The Effects of Mental Health on Knee Arthroplasty Outcomes

Statistical Analysis Plan

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Document Version History

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1.0	12/03/2025	N/A

Contents

1. Executive summary

Background

Patients with Mental Health (MH) disorders (MHD) are at higher risk of dissatisfaction, complications and chronic pain following knee arthroplasty (TKR). Chronic pain following knee arthroplasty alone costs the NHS £33,000,000 per Anum in direct care costs. Despite MH disorders being common problem, they are often underrepresented and overlooked in perioperative guidance.

Extensive literature has identified MHD as a key risk factor for poor outcome, the next translational step, patient level prediction of individuals at high risk has proven to be difficult, predominantly due to lack of granular MH data. Little research has considered the importance of specific diagnosis, severity and chronicity of the MHD.

Aim

Our overall aim is to explore mental health related risk factors which may place patients at risk of poor outcomes following knee replacement surgery.

Methodology

To achieve our aim, we will link and subsequently analyse patient data from 3 routine NHS data sources.

1.Discovery Data Service (DDS) - Holds linked patient data combining GP, Social service and Mental health records. It covers the population of North-East London (approximately 2 million people).

2.National Joint Registry (NJR) – A database for patient undergoing arthroplasty in the UK. Details include arthritis, surgery, and hospital data. It also has a linked Patient Reported Outcomes Score (PROMS) database, controlled by NHS England. Patients answer questionnaires about their general health and knee function before surgery and at approximately 6 months post operatively.

3.Hospital Episode Statistics (HES) - Is linked to the NJR. Provides details about patients' engagement with secondary health providers, and further inpatient data.

Outcomes

Knee Replacement Outcomes include

Patient knee function – As recorded using the Oxford Knee score at 6 months
Surgical complication – Any re-admission to hospital during the first 12 weeks after surgery Chronic pain – As recorded in the EQ5D Patient questionnaire at 6 months

Primary Objective

1. To estimate the prevalence and distribution of different mental health disorders diagnoses, in patients before they undertake a knee replacement within the NHS in Northeast London from January 2014 to January 2024.

2. Estimate the association between different mental health disorder diagnoses and knee replacement outcomes within the NHS in Northeast London from January 2014 to January 2024.

Secondary Objective

3. To estimate the level of association between severity of disease (for depression, anxiety, mixed anxiety and depression only), and timing of diagnosis on the three outcomes of interest following knee replacements within the NHS in Northeast London from January 2014 to January 2024.

Analysis Plan

Initial analysis will describe the distribution and prevalence of mental health disorders diagnosis at the time of surgery, for patients undergoing knee arthroplasty.

Following this regression analysis will be conducted to investigate the effects of mental health disorder diagnosis, severity and timing on the outcomes of interest following knee replacement. Outcomes will be measured at 6 months considering baseline score and other health confounder variables.

2. General

2.1 SAP scope

The scope of this SAP is to state the variables of interest from the 3 data sources, define the populations we intend analyse and describe the methods that will be employed to analyse the data.

2.2 Glossary

DDS – Discovery Data Service
NJR – National Joint registry
TKR – Total Knee Replacement
MHD – Mental Health Disorders
MH – Mental Health
OKS – Oxford Knee Score
EQ5D – EuroQol 5 Dimension
EQVAS – EuroQol Visual Analogue Scale

3. Summary of project and methods of data collection

This project aims to explore the association between mental health disorders and poor outcomes following knee replacement.

To achieve this, we will conduct a retrospective cohort study of routinely collected electronic NHS healthcare data. We will link data from primary care (GP and community), secondary care (hospital), and arthritis / arthroplasty specific data (held by the National Joint Registry). All data will be taken from databases that record data as part of standard practice in the UK. A description of each database to be used is in Table 1.

Table1 – Database description

Discovery Data Service (DDS)	A clinical partnership programme in London and recently expanding across the UK. The data service combines all health care monitoring systems in the NE London area, including GP, Social service and Mental health records. It covers approximately 6 million people. It has a data completeness of 95%, and contains demographics, diagnosis codes, health resource use, prescribing data and investigation results. The primary data vocabulary is snowmed CT codes.

National Joint Registry (NJR)	The NJR collects data on all joint replacement surgeries, surgeons, and implants in the United Kingdom. The NJR has previously been linked to the national Patient Reported Outcome Measure where patients answer questions about their joint function and general health, pre-operatively
	and at 6 months post operatively. It has already been proven to be representative of the UK population. It records 2 general wellbeing scores EuroQoL 5D (EQ-5D), EQ visual analogue scale (EQ VAS), in which there are questions also relating to patients Mental Health. It also containing the Oxford Knee Score (OKS), a specific score about knee joint function.
Hospital Episode Statistics (HES)	A nation-wide 'data product' providing robust details about a patient's engagement with any hospital in the United Kingdom. It contains information in 4 major categories – inpatient admissions, outpatient appointments, accident and emergency attendances, critical care admissions. The data controlled is NHS England, and the data is used to guide NHS leaders, government and other national bodies / regulators.

After gaining ethical approval, data access and completing the required data protection impact assessment, we will then perform an encrypted linkage process. In this process each patient is given a pseudonymised patient number (study ID), via an online encryption software. We will then match the study IDs across the 3 databases to collate a database with granular patient level detail about patients undergoing knee replacement in Northeast London and their respective mental health disorders.

The outcomes of interest are poor patient knee function, complication rate, and the development of 'Chronic Pain'. Described in full in section 6.

Main Exposures of interest include mental health diagnosis, the severity of disease, and the timing of disease diagnosis. Described in full in section 6.

Details of the data extracted about each patient is included in full in the extraction plan. This has been constructed previously and is published online. Key variables are included in section 6.1

4. Data selection for study

Data will be selected for the analysis in the SAP based on the following criteria.

1. Patients in the Northeast London area as determined by their GP location.
2. Patients with a TKR in any NE London NHS hospital from January 2014 to January 2024. These include Gateway Surgical Centre, King George Hospital, North Middlesex Hospital, Royal Free Hospital, Whips Cross University Hospital, Homerton Hospital, Royal London Hospital, Wittington Hospital, University College London Hospital, Barnet Hospital, Chase Farm Hospital, Queens Hospital, Basildon Hospital, Broomfield Hospital and Braintree Hospital.
3. Patients with linked data from the NJR and DDS.

Patients will be excluded if:

1. They had revision knee arthroplasty, partial or 'uni' knee replacements,
2. knee replacements performed privately
3. Data not linked across more than 1 database.

5. Study details

5.1 Study Objectives

The overall aim of the study:

To explore the relationship between mental health disorders and poor function, surgical complications and chronic pain following knee replacements in the NHS.

5.2 Analysis objectives

5.2.1 Primary objectives

The primary objectives for the statistical analysis are

1. To estimate the prevalence and distribution of different mental health disorders diagnoses, in patients before they undertake a knee replacement within the NHS in Northeast London from January 2014 to January 2024.

2. Estimate the association between different mental health disorder diagnoses and (i) patient knee function, (ii) surgical complication rates, and (iii) chronic pain, following knee replacements within the NHS in Northeast London from January 2014 to January 2024. Patient knee function will be determined by the oxford knee score (described section 6.1), Complication rate by re-admission to hospital and chronic pain by EQ5D Question response. (described section 6.1)

5.2.2 Secondary objectives

The secondary objectives for the statistical analysis are:

To estimate the level of association between severity of disease (for depression, anxiety and mixed anxiety and depression only), and timing of diagnosis (relative to surgery), on patient knee function, surgical complication rates, and chronic pain, following knee replacements within the NHS in Northeast London from January 2014 to January 2024.

5.3 Study design

Design
Retrospective observational cohort study using electronic health records.

Setting
Patients in the Northeast London area (as determined by their GP) and receiving a TKR in any NE London NHS hospital (previously listed) from January 2014 to January 2024.

Target population
Patients undertaking a knee replacement in the NHS.

Nature of follow-up
6 months post operation, when patients are requested to answer a post operative questionnaire as part of standard follow up care. The outcomes of interest will be assessed at this point.

Endpoints
Primary endpoints are

1. Oxford knee score reported by the patient at 6 months post operation.
2. Any attendance to AE or admission to hospital in the 6 months immediately following Knee replacement
3. EQ5D questionnaire reported by the patient at 6 months post operation.

Sample size justification
The NJR publishes aggregate statistics on knee replacement outcomes of operating for each hospital online. Data from 01/2020-01/2023 displays 1,832 number of knee replacements were conducted in all hospitals in Northeast London. Extrapolating this to 10 years equates to 6,045 knee operations, although this is a conservative estimate because COVID lockdowns in 2020 led to fewer knee operations.

The NJR has a PROMS completion rate of approximately 60%[(1)], resulting in an expected 3,627 patients. A conservative estimate for mental health disorders in the arthroplasty population is 10%, however the true number is unknown. With this assumption 360 patients would have our exposure of interest (Mental health disorder) in comparison with 3,267 patients without mental health disorders.

The rate of poor outcomes (as defined by a poor patient score) following knee replacement is estimated between 10 - 20%. The true effect size of mental health disorders is unknown, however assuming a conservative estimate of 20% poor outcome in the exposure group vs 14% in the control group (effect size of -0.094) between the two groups will provide approximately 83.7% to test for a difference between groups at the 5% level. We therefore find that our study is adequately powered to detect relatively small but clinically meaningful differences.

6. Analysis

6.1 Definition of analysis data sets

Primary analysis

The analysis set will be all patients included in the previously constructed database described in section 3.

Variables Primary Exposure
This is the specific diagnosis of mental health disorder. This will be extracted from the discovery data service. Due to the complexity and large number of codes used to describe mental health, patients will be grouped into broad diagnostic groups. These groups are mapped to the DSM5 classifications, which are a validated grouping for MH research. The groups are:

1. No MHD
2. Depression (only)
3. Anxiety (only)
4. Mixed Anxiety + Depression
5. Serious Mental Illness (SMI), includes schizophrenia, psychosis + bipolar

Secondary Exposures

1. Mental Health Severity. This will be determined using Discovery Data Service data and guided by NHS guidelines for treating MH. Severity variables will be applied to groups 2, 3 and 4 (Depression, Anxiety, Mixed Anxiety and Depression). Severity will not be applied to SMI, as the nature of this diagnosis is more severe requiring more intense treatment and follow ups. Severity groupings will be defined as:

1) No MHD (Control)
2) MHD with one attendance to GP with Mental Health Disorder at any point preoperatively.
3) MHD with multiple attendances to GP with a Mental Health Disorder at any point preoperatively.
4) MHD and on active treatment for MHD (talking therapies or medication)

2. Timing of diagnosis. This will be determined using Discovery Data Service data. Timing variables will be applied to 2, 3 and 4 only, for the previously stated reasons. MHD timing will be based on time from GP appointment (for MHD related complaint) to timing of surgery. Timing of diagnosis will be grouped as:

1) No MHD (Control)
2) MHD with no appointments with GP in year leading up to surgery
3) MHD with appointment with GP in year leading up to surgery
4) MHD with appointment with GP within 3 months leading up to surgery.

Outcomes

Knee function – As recorded in the National Joint Registry. The Oxford knee score is a validated questionnaire[(2)] on a patient's knee function. Patients submit their questionnaire pre-operatively and 6 months post operatively. The questionnaire needs to be completed in full to be considered in the complete case analysis.

Complication Rate – As recorded in the Hospital Episode Statistics and National Joint Registry, defined as any attendance to AE or re-admission to hospital in the 6 months post operation. We will include readmission to any medical specialty to make sure to capture non orthopaedic complications.

Chronic Pain – As recorded in the National Joint Registry. The EQ5D is a validated questionnaire relating to patient health. It has questions about chronic pain included as a component of the questionnaire. Patients submit their score pre-operatively and 6 months post operatively. Patients reporting pain as moderate or severe at 6 months will be considered to have chronic pain.

Confounders

Risk factors associated with poor outcomes following TKR, and mental health status, previously confirmed by systematic review. We will consider the following:

Pre-operative OKS score, sex, age, ethnicity, deprivation status (IMD quintile), High BMI, smoking status, frailty, medical diagnosis (including Arterial disease, cardiac disease, Stroke, Resp disease, Chronic Kidney disease, Diabetes), pre-operative analgesia (neuropathic and opiate). This data is included across the Discovery Data Service (as snowmed codes) and National Joint registry.

Demographic data such as sex, age, ethnicity, index of multiple deprivation (IMD) ranking based on resident postcode, is also recorded for each patient and stored in the discovery data service.

6.2 Definition of the analysis subgroups

Pre-defined subgroups for analysis include are:

- Sex (Male / Female)
- Age group (<50, 50 – 59, 60 – 69, 70 – 79, 80+)
- Ethnicity (White, Black African/Caribbean/British; South Asian (Bangladeshi/Pakistani/Indian); Other including Mixed and Chinese; Not Reported)
- Deprivation level (IMD Quintile)

6.3 General principles

Quantifying uncertainty
Unless stated otherwise, all statistical tests will be two-sided, and 95% confidence intervals will be used to quantify uncertainty. Where presented, P-values will be given to 2 significant digits without reference to a cut-off or reference to statistical significance. There will be no adjustments for multiple testing.

Missing data
The NJR and DDS has a completion rate of 97% for hospital and community data. We expect the link to have a success rate above 95%, due to the nature of the GP / secondary care referral process. This will allow for a high completion rate for demographic and confounder variable data.

Confounder data related to medical diagnosis will be collected via snowmed codes. If a code is not present, then it will be assumed that patient has not had that condition.

The PROMS outcome is likely to have a response rate of 60%; so substantial missing data are expected.

To allow for analysis of missing outcome PROMS data, we will evaluate data on patients who do not complete their PROMS at 6 months. Patient demographics, confounders and pre-operative PROMS outcomes will be compared between those with complete outcomes and those without.

The primary analysis will be a complete case analysis. A case is considered to be complete if it has a fully completed PROMS outcome (Oxford knee and Eq5D) at both pre-operative and 6 months post operative.

Depending on the level and type of data missing, further sensitivity analysis will be performed to evaluate the robustness of results. This is likely to include use of multiple imputation.

Descriptive analysis

Descriptive analysis will include all methods in the 'Strengthening the Reporting of Observational Studies in Epidemiology' (STROBE) checklist [3]. Basic summary statistics (count data and percentages) will be used to report the prevalence of confounders / mental health data, demographic data and outcomes. Continuous variables will be reported with means and 95% Confidence intervals for these.

Statistical models

Exploratory analysis will first explore relationship between all potential confounders and exposure variables. Distributions, averages and count data will be considered. Adjustment in the model for these factors will only be done if they are likely to be confounding variables (i.e. associated with response, associated with exposure of interest, and unlikely to be on the causal pathway between exposure and response).

Adjusted and unadjusted analyses will be both be reported.

All analyses will use generalized linear models (see table 6 for further model details).

Generalized linear models will be fitted for each outcome of interest, and each exposure.

6.4 Software

Analyses will be performed in R, with a version greater than 4.0.

6.5 Analysis

Objective 1

1. To estimate the prevalence and distribution of different mental health disorders diagnoses, in patients before they undertake a knee replacement within the NHS in Northeast London from January 2014 to January 2024.

Demographic data will be reported as shown in Table 1, and graphs produced where appropriate (histograms for continuous data, bar-charts for categorical). The same will be applied to outcomes (oxford knee score, EQ5D, EQVAS) and all potential confounders, to visualise the data.

The distribution and prevalence of mental health disorders diagnosis at the time of surgery, for patients undergoing knee arthroplasty will be presented as shown in Table 2.

Secondary analysis will firstly describe the distribution of mental health severity. Severity will be grouped as previously described. Count data and percentages will be used. Please see example table 3 for example results table.

Final secondary analysis will describe the distribution of mental health diagnosis timing. Timing will be grouped as previously described. Count data and percentages will be used. Please see example table 4 for example results table.

Objective 2

2: Estimate the association between different mental health disorder diagnoses and (i) patient knee function, (ii) surgical complication rates, and (iii) chronic pain

Primary

Separate regression models will be used for each of the outcomes of interest, (PROMS, Complication rate, Chronic Pain). Exposure groups will be compared with the control population without MHD. For all regression models the crude coefficients/odds ratios and adjusted coefficient/odds ratios will be presented. Where relevant comparisons between groups will be conducted with the appropriate statistical test and presented with a p value and confidence intervals. Model fit will be partially evaluated using the R squared statistic.

Please see table 5 in the appendix for example results table. The differing models are listed in table 6.

Secondary

The secondary analysis will be limited those patients in group 2, 3 and 4 only (depression, anxiety and mixed anxiety and depression). Exposures of interest will be the previously mentioned severity of mental health disease and timing of diagnosis. Participants will be grouped as previously described, with regression model parameters as described for the primary objective and in section 6.3. The differing models are listed below in table 6. Methodology for crude ratios, confounders and model construction will be the same as used for the primary analysis.

Table 6 - Regression models for primary and secondary analysis

Analysis	GLM	Exposure	Outcome
2A	Linear	Mental Health Diagnosis	Function (OKS)
2B	Logistic	Mental Health Diagnosis	Complications Rate
2C	Logistic	Mental Health Diagnosis	Chronic Pain
3A	Linear	Disease Severity	Function (OKS)
3B	Logistic	Severity	Complications Rate
3C	Logistic	Severity	Chronic Pain
4A	Linear	Disease Timing	Function (OKS)
4B	Logistic	Timing	Complication Rate
4C	Logistic	Timing	Chronic Pain

6.6 Sensitivity Analyses

In general, missing data will be evaluated as previously noted in section 6.3.
The timing and severity criteria in the analysis will be considered, with adjusted parameters for each of the groups. E.g. – more appointments with GP required for higher severity. Group parameters may be adjusted to allow for even distribution of participants with MHD across the four exposure groups.

Outcome classification will be considered with different parameters considered for OKS, complication rate and chronic pain. Different modalities of outcome recording may be considered (e.g. – prescription data for chronic pain, rather than PROMS score).

Further sensitivity analysis will examine the impact of varying model specifications, outlier treatment and other potential sources of bias as identified during our primary analysis.

6.7 Exploratory analysis

Following the main analysis, ad-hoc further exploratory analysis may be conducted, including to:

- Considering different methods for measuring outcome (e.g. - prescription data for chronic pain)
- Considering OKS as a binary outcome with patients achieving the MCID
- Creating a generalized prediction model for knee arthroplasty outcomes
- The effects of mental health disorder on knee arthroplasty revision rate
- The effects of mental health disorder on EQVAS Score
- The effects of mental health disorder on return to work
- More specific investigation into chronic pain outcomes and exposures
- Considering mental health as an outcome variable
- Treated vs Untreated Mental health disorders

7.0 Signatures of Approval

The sign-off relates to the SAP version 1.0, dated 12/03/2025

Name	Role	Signature	Date
Mr. Gabbott	PI		12/03/25

Appendix 1: Dummy Tables

Table 1; Demographic Data for Complete Cases

Demographic		Total Number (% / CI)
Sex	Male	N(%)
	Female	N(N)
Mean Age		N(CI)
Ethnicity	White	N(N)
	Black	N(N)
	South Asian	N(N)
	Other	N(N)
BMI		N(N)
Smoking Status	Current	N(N)
	Past	N(N)
	Non-Smoker	N(N)
Medical Diagnosis	Arterial Disease	N(N)
	Cardiac Disease	N(N)
	Stroke	N(N)
	Respiratory	N(N)
	CKD	N(N)
	Diabetes	N(N)
Outcomes (PROMS)	OKS	N(CI)
	EQ5D	N(CI)
	EQVAS	N(CI)
Outcomes (PROMS)	OKS	N(CI)
	EQ5D	N(CI)
	EQVAS	N(CI)
Complication Rate		N(N)

Table 2 – Mental Health Diagnosis Data for Complete Cases

Diagnosis		Total Number (% of TKR population)	Oxford Knee Score (Mean (95% CI)	Readmission rate (%)	Chronic Pain (%)
No MH		N(N)			
Depression (only)		N(N)			
Anxiety (only)		N(N)			
Mixed Anxiety and Depression		N(N)			
Serious Mental Illness		N(N)			

Table 3 –Mental Health Severity data for Complete Cases

Severity Level		Total Number (% of population)	Oxford Knee Score (Mean (95% CI)	Readmission rate (%)	Chronic Pain (%)
One attendance to GP		N(N)			
Multiple attendances		N(N)			
Required treatment		N(N)			

Table 4 – Mental Health Timing data for Complete Cases

Timing of diagnosis		Total Number (% of Population)	Oxford Knee Score (Mean (95% CI)	Readmission rate (%)	Chronic Pain (%)
1 year +		N(N)			
Within 1 year		N(N)			
Within 3 months		N(N)			

Table 5 – Generalized Linear Model Results for Readmission at 6 weeks

Exposure	Univariate Odds Ratio	Adjusted Odds Ratio	P
MH Diagnosis			
Sex			

Age			
Deprivation			
BMI			
Smoking			
Frailty			
Medical diagnosis			
Pre op PROMS			

Reference group – Patients with No MHD Adjusted for:

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