						
Young 2006	RCT	A Randomized Depression Prevention Trial Comparing Interpersonal Psychotherapy-- Adolescent Skills Training to Group Counseling in Schools. Prev Sci 2016;17(3): 314-24.	<input type="checkbox"/>						

Andersson et al. 2005	RCT	Internet-based self-help for depression: randomised controlled trial. Br J Psychiatry. 2005;187(5):456-461						<input type="checkbox"/>		
Beevers et al. 2017	RCT	Effectiveness of an internet intervention (Deprexis) for depression in a united states adult sample: a parallel-group pragmatic randomized controlled trial. J Consult Clin Psychol. 2017;85(4):367-380.						<input type="checkbox"/>		
Berger et al. 2011	RCT	Internet-based treatment of depression: a randomized controlled trial comparing guided with unguided self-help. Cogn Behav Ther. 2011;40 (4):251-266.					<input type="checkbox"/>	<input type="checkbox"/>		
Choi et al. 2012	RCT	Culturally attuned Internet treatment for depression amongst Chinese Australians: a randomised controlled trial. J Affect Disord. 2012;136(3):459-468.						<input type="checkbox"/>		
Christensen et al. 2004	RCT	Delivering interventions for depression by using the internet: randomised controlled trial. BMJ. 2004; 328(7434):265.					<input type="checkbox"/>	<input type="checkbox"/>		
de Graaf et al. 2011	RCT	Clinical effectiveness of online computerised cognitive-behavioural therapy without support for depression in primary care: randomised trial. Br J Psychiatry. 2009;195(1):73-80.					<input type="checkbox"/>	<input type="checkbox"/>		
Farrer et al. 2011	RCT	Internet-based CBT for depression with and without telephone tracking in a national					<input type="checkbox"/>	<input type="checkbox"/>		

		helpline: randomised controlled trial. PLoS One. 2011;6(11):e28099.							
Forand et al. 2017	RCT	Efficacy of guided iCBT for depression and mediation of change by cognitive skill acquisition. Behav Ther. 2018;49(2):295-307.					<input type="checkbox"/>		
Forsell et al. 2017	RCT	Internet delivered cognitive behavior therapy for antenatal depression: a randomised controlled trial. J Affect Disord. 2017;221:56-64.					<input type="checkbox"/>		
Geraedts et al. 2014	RCT	Short-term effects of a web-based guided self-help intervention for employees with depressive symptoms: randomized controlled trial. J Med Internet Res. 2014;16(5):e121					<input type="checkbox"/>		
Gilbody et al. 2015	RCT	Computerised cognitive behaviour therapy (cCBT) as treatment for depression in primary care (REEACT trial): large scale pragmatic randomised controlled trial. BMJ. 2015;351:h5627				<input type="checkbox"/>	<input type="checkbox"/>		
Gilbody et al. 2017	RCT	REEACT collaborative. Telephone-supported computerised cognitive-behavioural therapy: REEACT-2 large-scale pragmatic randomised controlled trial. Br J Psychiatry. 2017;210(5):362-367.					<input type="checkbox"/>		
Hallgren et al. 2016	RCT	Exercise and internet-based cognitive-behavioural therapy for depression: multicentre randomised controlled trial with					<input type="checkbox"/>		

		12-month follow-up. Br J Psychiatry. 2016;209(5):414-420							
Johansson et al. 2012	RCT	Tailored vs. standardized internet-based cognitive behavior therapy for depression and comorbid symptoms: a randomized controlled trial. PLoS One. 2012;7(5):e36905.					<input type="checkbox"/>		
Kessler et al. 2012	RCT	Therapist-delivered Internet psychotherapy for depression in primary care: a randomised controlled trial. Lancet. 2009;374(9690):628-634					<input type="checkbox"/>		
Kivi et al. 2014	RCT	Internet-based therapy for mild to moderate depression in Swedish primary care: short term results from the PRIM-NET randomized controlled trial. Cogn Behav Ther. 2014;43(4):289-298.					<input type="checkbox"/>		
Klein et al. 2016	RCT	Effects of a psychological internet intervention in the treatment of mild to moderate depressive symptoms: results of the EVIDENT study, a randomized controlled trial. Psychother Psychosom. 2016;85(4):218-228.				<input type="checkbox"/>	<input type="checkbox"/>		
Lintvedt et al. 2013	RCT	Evaluating the effectiveness and efficacy of unguided internet-based self-help intervention for the prevention of depression: a randomized controlled trial. Clin Psychol Psychother. 2013;20(1): 10-27.					<input type="checkbox"/>		

Meyer et al. 2009	RCT	Effectiveness of a novel integrative online treatment for depression (Deprexis): randomized controlled trial. J Med Internet Res. 2009;11(2):e15.				<input type="checkbox"/>	<input type="checkbox"/>		
Meyer et al. 2015	RCT	Effects of an internet intervention (Deprexis) on severe depression symptoms: randomized controlled trial. Internet Interventions. 2015;2(1):48-59				<input type="checkbox"/>	<input type="checkbox"/>		
Milgrom et al. 2016	RCT	Internet cognitive behavioral therapy for women with postnatal depression: a randomized controlled trial of MumMoodBooster. J Med Internet Res. 2016;18(3):e54.					<input type="checkbox"/>		
Mira et al. 2017	RCT	An Internet-based program for depressive symptoms using human and automated support: a randomized controlled trial. Neuropsychiatr Dis Treat. 2017;13:987-1006				<input type="checkbox"/>	<input type="checkbox"/>		
Mohr et al. 2013	RCT	A randomized controlled trial evaluating a manualized TeleCoaching protocol for improving adherence to a web-based intervention for the treatment of depression. PLoS One. 2013;8(8):e70086					<input type="checkbox"/>		
Montero-Marín et al. 2016	RCT	An internet-based intervention for depression in primary Care in Spain: a randomized controlled trial. J Med Internet Res. 2016;18(8):e231					<input type="checkbox"/>		

Moritz et al. 2012	RCT	A randomized controlled trial of internet based therapy in depression. Behav Res Ther. 2012; 50(7-8):513-521.				<input type="checkbox"/>	<input type="checkbox"/>		
Perini et al. 2009	RCT	Clinician-assisted Internet-based treatment is effective for depression: randomized controlled trial. Aust N Z J Psychiatry. 2009;43(6):571-578.					<input type="checkbox"/>		
Phillips et al. 2014	RCT	Randomized controlled trial of computerized cognitive behavioural therapy for depressive symptoms: effectiveness and costs of a workplace intervention. Psychol Med. 2014;44(4):741-752.				<input type="checkbox"/>	<input type="checkbox"/>		
Pugh et al. 2016	RCT	A randomised controlled trial of therapist-assisted, internet-delivered cognitive behavior therapy for women with maternal depression. PLoS One. 2016; 11(3):e0149186.					<input type="checkbox"/>		
Richards et al. 2015	RCT	A randomized controlled trial of an internet-delivered treatment: its potential as a low-intensity community intervention for adults with symptoms of depression. Behav Res Ther. 2015;75:20-31					<input type="checkbox"/>		
Rosso et al. 2016	RCT	Internet-based cognitive behavior therapy for major depressive disorder: a randomized controlled trial. Depress Anxiety. 2017;34(3):236-245.					<input type="checkbox"/>		



Ruwaard et al. 2009	RCT	Standardized web-based cognitive behavioural therapy of mild to moderate depression: a randomized controlled trial with a long-term follow-up. Cogn Behav Ther. 2009;38(4):206-221						<input type="checkbox"/>		
Sheeber et al. 2012	RCT	Development and pilot evaluation of an Internet-facilitated cognitive-behavioral intervention for maternal depression. J Consult Clin Psychol. 2012;80(5):739-749						<input type="checkbox"/>		
Smith et al. 2017	RCT	Help from home for depression: a randomised controlled trial comparing internet-delivered cognitive behaviour therapy with bibliotherapy for depression. Internet Interv. 2017;9:25-37.						<input type="checkbox"/>		
Spek et al. 2007	RCT	Internet-based cognitive behavioural therapy for subthreshold depression in people over 50 years old: a randomized controlled clinical trial. Psychol Med. 2007;37(12):1797-1806					<input type="checkbox"/>	<input type="checkbox"/>		
Vernmark et al. 2010	RCT	Internet administered guided self-help versus individualized e-mail therapy: a randomized trial of two versions of CBT for major depression. Behav Res Ther. 2010;48(5):368-376						<input type="checkbox"/>		
Warmerdam et al. 2008	RCT	Internet-based treatment for adults with depressive symptoms: randomized controlled trial. J Med Internet Res. 2008;10(4):e44						<input type="checkbox"/>		

Williams et al. 2013	RCT	Positive imagery cognitive bias modification (CBM) and internet-based cognitive behavioral therapy (iCBT): a randomized controlled trial. J Affect Disord. 2015;178:131-141.					<input type="checkbox"/>		
Yeung et al. 2017	RCT	Outcomes of an online computerized cognitive behavioral treatment program for treating chinese patients with depression: a pilot study. Asian J Psychiatr. 2018;38:102-107.					<input type="checkbox"/>		
Zagorscak et al. 2018	RCT	Benefits of individualized feedback in internet-based interventions for depression: a randomized controlled trial. Psychother Psychosom. 2018;87(1):32-45.					<input type="checkbox"/>		
Clarke et al. 2002	RCT	Overcoming depression on the Internet (ODIN): a randomized controlled trial of an Internet depression skills intervention program. J Med Internet Res. 2002;4(3):E14.				<input type="checkbox"/>			
Clarke et al. 2005	RCT	Overcoming Depression on the Internet (ODIN) (2): a randomized trial of a self-help depression skills program with reminders. J Med Internet Res. 2005; 7(2):e16.				<input type="checkbox"/>			
Clarke et al. 2009	RCT	Dickerson J, Gullion C. Randomized effectiveness trial of an Internet, pure self-help, cognitive behavioral intervention for depressive symptoms in young adults. Cogn Behav Ther. 2009;38(4):222-234				<input type="checkbox"/>			

Kleiboer et al. 2015	RCT	A randomized controlled trial on the role of support in Internet-based problem solving therapy for depression and anxiety. Behav Res Ther. 2015;72(6):63-71.					□			
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## Appendix 6. Summary of included reviews for depression

Citation; country	Review type; No. of studies relevant to our review	Population	Analytical approach used for examining effects by SES	Intervention	Outcomes assessed; Follow-up period	SES measure	Results	Reported risk of bias in review
Caldwell et al. 2019; <sup>24</sup>  United Kingdom	Systematic review & Meta-analysis  19 (137) Randomised & quasi-randomized trials	School-based children and young people aged 4–18 years	Post hoc sub-group analysis	School-based Cognitive Behavioural Therapy	Self-reported depression:  DSM-5; self-reported wellbeing; self-reported suicidal ideation, behaviour, or self-harm  <i>13-24 months (long term)</i>	Low SES in primary school	SMD -0.23 (95% CI: -0.60 to 1.13)	Unclear risk
						High SES primary school	SMD -0.05 (95% CI: -0.55 to 0.45)	
						Low SES in secondary school	SMD 0.04 (95% CI: -0.06 to 0.15)	
						High SES in secondary school	SMD -0.07 (95% CI: -0.20 to 0.06)	
Kavanagh et al. 2009; <sup>28</sup>  United Kingdom	Systematic review & Meta-analysis  6 (17) Randomized trials	School-based young people aged 11–19	Post hoc sub-group analysis	School-based Cognitive Behavioural Therapy	Reduction in depressive symptoms:  Children's Depression Inventory; Beck Depression Inventory	Low SES	Two studies (n=57)  Standardised mean differences [(SMD): 0.44, 95% CI: -0.09 to 0.97]	High quality
						Middle SES	Two studies (n=2,003)	

Citation; country	Review type; No. of studies relevant to our review	Population	Analytical approach used for examining effects by SES	Intervention	Outcomes assessed; Follow-up period	SES measure	Results	Reported risk of bias in review
					<i>Up to 4 weeks</i>		(SMD: -0.28, 95% CI: -0.44 to -0.11)	
						High SES	Two studies (n=283)  (SMD: -0.31, 95% CI: -0.54 to -0.07)	
Finegan et al. 2018; <sup>25</sup>  United Kingdom	Systematic review & Meta-analysis  1 (17) Randomized control trial	Community-based adult patients over 18 years of age, who received a form of psychotherapy for a common mental health problem (unipolar depression, anxiety disorders)	Not reported	Cognitive Behavioural Therapy	Severity of depressive symptoms:  Beck Depression Inventory-II  <i>Follow-up period not reported</i>	Educational level (more than/less than A level)	No relationship was found between level of education and treatment outcomes following CBT	Good quality
Karyotaki et al. 2017; <sup>27</sup>  Netherlands	Meta-analysis of Individual Participant Data  10 (16)	Community-based adults aged 42.0 (11.7) years; with elevated symptoms of depression	Moderator analysis	Self- guided Internet-Based Cognitive Behavioural Therapy	Depressive symptom response:  Standardized $\beta$ weights of the composite z	Educational level (primary, secondary and tertiary)	Educational level did not significantly moderate outcomes after treatment:	Low risk

Citation; country	Review type; No. of studies relevant to our review	Population	Analytical approach used for examining effects by SES	Intervention	Outcomes assessed; Follow-up period	SES measure	Results	Reported risk of bias in review
	Randomized clinical trials	based on any diagnosis or any self-report scale of depression			<p>scores of the Beck Depression Inventory; Center for Epidemiological Studies– Depression Scale; and 9-item Patient Health Questionnaire scores</p> <p><i>Follow-up period not reported</i></p>		<p>Secondary vs. primary (<math>\beta =</math> 0.15;P = 0.21)</p> <p>Tertiary vs primary (<math>\beta =</math> 0.03;P =0.79)</p>	
						Employment status (employed or unemployed)	Employment status did not significantly moderate outcomes after treatment ( $\beta =$ 0.12;P =0.11)	
					Treatment response:  Standardized $\beta$ weights of the composite z scores of the Beck Depression Inventory; Center for Epidemiological Studies– Depression Scale; and 9-item Patient Health Questionnaire scores	Educational level (primary, secondary and tertiary)	<p>Educational level was not significantly associated with treatment response:</p> <p>Secondary vs. primary (<math>\beta =</math> -0.40;P = 0.31)</p> <p>Tertiary vs primary (<math>\beta =</math> -0.16;P = 0.68)</p>	
						Employment status (employed or unemployed)	Employment status was not significantly associated with	

Citation; country	Review type; No. of studies relevant to our review	Population	Analytical approach used for examining effects by SES	Intervention	Outcomes assessed; Follow-up period	SES measure	Results	Reported risk of bias in review
					<i>Follow-up period not reported</i>		treatment response ( $\beta = -0.34; P = 0.12$ )	
Karyotaki et al. 2021; <sup>26</sup>  United States of America	Systematic Review and Individual Patient Data Network Meta-analysis  39 (39) Randomized clinical trials	Community-based adults; with self-reported or diagnosed depression	Effect size modification	Guided Internet-Based Cognitive Behavioural Therapy (delivered by a professional or a paraprofessional)	Depression symptom severity:  Patient Health Questionnaire–9 (PHQ-9) scores  6 & 12 months	Employment status (employed, unemployed, student, other) at 6 months         Employment status (employed, unemployed, student, other) at 12 months	Other vs Treatment as Usual (TAU): (SD: 0.038; 95%CI, -0.096 to 0.052)  Student vs. TAU: (SD: 0.04; 95%CI, -0.076 to 0.081)  Unemployed vs TAU: (SD: 0.041; 95%CI, -0.119 to 0.043)  Other vs TAU: (SD: 0.038; 95%CI, -0.113 to 0.035)  Student vs. TAU: (SD: 0.046; 95%CI, -0.087 to 0.094)  Unemployed vs TAU: (SD: 0.037; 95%CI, -0.072 to 0.073)  Other vs TAU:	Low risk

Citation; country	Review type; No. of studies relevant to our review	Population	Analytical approach used for examining effects by SES	Intervention	Outcomes assessed; Follow-up period	SES measure	Results	Reported risk of bias in review
				Unguided Internet-Based Cognitive Behavioural Therapy		Employment status (employed, unemployed, student, other) at 6 months	(SD: 0.033; 95%CI, - 0.059 to 0.071) Student vs. TAU: (SD: 0.034; 95%CI, -0.075 to 0.058) Unemployed vs TAU: (SD: 0.03; 95%CI, -0.068 to 0.05)	
						Employment status (employed, unemployed, student, other) at 12 months	Other vs TAU: (SD: 0.03; 95%CI, -0.077 to 0.04) Student vs. TAU: (SD: 0.043; 95%CI, -0.092 to 0.078) Unemployed vs TAU: (SD: 0.032; 95%CI, -0.066 to 0.059)	
Kuyken et al. 2016; <sup>29</sup>  United Kingdom	Individual Patient Data Meta-analysis  9 (9)	Community-based adults, aged 47.1 (11.9) years; with major depressive disorder in full	Moderator analysis	Mindfulness-Based Cognitive Therapy	Relapse to depression  <i>Within 60 weeks of follow-up</i>	Educational level (no qualifications, qualifications below degree level, and	There is no support for MBCT having differential effects on relapse to depression	Low risk

Citation; country	Review type; No. of studies relevant to our review	Population	Analytical approach used for examining effects by SES	Intervention	Outcomes assessed; Follow-up period	SES measure	Results	Reported risk of bias in review
	Randomized trials	or partial remission according to a formal diagnostic classification system				degree or higher)	based on educational level	
Saad et al. 2021; <sup>30</sup>  Canada	Equity- focused systematic review  1 (18) Randomized control trial	New mothers with postpartum depression Pregnancy stage: postnatal	Not reported	Mobile Cognitive Behaviour Therapy	Severity of postpartum depression Symptoms:  The Edinburgh Postnatal Depression Scale (EPDS)— Persian version  <i>Up to 3 months</i>	Educational level	Post-intervention correlation p=0.44 and p=0.89 for the intervention and control groups, respectively	High risk



## Appendix 7. Association of SES and clinical outcomes for depression

Intervention	Outcome	SES Parameter	Overall Summary	Does the intervention favour advantaged or disadvantaged populations
School-based CBT	Self-reported depression	Low vs. high SES in primary school	There was no evidence of a difference by socioeconomic status for depression in primary school settings. <sup>24</sup>	No evidence of differential impact
		Low vs. high SES in secondary school	In secondary school settings, results suggest that interventions delivered in lower socioeconomic status settings were less effective than those in higher or mixed socioeconomic status settings. <sup>24</sup>	Favours advantaged populations
	Reduction in depressive symptoms	Low vs. middle vs. high SES	Limited evidence (6 primary studies) show that CBT may be more effective for young people from families with middle to high SES than for those from low SES backgrounds. <sup>28</sup>	Favours advantaged populations
Community-based online CBT	Severity of depressive symptoms	Educational level	No relationship was found between level of education and treatment outcomes following CBT. <sup>25</sup>	No evidence of differential impact
Guided internet-based CBT	Depression symptom severity	Employment status	Not being employed was associated with poorer outcomes. <sup>26</sup>	Favours advantaged populations

<b>Intervention</b>	<b>Outcome</b>	<b>SES Parameter</b>	<b>Overall Summary</b>	<b>Does the intervention favour advantaged or disadvantaged populations</b>
Self-guided internet-based CBT	Depressive symptom response	Educational level	Educational level did not significantly moderate outcomes after treatment. <sup>27</sup>	No evidence of differential impact
		Employment status	Not being employed was associated with poorer outcomes. <sup>26</sup>	Favours advantaged populations
	Treatment response	Educational level	Educational level was not significantly associated with treatment response. <sup>27</sup>	No evidence of differential impact
Mindfulness-based CBT	Relapse to depression within 60 weeks of follow-up	Educational level	There is no support for MBCT having differential effects on relapse to depression based on educational level. <sup>29</sup>	No evidence of differential impact
Mobile CBT	Severity of postpartum depression symptoms	Educational level	The effectiveness of postnatal CBT interventions was not associated with women's education. <sup>30</sup>	No evidence of differential impact

## Appendix 8. Characteristics of OA included studies

Citation; country	Study design; type of analysis	Setting and participants	Intervention	Outcome	Mean follow-up time	SES Measure	Results
Cankaya et al. 2016; <sup>32</sup>  Turkey	Prospective Cohort;	Orthopaedics and Physical Medicine and Rehabilitation departments; Knee OA; 70 patients; Mean age (SD): 67.3(8) years; 75.7% female	Total knee arthroplasty	Functional improvement	6 months	Place of residence	Rural vs. urban $P = 0.881$
						Employment status	Employed vs. unemployed $P = 0.521$
						Educational level	Illiterate vs. primary vs. high vs. university $P = 0.521$
				Quality of life	6 months	Place of residence	Rural vs. urban $P = 0.112$
						Employment status	Employed vs. unemployed $P = 0.341$
						Educational level	Illiterate vs. primary vs. high vs. university $P = 0.028$
Davis et al. 2017; <sup>33</sup>  Canada	Prospective Cohort;	Tertiary care centres; OA; 418 patients; Mean age (SD): 65.0 (10) years; 64% female	Total knee replacement	Change in frequency in engagement in life activities	12 months	Educational level	More than high school; beta = -0.81; 95% CI -2.66 to 1.04; $P = 0.4$
				Late Life Disability Index			
Dell'Isola et al. 2020; <sup>34</sup>  Sweden	Prospective Cohort;	Various care centres; Knee OA; 16,547 patients; Mean age (SD): 66.3 (9.02); 70.2% female	Better management of patients with osteoarthritis (BOA) self-management programme	Pain reduction	3 months	Educational level	Regression Coefficients= -0.12 (-0.19 to - 0.05)
					12 months		Regression Coefficients= -0.24 (-0.32 to - 0.16)
		3 months			High education (>14 years) vs.		Regression Coefficients= -0.13 (-0.23 to - 0.02)
		Various care centres, Sweden; Hip OA;					

Citation; country	Study design; type of analysis	Setting and participants	Intervention	Outcome	Mean follow-up time	SES Measure	Results
		6,762 patients; Mean age (SD): 67.1 (9.14); 70.6% female			12 months	Low education (0-14 years)	Regression Coefficients= -0.16 (-0.28 to -0.38)
Dumenci et al. 2019; <sup>35</sup> USA	RCT;	University-based Sites; Knee OA; 384 patients; Mean age (SD): 63.2 (8.0); 67% female	Knee arthroplasty	WOMAC Pain	12 months	Income	Lower income; OR = 0.33; 95% CI 0.15 to 0.715; <i>P</i> = 0.004
Fatimah et al. 2016; <sup>36</sup> Pakistan	Prospective Cohort;	Female Rheumatology Department; Knee joint OA; 124 patients; Age (range): 30 to 80 years; 100% female	Intra-articular steroid injections	WOMAC Pain WOMAC Function	3 months	SES status	*No relationship could be established between socioeconomic status and response
Johnsen et al. 2021; <sup>37</sup> Denmark	Prospective Cohort;	Orthopaedics and Physical Medicine and Rehabilitation departments; 22,588 patients; Knee and hip OA; Mean age (SD): 65.0 (9.3)	Good Life with osteoArthritis in Denmark (GLA:D) education and exercise program	Pain intensity	3 months	Educational level (ref: Primary)	Secondary: -1.1mm (-2.3 to 0.1)
							Short-term: -0.7mm (-1.7 to 0.3)
							Middle-term: -0.2mm (-1.1 to 0.7)
							Long-term: 2.0mm (0.8 to 3.1)
						Employment status (ref: Retired)	Employed/student: -2.2mm (-2.9 to -1.5)
							Unemployed: -1.6mm (-3.8 to 0.7)
							Sick leave (part/full time): -3.4mm (-4.9 to -1.9)
							Early retirement: -2.0mm (-3.9 to -0.2)
			12 months	Educational	Secondary: -0.3mm (-1.8 to 1.2)		

Citation; country	Study design; type of analysis	Setting and participants	Intervention	Outcome	Mean follow-up time	SES Measure	Results
						(ref: Primary)	Short-term: 0.8mm (-0.5 to 2.1) Middle-term: 0.9mm (-0.2 to 2.0) Long-term: 2.0mm (0.6 to 3.4)
						Employment status (ref: Retired)	Employed/student: mm -1.3 (-2.1 to -0.5) Unemployed: 2.6mm (-0.3 to 5.4) Sick leave (part/full time): -4.5mm (-6.4 to -2.6) Early retirement: -2.8mm (-5.1 to -0.6)
Jones et al. 2017; <sup>38</sup>  USA	Prospective Cohort;	Academic medical centers; 1,512 patients; Post-Traumatic OA; Age (median): 23 years; 56% male	Anterior cruciate ligament reconstruction (ACLR)	Function (IKDC scores) KOOS Symptom Scores KOOS Pain KOOS ADL KOOS Sports/recreation KOOS QoL Marx Activity Level	6 years	Educational level (12 vs 16 years)	OR=1.35 (1.11–1.64) OR=1.48 (1.21–1.81) OR=1.39 (1.14–1.70) OR= 1.57 (1.27–1.93) OR= 1.42 (1.16–1.74) OR=1.30 (1.06–1.59) OR=1.22 (1.02–1.45)
Lawford et al. 2018; <sup>39</sup>  Australia	RCT;  Moderator analysis	Community based; 148 patients; Knee OA; Mean age (SD): 60.8 (6.5); 56.1% female	Internet-delivered exercise, education, and pain coping skills training	WOMAC function subscale (difference between intervention-control) - walking pain	3 months  9 months	Educational level ( $P = 0.22$ )  Educational level ( $P = 0.58$ )	Tertiary education: mean difference = 1.87 (1.10, 2.64) No tertiary education: mean difference = 0.96 (-0.29, 2.21) Tertiary education: mean difference = 1.08 (0.18, 1.97) No tertiary education: mean difference = 0.57 (-0.97, 2.12)

Citation; country	Study design; type of analysis	Setting and participants	Intervention	Outcome	Mean follow-up time	SES Measure	Results	
					3 months	Employment status ( <i>P</i> = 0.02)	Not employed: mean difference = 0.86 (−0.13, 1.85) Employed: mean difference = 2.38 (1.52, 3.23)	
					9 months	Employment status ( <i>P</i> = 0.86)	Not employed: mean difference = 1.06 (−0.13, 2.25) Employed: mean difference = 1.20 (0.17, 2.22)	
				Physical function	3 months	Educational level ( <i>P</i> = 0.22)	Tertiary education: mean difference = 10.44 (6.41, 14.48) No tertiary education: mean difference = 5.66 (−0.88, 12.20)	
					9 months	Educational level ( <i>P</i> = 0.25)	Tertiary education: mean difference = 7.75 (3.86, 11.64) No tertiary education: mean difference = 3.25 (−3.46, 9.96)	
					3 months	Employment status ( <i>P</i> = 0.14)	Not employed: mean difference = 6.88 (1.74, 12.01) Employed: mean difference = 11.94 (7.48, 16.41)	
					9 months	Employment status ( <i>P</i> = 0.81)	Not employed: mean difference = 6.72 (1.50, 11.93) Employed: mean difference = 7.57 (3.05, 12.08)	
Neuprez et al. 2020; <sup>40</sup>	Prospective Cohort;	University Hospital of Liege; 626 patients; Late stage knee and hip OA; Median age (IQR): 66 (59-73)	Total joint replacement		WOMAC total (Pain, stiffness and physical function)	5 years	Educational level	beta=7.33 (1.99 to 12.38), <i>P</i> <0.01
Pihl et al. 2020; <sup>41</sup>	Prospective Cohort;	Orthopaedics and Physical Medicine and Rehabilitation departments; Knee	Good Life with osteoArthritis in Denmark (GLA:D) education and		Change in pain (VAS) Change in QoL (EQ-5D)	8 weeks	Educational level 5-point scale ranging from primary school	*No difference observed (forest plot) in pain scores, or QoL by educational level

Citation; country	Study design; type of analysis	Setting and participants	Intervention	Outcome	Mean follow-up time	SES Measure	Results
		and hip OA; 35,496 patients total; Age	exercise program			to long-term education.	
Sveikata et al. 2017; <sup>42</sup> Lithuania	Prospective Cohort;	Republican Vilnius University Hospital; 294 patients; Knee OA; Mean age (SD): 70.86 (8.28)	Total Knee Arthroplasty	Pain	1 year	Educational level	There was no statistically significant difference ( $P = 0.168$ ) in pain scores between participants with low and high levels of education 1 years post TKA.
			Stiffness	There was no statistically significant difference ( $P = 0.59$ ) in stiffness scores between participants with low and high levels of education 1 years post TKA.			
			Function	There was no statistically significant difference ( $P = 0.225$ ) in function scores between participants with low and high levels of education 1 years post TKA.			
			Mental health (SF-12)	There was no statistically significant difference ( $P = 0.461$ ) in mental health between participants with low and high levels of education 1 years post TKA.			
			Physical health (SF-12)	There was no statistically significant difference ( $P = 0.594$ ) in physical health between participants with low and high levels of education 1 years post TKA.			
Unevik et al. 2020; <sup>43</sup>	Prospective Cohort;	Clinical and/or radiographic		Difficulties with walking	3 months		Compulsory only: OR=1.12 (1.03–1.20); $P > 0.0$ )

Citation; country	Study design; type of analysis	Setting and participants	Intervention	Outcome	Mean follow-up time	SES Measure	Results
Sweden		departments; 22,741 patients; OA; Mean age (SD): 66.3 (9)	BOA self-management programme			Educational level (ref: university)	Upper secondary: OR=1.02 (0.95–1.10)
					1 year		Compulsory only: OR=1.16 (1.03–1.20); <i>P</i> > 0.05
							Upper secondary: OR=1.06 (0.99–1.14)
					3 months	Birth place (Domestic born)	Foreign born: OR=1.14 (1.02–1.27); <i>P</i> > 0.05
					1 year		Foreign born: OR=1.16 (1.04–1.30); <i>P</i> > 0.05
					Suffers from impairment in any joint that they are willing to undergo surgery	3 months	Educational level (ref: university)
						Upper secondary: OR=1.20 (1.07–1.35); <i>P</i> > 0.05	
				1 year		Compulsory only: OR=1.23 (1.12–1.35); <i>P</i> > 0.05	
						Upper secondary: OR=1.12 (1.03–1.23); <i>P</i> > 0.05	
				3 months		Birth place (Domestic born)	Foreign born: OR=1.09 (0.93–1.27)
				1 year			Foreign born: OR=1.07 (0.94–1.22)
				EQ-5D-3L scores	3 months	Educational level	Compulsory only: Mean=0.70 (0.70–0.70); <i>P</i> > 0.05
							Upper secondary: Mean=0.71 (0.71–0.71); <i>P</i> > 0.05
							University: Mean= 0.72 (0.71–0.72)
1 year	Compulsory only: Mean=0.67 (0.67–0.67); <i>P</i> > 0.05						
	Upper secondary: Mean=0.67 (0.67–0.68); <i>P</i> > 0.05						



Citation; country	Study design; type of analysis	Setting and participants	Intervention	Outcome	Mean follow-up time	SES Measure	Results
							University: Mean= 0.68 (0.68–0.69); <i>P</i> > 0.05
					3 months	Birth place	Foreign born: Mean=0.69 (0.69–0.70); <i>P</i> > 0.05
					1 year		Domestic born: Mean= 0.71 (0.71–0.71); <i>P</i> > 0.05
							Foreign born: Mean= 0.66 (0.65–0.66)
							Domestic born: Mean=0.68 (0.68–0.68); <i>P</i> > 0.05
				NRS Pain Score	3 months	Educational level	Compulsory only: Mean=4.0 (4.0–4.1); <i>P</i> > 0.05
							Upper secondary: Mean=4.0 (3.9–4.0); <i>P</i> > 0.05
							University: Mean= 3.8 (3.8–3.8); <i>P</i> > 0.05
					1 year		Compulsory only: Mean=4.5 (4.4–4.5); <i>P</i> > 0.05
							Upper secondary: Mean=4.3 (4.3–4.4); <i>P</i> > 0.05
							University: Mean=4.1 (4.1–4.2); <i>P</i> > 0.05
					3 months	Birth place	Foreign born: Mean=4.0 (3.9–4.1); <i>P</i> > 0.05
					1 year		Domestic born: Mean= 3.9 (3.9–4.0); <i>P</i> > 0.05
							Foreign born: Mean=4.5 (4.4–4.6); <i>P</i> > 0.05
							Domestic born: Mean=4.3 (4.3–4.3); <i>P</i> > 0.05

## Appendix 9. Association of SES and clinical outcomes for OA

Type of intervention	Intervention	Outcome	SES parameter	Overall summary	Does the intervention favour advantaged or disadvantaged populations
Education and self-management	Good Life with osteoArthritis in Denmark (GLA:D) education and exercise program	Pain	Educational level Employment status	Improvements in pain after supervised exercise therapy and education in patients with knee and hip OA did not substantially differ by educational level or employment status at 8 weeks, <sup>41</sup> 3 months and 12 months. <sup>37</sup>	No evidence of differential impact
		Quality of Life (QoL)	Educational level	Improvements in QoL after supervised exercise therapy and education in patients with knee and hip OA did not substantially differ by educational level at 8 weeks. <sup>41</sup>	No evidence of differential impact
	Better management of patients with osteoarthritis (BOA) self-management programme	Pain	Educational level	Higher educational levels is associated with decreased pain at 3 and 12 months follow-up. <sup>34</sup>	Favours advantaged populations
			Birth place	At 3 and 12 months, pain scores were lower for domestic born participants. <sup>43</sup>	Favours advantaged populations
		Walking difficulty	Educational level	At 3 and 12 months, those with lower levels of education were more likely than those with university education to report difficulties with walking. <sup>43</sup>	Favours advantaged populations
			Birth place	At 3 and 12 months, foreign born participants were more likely than domestic born participants to report difficulties with walking. <sup>43</sup>	Favours advantaged populations

Type of intervention	Intervention	Outcome	SES parameter	Overall summary	Does the intervention favour advantaged or disadvantaged populations
		Joint impairment	Educational level	At 3 and 12 months, those with lower levels of education were more likely than those with university education to suffer enough impairment to consider surgery. <sup>43</sup>	Favours advantaged populations
			Birth place	At 3 and 12 months, foreign born participants were more likely than domestic born participants to suffer enough impairment to consider surgery. <sup>43</sup>	Favours advantaged populations
		QoL	Educational level	At 3 and 12 months, EQ-5D-3L scores were higher for those with higher levels of education. <sup>43</sup>	Favours advantaged populations
			Birth place	At 3 and 12 months, EQ-5D-3L scores were higher for domestic born participants. <sup>43</sup>	Favours advantaged populations
	Internet-delivered exercise, education, and pain coping skills training	Pain	Educational level	There was no statistically significant moderation effect of education level on change in walking pain scores at 3 months and 9 months. <sup>39</sup>	No evidence of differential impact
			Employment status	A statistically significant moderation effect of employment was found at 3 months follow up. Among those employed, the intervention group had greater reductions in pain than those in the control group at 3 months. <sup>39</sup>  Among unemployed participants, the difference between the intervention and control group in the reduction in pain at 3 months was smaller. However, there was no significant moderation effect at 9 months. <sup>39</sup>	Favours advantaged populations - short term  No evidence of differential impact – long term
		Function	Educational level	There was no statistically significant moderation effect of education level on	No evidence of differential impact

Type of intervention	Intervention	Outcome	SES parameter	Overall summary	Does the intervention favour advantaged or disadvantaged populations
				change in physical function scores at 3 and 9 months. <sup>39</sup>	
			Employment status	There was no statistically significant moderation effect of employment on change in physical function scores at 3 and 9 months. <sup>39</sup>	No evidence of differential impact
Pharmacological	Intra-articular steroid injections	Pain	Not reported	No relationship could be established between socioeconomic status and improvement in pain or functional outcomes at 3 months. <sup>36</sup>	No evidence of differential impact
		Function			
Surgical	Total knee arthroplasty	Function	Place of residence	There was no relationship between KOOS-PS score changes and place of residence (rural or city) at 6 months. <sup>32</sup>	No evidence of differential impact
			Employment status	There was no relationship between KOOS-PS score changes and employment status at 6 months. <sup>32</sup>	No evidence of differential impact
			Educational level	The functional status of patients with a higher educational level improved statistically significantly more than that of patients with lower educational levels at 6 months. <sup>32</sup>  There was no statistically significant difference in function scores between participants with low and high levels of education 1 years post TKA. <sup>42</sup>	Favours advantaged populations in the short term  No evidence of differential impact in the long-term
		QoL	Place of residence	There was no relationship between SF-36 physical component score changes and place of residence (rural or city) at 6 months. <sup>32</sup>	No evidence of differential impact
			Employment status	There was no relationship between SF-36 physical component score changes and employment status at 6 months. <sup>32</sup>	No evidence of differential impact

Type of intervention	Intervention	Outcome	SES parameter	Overall summary	Does the intervention favour advantaged or disadvantaged populations
			Educational level	The QoL status of the patients with a higher educational level improved statistically significantly more than that of patients with a lower educational level at 6 months. <sup>32</sup>	Favours advantaged populations
		Change in frequency in engagement in life activities	Educational level	At 12 months, higher levels of education is not significantly associated with changes in frequency in engagement in life activities. <sup>33</sup>	No evidence of differential impact
		Pain 2	Income	Lower income was associated with an increased likelihood of being in the poor outcomes class for WOMAC Pain scores. <sup>35</sup>	Favours advantaged populations
			Educational level	There was no statistically significant difference in pain scores between participants with low and high levels of education 1 years post TKA. <sup>42</sup>	No evidence of differential impact
		WOMAC Total (pain, stiffness and physical function)	Educational level	Higher levels of education was significantly associated with an improvement in pain, stiffness and physical function, five years after knee arthroplasty.	Favours advantaged populations
		Stiffness	Educational level	There was no statistically significant difference in stiffness scores between participants with low and high levels of education 1 years post TKA. <sup>42</sup>	No evidence of differential impact
		Mental health	Educational level	There was no statistically significant difference in mental health between participants with low and high levels of education 1 years post TKA. <sup>42</sup>	No evidence of differential impact
		Physical health	Educational level	There was no statistically significant difference in physical health between participants with low and high levels of education 1 years post TKA. <sup>42</sup>	No evidence of differential impact
		Function	Educational level		

Type of intervention	Intervention	Outcome	SES parameter	Overall summary	Does the intervention favour advantaged or disadvantaged populations
	Anterior cruciate ligament reconstruction	Symptom Scores Pain ADL Sports/recreation QoL Marx Activity Level		Higher levels of education was associated with better KOOS function, symptom scores, pain, ADL, sports/recreation, quality of life scores and Marx activity levels scores at 2 and 6 years. <sup>38</sup>	Favours advantaged populations

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