Supplementary data

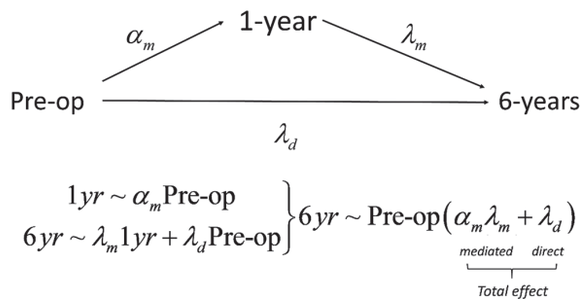

Figure 2. Mediation analysis of the effect of the preoperative PROM on 6-year PROM values where the 1-year follow-up measurement acts like a mediator. The regression coefficients λ_d, α_m, λ_m and λ_d denote the change in outcome when the continuous regressors change with one unit or absolute differences in outcome between the reference and the other levels of a categorical variable.

APPENDIX

1. Missing PROMs data

There are two main causes of missing PROMs data. The foremost cause of missingness is the sequential introduction of the PROMs programme. At the inception of the programme only a handful of hospitals participated. More hospitals gradually joined and the programme reached full coverage by 2008. Therefore, most patients with missing PROMs data were never invited to respond to the questionnaire. It has not been recorded whether a patient was invited or not to respond.

While missing data is generally defined as "values that are not available and that would be meaningful for analysis if they were observed" we should delimitate this kind of missing data from non-respondents. We cannot fully assume that the PROM values in a data set are missing completely at random (MCAR), but missing at random (MAR) as missingness can be fully accounted for by the date on introduction of the hospital in the PROMs programme, a variable where there is complete information. Presenting this information greatly exceeds the scope of the present paper.

Although the mechanism for missingness for these data appoints is MAR we do not expect biased results.

Preoperative PROMs

Respondents and non-respondents had similar sex distribution, same age and diagnosis distribution (Table 1).

1-year follow-up

Responders and non-responders had similar sex distribution, same age and diagnosis distribution (Table 2).

Table 1. Differences between patients with and without preoperative PROM data

Missing:	No n = 21,051	Yes n = 34,506
Diagnosis, n (%)		
Primary osteoarthritis	19,508 (92.7)	31,384 (91.0)
Inflammatory joint disease	515 (2.4)	908 (2.6)
Sequelae childhood hip disease	497 (2.4)	873 (2.5)
Femoral head necrosis	522 (2.5)	1222 (3.5)
Other secondary osteoarthritis	9 (0.0)	118 (0.3)
Age, mean (sd)	67.9 (10.8)	68.1 (11.1)
Sex: Female, n (%)	12,084 (57.4)	19,885 (57.6)

Table 2. Differences between patients with and without 1-year PROM data

Missing:	No n = 19,230	Yes n = 1,812
Diagnosis, n (%)		
Primary osteoarthritis	17860 (92.9)	1640 (90.5)
Inflammatory joint disease	455 (2.4)	60 (3.3)
Sequelae childhood hip disease	440 (2.3)	57 (3.1)
Femoral head necrosis	467 (2.4)	54 (3.0)
Other secondary osteoarthritis	8 (0.0)	1 (0.1)
Age, mean (sd)	68.0 (10.6)	67.0 (12.6)
Sex: Female, n (%)	11069 (57.6)	1010 (55.7)

Table 3. Differences between patients with and without 6-year PROMs data

Missing:	No n = 15,755	Yes n = 3,475
Diagnosis, n (%)		
Primary osteoarthritis	14,680 (93.2)	3,180 (91.5)
Inflammatory joint disease	356 (2.3)	99 (2.8)
Sequelae childhood hip disease	384 (2.4)	56 (1.6)
Femoral head necrosis	328 (2.1)	139 (4.0)
Other secondary osteoarthritis	7 (0.0)	1 (0.0)
Age, mean (sd)	67.1 (10.2)	72.2 (11.3)
Sex: Female, n (%)	9,123 (57.9)	1,946 (56.0)

6-year follow-up

Respondents and non-respondents had similar sex and diagnosis distribution (Table 3). Patients with no 6 year follow-up were 5 years older at the time of the operation than patients with existing data.

Table 4. Reoperated within 7 years

	No n = 21,051	Yes n = 716
Diagnosis, n (%)		
Primary osteoarthritis	19,508 (92.7)	632 (88.3)
Inflammatory joint disease	515 (2.4)	30 (4.2)
Sequelae childhood hip disease	497 (2.4)	21 (2.9)
Femoral head necrosis	522 (2.5)	31 (4.3)
Other secondary osteoarthritis	9 (0.0)	2 (0.0)
Age [a]	67.9 (10.8)	72.2 (11.3)
Sex: Female, n (%)	12,084 (57.4)	1,946 (56.0)
EQ-5D index preoperatively [a]	0.40 (0.32)	0.38 (0.32)
EQ-5D index 1 year [a]	0.78 (0.24)	0.66 (0.32)
Pain VAS preoperatively [a]	61.5 (16.9)	61.3 (17.2)
Pain VAS 1 year [a]	14.1 (17.8)	25.0 (25.3)
EQ VAS preoperatively [a]	52.9 (22.3)	52.1 (22.3)
EQ VAS 1 year [a]	75.6 (20.1)	67.7 (24.2)
Charnley class, n (%) preop.		
A	9,085 (43.2)	290 (40.6)
B	2,938 (14.0)	83 (11.6)
C	9,019 (42.9)	341 (47.8)
Charnley class, n (%) 1 year		
A	8,456 (44.0)	221 (38.4)
B	2,213 (11.5)	58 (10.1)
C	8,569 (44.5)	297 (51.6)

[a] Values are mean (standard deviation)

2. Reoperated patients

Patients are excluded from the routine PROMs follow-up program if they undergo a re-operation. We compared those re-operated within 7 years to patients without a registered reoperation. There were differences in age, diagnosis at surgery and Charnely class distribution but not preoperative PROMs. Those who were not reoperated before their 1-year follow reported worse EQ-5D, EQ VAS, hip pain VAS and less satisfaction (Table 4).

3. Sensitivity analysis for the mediation analysis

Ignorability

Mediation analysis assumes that the ancestor is ignorable given the covariates that chronologically precede them and that the mediator is assumed to be ignorable given the observed value of the ancestor variable and covariates that chronologically precedes them.

Mediation is often tested with linear structural equation modelling which is based on the following system of linear equations:

i) $6yr = \gamma_1 + \lambda_d \text{Preop} + \varepsilon_{i1}$

ii) $1yr = \gamma_2 + \alpha_m \text{Preop} + \varepsilon_{i2}$

iii) $6yr = \gamma_3 + \lambda_m 1yr + \lambda_d \text{Preop} + \varepsilon_{i3}$

where γ_1, γ_2 and γ_3 are the intercepts, the value of the outcome variable when all continuous regressors are zero and all categorical regressors have the reference value. The regression coefficients λ_d, α_m, λ_m and λ_d denote the change in outcome when the continuous regressors change with one unit or absolute differences between in outcome between the reference and the other levels of a categorical variable. The residuals ε_{i1}, ε_{i2} and ε_{i3} represents the difference between the observed and predicted follow-up values.

Often the ignorability assumption is too strong in applied settings, such as in the present case. Unmeasured covariates can confound the relationship between the mediator and the outcome. Thus sensitivity analysis is required.

The ignobility assumption assumes that the residuals from ii) and iii) have correlation zero:

$$\rho = Corr(\varepsilon_{i2}, \varepsilon_{i3}) = 0$$

The EQ-5D index

Figure 1 shows the results of the sensitivity analysis for the EQ-5D index based on residual correlation. The analysis suggests that conclusion about the sign of the estimated mediated effect would be valid unless the sensitivity parameter ρ

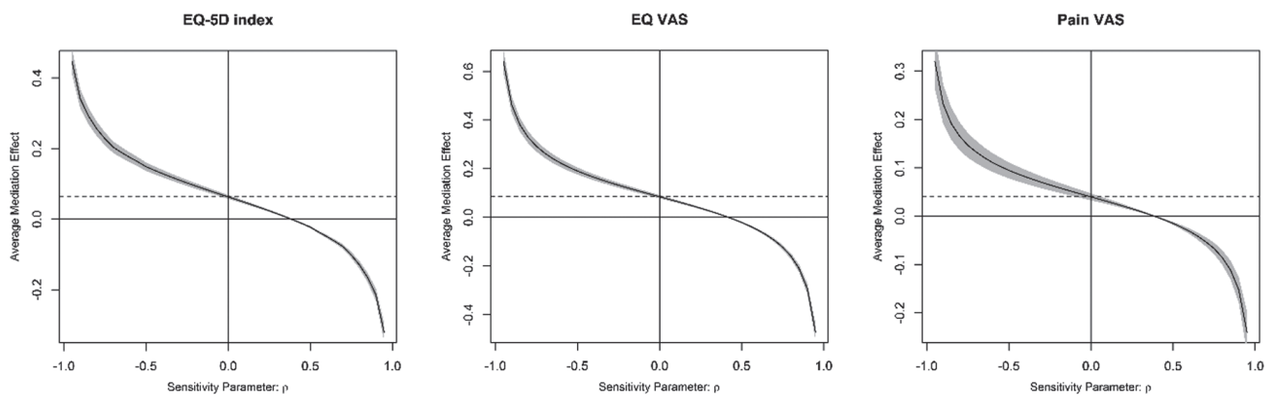

Figure 1. Sensitivity analysis for the EQ-5D index, EQ VAS and Pain VAS. The horizontal line represents the estimated indirect effect. The solid line indicates the value that indirect would take for differing values of the sensitivity parameter ρ.

>0.45. This indicates that the results are acceptable even if there are large departures from the ignorability assumption for the mediator.

The EQ VAS

Figure 1 shows the results of the sensitivity analysis for the EQ VAS based on residual correlation. The analysis suggests that conclusion about the sign of the estimated mediated effect would be valid unless the sensitivity parameter ρ >0.45. This indicates that the results are acceptable even if there are large departures from the ignorability assumption for the mediator.

The Pain VAS

Figure 1 shows the results of the sensitivity analysis for the EQ VAS based on residual correlation. The analysis suggests that conclusion about the sign of the estimated mediated effect would be valid unless the sensitivity parameter ρ >0.40. This indicates that the results are acceptable even if there are large departures from the ignorability assumption for the mediator.

Confounding variables

Unmeasured confounding variables might lead to an overestimation of the indirect effect and the mediation (Judd & Kenny, 2010). The omission of these variables might seriously distort the dependence of interest (Cox & Wermuth, 2004). We have controlled for two important background variables, age and sex; however, there are likely other confounders we should have considered. The sensitivity analysis concluded that the results are robust against the violation of the assumption of ignorability. There are no statistical remedies for the violation of this assumption. In addition to sensitivity analysis theoretical and empirical arguments are needed for the plausibility of the mediation process. We postulate that the causal assumption, of greatest importance, has not been violated. Statistically we are unable to prove the existence of causality, however the strength and validity of our inference is inherent in the validity of the design (Pearl 2010). Here, we subscribe to a more mechanistic view of causality (Aalen and Frigessi 2007, Aalen et al. 2012). This mechanistic view arises from the Granger-Schweder definition of causality that states that the prediction of the outcome based on all predictors should be better than the prediction with the ancestor omitted. We observed that the ancestor variable, the pre-operative PROMs, explained a large portion of the variability of the mediator, the 1-year PROMs. The mediator explained the majority of the variability of the 6-year PROM outcome. This, along with the chronological order of these three measurement points suggests that we can assume a possible causal relationship between the ancestor, mediator and outcome.

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