**FACE TO FACE OR DIGITALLY? A COMPARISON OF FIRST-LINE INTERVENTIONS DELIVERY FOR PEOPLE WITH HIP OR KNEE OSTEOARTHRITIS (NCT04836988)**

**Background**

Osteoarthritis (OA) is among the leading causes of disability worldwide and due to its raising prevalence, the identification of appropriate care and care delivery modalities is a priority for the health care systems [1, 2]. Exercise and education constitute the first-line intervention for people with knee and hip OA and have been shown to be effective regardless of symptoms and disease severity [3, 4]. Unfortunately, there is a discrepancy between recommended treatment and what patients receive. Less than 40% of people with OA seeking care seem to receive recommended first line management internationally [5]. To implement those guidelines, the Better Management of Patients with OsteoArthritis (BOA), a face-to-face concept including education and an option to exercise, has been developed and are offered at primary care clinics in Sweden since 2008 [6]. However, traditional face to face interventions present barriers, such as limited access and lack of flexibility, which may limit the patients' adherence with the interventions [7]. Digital delivery of the management program may be one way of overcoming such barriers [8, 9]. In light of the current Covid-19 pandemic, digitally delivered treatments may gain even further awareness as a feasible treatment option. Both delivery methods have been reported to reduce OA symptoms in patients with hip and/or knee OA [10, 11], but little is known whether the results of digital interventions are comparable with traditional face-to-face rehabilitation programs.

**Aim**

To compare the outcomes (average treatment effect) of two different modalities of first-line treatment delivery (face-to-face vs. digitally) after 3 months of program participation.

**Hypothesis**

There will be no difference in the average treatment effect of the main outcome between the two delivery methods.

**Methods**

This is a retrospective observational registry-based study comparing outcomes of a face-to-face and a digital OA management program.

The study was approved by the regional ethics committee of the Swedish Ethical Review Authority (Dnr 2019-06288, decision date 2020-02-11 and is pre-registered at ClinicalTrials.gov (NCT04836988). Participants were informed that data generated from the register may be used for research purposes at registration (BOA) or provided digital informed consent for the same purpose at registration (JA). The study adheres to the STROBE guidelines for observational studies.

**Data sources**

BOA (face-to-face): The BOA registry was started in 2008 and currently includes more than 100,000 individuals with OA who have registered for an evidence-based self-management program, including education, exercise and weigh management if needed at a primary care clinic.

Joint Academy (digital program): The digital self-management program started in 2014 and was originally inspired by the Swedish evidence based face-to-face BOA self-management treatment program [9]. The associated registry currently includes more than 30 000 individuals with OA. The intervention consists of a digital OA self-management program (Joint Academy®) [11, 12] comprising text lectures on OA with accompanying quizzes, physical activity and self-management in OA. The participant also receives exercises aiming at improving strength and neuromuscular control of various levels based on each individuals' progression in the program.

**Data extractions and linkages**

All data extracted from the digital self-management program (JA) and BOA registries. Criteria for inclusion in the data extraction are:

- Clinical diagnosis of OA, with knee or hip OA as their index (most symptomatic) joint
- Enrolled in either of the two programs between April 1, 2018 and December 31, 2019
- Provided 3-month follow-up data for the main outcome on or before March 31, 2020
- Program adherence of 80% or higher.

The data from the two registers will be linked using personal identity numbers to identify individuals that may have participated in both programs during the specific time window. Patients that participated in both programs will be excluded from further analysis.

The JA participants will be matched 1:1 to participants in the BOA register using the propensity scoring approach described below.

**Main exposures and outcomes**

*Exposures*

Three months of first-line OA treatment delivered either face-to-face or digitally with a program adherence of 80% or higher. The choice of this cut-off was based on recommendations in the Swedish Guidelines for management of knee and hip osteoarthritis by the National Board of

Health and Welfare. Adherence defined as ≥ 80% completed education videos, exercises and questionnaires offered in the digital program and participation in two out of three educational lessons and at least 10 of the 12 supervised group exercise sessions offered in the BOA program.

*Main outcome*
Main outcome will be self-reported change in pain on the NRS-scale between baseline and three months follow-up. The NRS comprises an 11-point scale where 0 indicates no pain and 10 indicates the worst possible pain [13] (Table 1).

*Secondary outcomes*
Secondary outcomes will be change in self-reported walking difficulties (dichotomous reply, yes/no), willingness for joint surgery (dichotomous reply, yes/no) and health-related quality of life, assessed with the EuroQol – 5 dimension descriptive system (EQ-5D-3L)[14] between baseline and three months follow-up (Table 1).

**Sample size**
As this study aims at estimating treatment effects, the important issue to assess is not power (related to a hypothesis), but precision – i.e. the width of the confidence interval. To illustrate this, consider the example of an RCT to compare mean joint pain after exercise intervention for OA, between persons that receive the treatment in different modalities. The minimum clinically important difference is typically considered one unit on a 0-10 NRS scale. To obtain a 95% confidence interval for the between-group difference with a width of at most 0.5 units (i.e. very precise) in a sample with a typical standard deviation of 1.5, with 99% probability, we will need ~630 patients in total. Considering our cohort size of >2000 persons who underwent the intervention, we will be able to estimate between-group differences also in subgroups, by sex, BMI, etc.

**Statistical analysis**
In this study we will use observational data to emulate an equivalence trial comparing the effect on joint pain of a digitally delivered first-line intervention and of an in-person delivered first line intervention for people with OA of the hip or knee.

*Main outcome analysis*
The main outcome will be analyzed using a propensity score matching approach [17]. We will estimate the propensity score using a logistic regression model, in which we will regress the treatment status on the observed baseline characteristics of the participants. The characteristics to include in the propensity score will be selected using the disjunctive cause

criteria [16], including factors in the analysis identified as causes of treatment allocation(exposure) and/or the pain change (outcome) (Table 2). We will use nearest neighbor matching to select controls (BOA participants) whose propensity score is closest to that of the treated subject. Furthermore, we will use an optimal matching strategy to minimize the total within-pair difference of the propensity score. Within-pair differences in main outcome will be analysed using a paired t-test. Finally, we will adjust the analysis for baseline pain using linear regression in order to increase the precision of the estimates and minimize the regression to the mean effect [17, 18].

*Assessing propensity score balance*
Balance of baseline variables between treated and control subjects in the matched study population will be assessed using standardized difference [19].

*Equivalence bounds*
In order to establish equivalence between the interventions the pain change after the intervention should differ of less than 1-point on a 0-10 NRS pain scale. This cut off was selected based on previous work identifying 1-point change as the MCID in people with OA [20].

*Sensitivity analysis*
In order to evaluate and contrast the influence of choice of analysis method on study results, linear regression analysis based on the same adjustment set used for the propensity score, representing the causal effect studied, will be applied and both adjusted and unadjusted estimates will be presented, discussed and contrasted against results from the propensity score matched analysis.

*Missing data*
Data on study drop-outs will be summarized by treatment group using frequency counts to assess any imbalance. If the fraction of missing study data is non-ignorable (i.e. 5% or more with missing data in either outcome and/or any adjustment variable), then multiple imputation techniques, such as MICE [21] will be applied to the analysis of the primary outcome. The analysis method will also be altered to a linear regression approach, as opposed to that of propensity score matching, in order to facilitate incorporation of missing data methods in the analysis procedure. However, when the fraction of missing data is small (i.e. 5% or more with missing data in either outcome and/or any adjustment variable), the primary analysis will be performed using a complete case approach.

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**Table 1.** Variables in BOA and Joint Academy registers

| Variable | Role | Used for matching |
|---|---|---|
| Age | Confounder | Yes |
| Sex | Confounder | yes |
| Weight | Confounder | yes |
| Height | Confounder | yes |
| Education level | Confounder | yes |
| Working status | Confounder | yes |
| Most affected Joint | Confounder | yes |
| Other affected joints | Confounder | Yes (used as number of joints) |
| On Waiting list for surgery | Confounder | No (very rare) |
| Wish for surgery | Secondary outcome | yes |
| Physical activity (training) | Confounder | yes |
| Physical activity (every-day exercise) | Confounder | yes |
| Overall health | Confounder | yes |
| Walking difficulties | Secondary outcome | yes |
| Pain | Outcome | Yes (baseline pain) |
| EQ-5D | Outcome | |
| Fear of movement | Confounder | yes |
| Compliance with the intervention | Inclusion criteria | No |
| Previous surgery index joint | Confounder | No |