BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019426
Article Type:	Protocol
Date Submitted by the Author:	04-Sep-2017
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Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Geriatric medicine, Mental health, Anaesthesia
Keywords:	postoperative, delirium, total joint arthroplasty, incidence

TITLE

Protocol for a Single-Centre Prospective Observational Study of Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

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Word count: 3713

Keywords: postoperative, delirium, total joint arthroplasty, incidence

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ABSTRACT

Introduction

Postoperative delirium is a serious and common complication in older adults following Total Joint Arthroplasties (TJA). It is associated with increased risk of postoperative complications, mortality, length of hospital stay and postdischarge institutionalisation. Thus, it has a negative impact on the health-related quality of life of the patient and poses a large economic burden. This study aims to characterise the incidence of postoperative delirium following TJA in the South East Asian population, and investigate any risk factors or associated outcomes.

Methods and analysis

This is a single-centre prospective observational study, recruiting patients between 65 and 90 years old undergoing elective Total Knee Arthroplasty or Total Hip Arthroplasty. Exclusion criteria included patients with clinically diagnosed dementia. Preoperative and intraoperative data will be obtained prospectively. The primary outcome will be the presence of postoperative delirium assessed using the Confusion Assessment Method on postoperative day 1, 2, 3 and day-of-discharge. Other secondary outcomes assessed postoperatively will include hospital outcomes, pain at rest, knee function, health-related quality of life and POMS-defined morbidity. Data will be analysed to calculate the incidence of postoperative delirium. Potential risk factors and any associated outcomes of postoperative delirium will also be determined.

Ethics and dissemination

This study has been approved by the Singapore General Hospital Institutional Review Board (SGH IRB) (CIRB Ref: 2017/2467) and is registered on the ClinicalTrials.gov registry (Identified: NCT03260218). An informed consent form will be signed by all participants before recruitment and translators will be made available to non-English speaking participants. The results of this study will be presented at international conferences and submitted to a peer-reviewed journal. The data collected will also be made available in a public data repository.

STRENGTHS AND LIMITATIONS

Strengths

1. This study is the first to evaluate the incidence of postoperative delirium in the elderly above 65 years old following TKA and THA in Singapore.
2. Association of variables to occurrence of postoperative delirium that have not been well studied such as hand grip strength, STOP-Bang score and long-term outcomes including knee function and HRQoL will be analysed.
3. The Confusion Assessment Method (CAM) will be used, which is a gold standard measure for detection of delirium.

Limitations

1. The study is conducted in a single centre in Singapore which may limit the generalisability of the results of the study.
2. Delirium will be only assessed once a day, and the presence of delirium may be missed due to the fluctuating nature of the condition.

INTRODUCTION

Delirium is a neurocognitive disorder characterised by a disturbance in attention, level of consciousness and cognition, in which symptoms are acute in onset and may fluctuate in severity throughout the day[1]. Delirium occurs as a serious and common perioperative complication in older adults following total joint arthroplasty (TJA). A recent meta-analysis by Scott et al reported an incidence of 17%, but the rates reported by individual studies varied substantially[2]. In particular, a study of the Asian population in China by Chen et al reported an incidence of 16.5% following TJA in elderly above 60 years old[3]. However, the incidence has not yet been well-documented in the South-East Asian population, exposing a knowledge gap. With the demand for total hip arthroplasty (THA) expected to rise by almost 2-fold and that for total knee arthroplasty (TKA) by almost 7-fold by 2030[4], postoperative delirium is likely to become a significant health burden.

Postoperative delirium has been associated with increased morbidity and cost. Patients with delirium after surgery have an increased risk of major postoperative complications and increased mortality (8% vs 2%)[5,6]. They also experience significantly longer hospital stay (median 6 days longer) and are at increased risk of subsequent postdischarge institutionalisation (OR 1.77-3.29)[6–8], which are associated with higher total procedural cost[9]. Therefore, postoperative delirium can not only impact the health-related quality of life of the patient, but also pose a large economic burden both in the short and long term. Poor compliance with postoperative therapy may be a reason for the worse outcomes associated with postoperative delirium. Low cognitive function has been shown to be a significant predictor of exercise adherence in older women[10], which is part of standard rehabilitation after TKA.

Identifying risk factors of postoperative delirium may be important for preventing its occurrence and consequences, and guide treatment of patients with delirium. As most TJA operations are elective, there may be opportunity to address the modifiable risk factors to optimise the patient before the surgery or implement perioperative management strategies which can decrease the negative outcomes of postoperative delirium. Age has been reported as an important predisposing risk factor[11,12], which makes the population under study particularly at risk of postoperative delirium. The average age of this population is 71, and majority of patients are 65 years or older (81.3% for TKR and 69.5% for THR)[9]. Other reported predisposing risk factors include pre-existing cognitive impairment (OR 2.6-6.5), poor physical status (OR 1.7-5.7), alcohol abuse (OR 1.9-5.5)[7,11,12]. A meta-analysis by Yuan et al identified precipitating risk factors, such as low postoperative O_2 saturation (OR 1.59-4.18) and pain at rest (OR 1.63-6.20)[13]. However, few studies have investigated the risk factors associated with postoperative delirium following TJA specifically.

Given the limited knowledge about postoperative delirium especially in the South East Asian population, together with the increasing number of older adults undergoing TJA, this study aims to characterise the incidence of delirium in older adults undergoing elective TJA. We hypothesise that the incidence detected will be similar to that in Western studies, as the incidence in the Asian population reported in the study in China was comparable to the values seen in the Western population. This study also aims to identify risk factors of postoperative delirium following elective TJA, including demography, comorbidities, clinical laboratory data and drugs used in the perioperative period. This will enable the provision of better perioperative care for prospective patients undergoing TJA.

METHODS AND ANALYSIS

Study design

Institutional Review Board approval was obtained (Singhealth CIRB 2017/2467) prior to starting the study. This is a single centre, prospective observational study conducted at a tertiary public hospital in Singapore (Singapore General Hospital (SGH)). SGH is the largest hospital in Singapore with 1,597 beds in 2013[14]. 1,500 TKA surgeries were performed in SGH in 2007, accounting for 65% of all TKA surgeries in Singapore[15].

Study population

Patients aged between 65 and 90 undergoing elective total joint (hip or knee) replacement surgery in Singapore General Hospital will be screened for eligibility. Exclusion criteria includes patients who are unable to give their own consent for the surgery and anaesthesia. Patients with clinically diagnosed dementia will also be excluded from the study as they are deemed not to have capacity for consent.

All eligible patients will be identified from the appointment list of attendees of the preoperative evaluation clinic (PEC) at SGH where the patients attend for preoperative assessment and counselling by the anaesthetists. Patients between 65 and 90 years old undergoing TKA or THA will be approached and invited to enrol into the study. Informed consent will be obtained then.

Preoperative data

We will collect the patients' baseline characteristics preoperatively. This will allow for the identification of risk factors or correction of confounding factors during analysis of the results.

Data on cognitive status

Before the operation, each patient will be interviewed to assess their baseline cognitive status. The Mini–Mental State Examination (MMSE) will be used, which is a 11-question screening tool used to evaluate the cognitive aspects of mental function[16]. It measures domains of cognitive function including memory, attention, language, praxis and visuospatial ability. A score of 0-30 can be obtained with higher values denoting better cognitive function. A score of <24 suggests cognitive impairment. The test was adapted for use in Singapore, and the changes and reasons for the changes shown in Figure 1 below. In addition, the test will be administered in English, Chinese or Malay, according to the language the participant is most well-versed in. The Chinese version of MMSE that will be used was previously validated in Shanghai[17] and in Singapore[18]. The Malay version of MMSE that will be used was developed by translation from the English version. The Chinese and Malay versions of MMSE have similar test questions and are scored the same way as the English version, but there some differences shown in Figure 2. However, a recent study in Singapore has shown that there were significant ethnic differences in unadjusted MMSE scores using the different versions of MMSE. These differences were not eliminated after accounting for known correlates of MMSE performance such as socioeconomic status, comorbid illnesses, functional health status, and health-related behaviours[19].

Item no.	Original version	Adapted version	Reasons
1	"What is the season?"	Without looking at your watch, what time is it?"	There are no seasons in Singapore.
2a	"What county are we in?";	"What area/street are we in?";	Singapore is a city country; "Singapore" would only the only correct answer.
2b	"What town/city are we in?"	"Which part of Singapore (North/South/East/West) are we in?"	Singapore is a city country; "Singapore" would only the only correct answer.

Figure 1 - Changes in the adapted version for use in Singapore

Item no.	English version	Chinese version	Malay version
4	Spell the word "WORLD" backwards	请把这句话倒说一遍 – "天上有月亮"	Terbalikkan ejaan "DUNIA"
7	Repeat the following – "no ifs, ands, or buts"	请清除的重复一遍 – "四十四只石狮子"	Ulangan perkataan – "da dahulu, kini dan selamanya"

Figure 2 - Differences between the English, Chinese and Malay MMSE

CAM will also be performed prior to the operation to obtain the patient's baseline score. CAM is a screening instrument for delirium intended for use by non-psychiatrically-trained clinicians based on the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III-R criteria[20]. It involves an interview whereby delirium can be diagnosed using the CAM algorithm based on 4 criteria – (1) acute onset or fluctuating course, (2) inattention, (3) disorganised thinking and (4) altered level of consciousness. Delirium is said to be present if criteria 1 and 2 and either of 3 or 4 are present. CAM has a sensitivity of 94-100%, specificity of 90-95%, and high inter-observer reliability[21]. This enables a new case of delirium in the postoperative period to be detected.

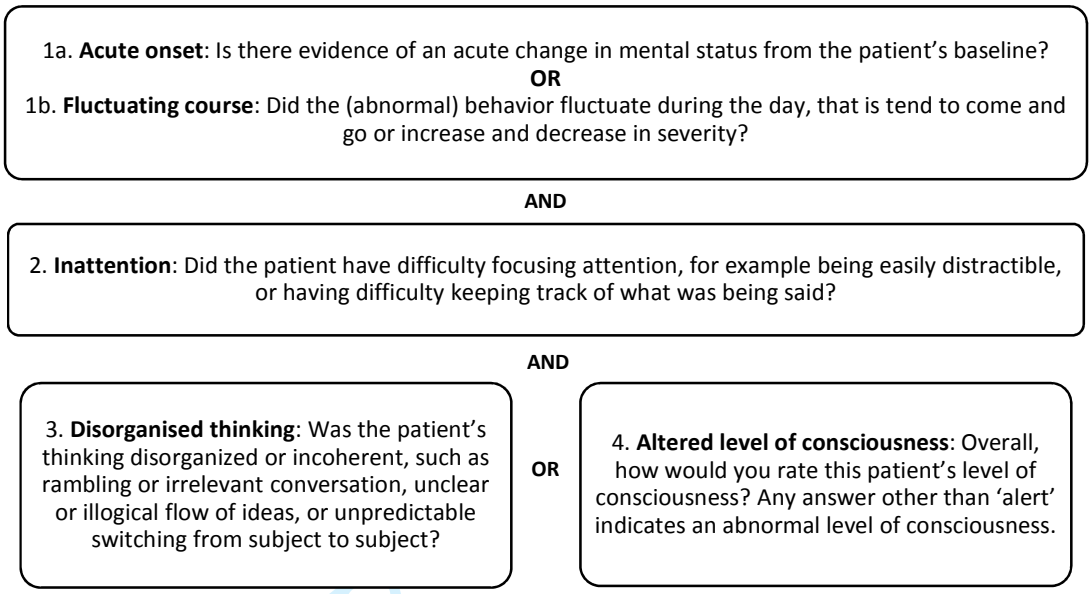

Figure 3 – CAM criteria: at least one criteria on each of the 3 rows must be met for a positive result

Other data

Sensory impairment will be assessed during the preoperative interviews. Patients will be asked to wear their visual or hearing aids during these interviews. A patient will be considered to have visual or hearing impairment if the research member conducting the interview is unable to perform the interview normally due to the sensory impairment, such as raising his/her voice for a patient with impaired hearing. The preoperative MMSE assessment provides a useful tool in assessing for visual impairment as it has several vision-dependent items (naming objects, following a written command, instructions to handle a piece of paper, writing a sentence, copying a diagram)[22].

The grip strength of each patient will also be measured using the JAMAR® Plus+ Digital Hand Dynamometer (Sammons Preston Inc, Bolingbrook, IL). Hand dynamometry has acceptable reliability and validity for measurement of grip strength[23], which can serve as an indicator of muscle function and physical fitness. The normative value of hand grip strength for elderly in Singapore has recently been published, decreasing from 18.6kg and 29.3kg for females and males respectively in the 65-69 age group to 12.4kg and 18.5kg in the 85+ age group[24].

The patient baseline characteristics will be obtained from the medical records. Perioperative data is available through the PEC database as well as the Orthopaedic Diagnostic Centre (ODC) total joint registry, which will be prospectively entered into the REDCap™ database. This will include data regarding patient's demographics, smoking history, alcohol history, pre-existing medical conditions, preoperative medications.

Each patient will also be rated preoperatively by an anaesthesiologist in the PEC based on the American Society of Anaesthesiologists (ASA) physical status classification[25]. It is a scale from 1 to 5, where 1 represents a completely healthy fit patient and 5 representing a moribund patient who is not expected to live 24 hour with or without surgery. For our analysis, we will be calculating each patient's perioperative risk based on the Charlson

Comorbidity Index (CCI)[26]. 19 different comorbid medical conditions are assigned weights of 1, 2, 3 and 6 according to the degree to which they predicted mortality, and the sum of these values gives the final score. It is a valid method of estimating risk of mortality resulting from comorbidities[27]. The STOP-Bang score will also be calculated for each patient. The STOP-Bang questionnaire was a good screening tool for diagnosing obstructive sleep apnoea, with a sensitivity of 89.0% and accuracy of 79.1%[28]. Preoperative laboratory results, including data about haemoglobin or creatinine level, will also be collected.

Intraoperative data

Data regarding the surgery will be collected. Intraoperative data includes type of arthroplasty performed (TKA or THA), type of anaesthesia (spinal, general or other anaesthesia), use of femoral nerve block, intraoperative drug use, tourniquet time, intra-articular injections and blood transfusion (number of pints transfused). Occurrence of hypotension, which is defined as a mean arterial pressure <60mmHg, and its duration will also be recorded.

Postoperative data

Primary outcome

The primary outcome will be the presence of postoperative delirium following TJA. Each patient will be assessed for delirium on postoperative day (POD) 1, 2 and 3 in the wards at 7am as well as the day of discharge. Delirium will not be evaluated on POD 0 due to difficulty in differentiating delirium from the effects of residual anaesthesia.

The Confusion Assessment Method (CAM) will be used to detect postoperative delirium and delirium severity. Delirium is said to be present if the patient meets the CAM criteria for any of the postoperative assessments. Patients assessed to have delirium will be referred to the psychiatrists for further management.

Short-term secondary outcomes

Postoperative complications will be assessed by the Postoperative Morbidity Survey (POMS). This is a 9-point survey that can be easily used by clinicians to characterise short-term postoperative morbidity in their respective settings[29]. It is designed to only identify morbidity of a type and severity that could prolong LOS. Using POMS, postoperative morbidity outcomes can be dichotomised into 2 categories – the absence and presence of morbidity. Initial data from our centre demonstrated a median LOS of 4 days following primary unilateral TKA[30]. This was assumed to represent an uncomplicated postoperative course, and any POMS-defined morbidity on POD 0-4 might be expected as part of the usual course of surgery. POMS will thus be assessed on POD 5, as it will have face validity in this cohort for identifying patients experiencing postoperative complication(s). It has also been reported to have good inter-rater reliability and acceptability to patients[31].

Other postoperative outcomes that will be obtained include postoperative nausea and vomiting (PONV), length of stay (LOS) and 30-day readmission rates. 30-day readmission is defined as readmission within 30 days of initial admission. The reason for readmission will also be obtained.

Long-term secondary outcomes

Longer-term outcomes such as functional and health-related quality-of-life (HRQoL) outcomes will also be recorded by the ODC total joint registry at 6 months, 1 year, 2 years and 5 years postoperatively. The ODC tracks clinical outcome measures during pre- and postoperative functional assessments of the patients in SGH. Their total joint registry contains data about outcomes from knee and hip arthroplasties.

Knee function will be measured using the new Knee Society Knee Score (KSKS) and Function Score (KSFS)[32]. The physician-derived KSKS measures alignment, stability, joint motion and symptoms experienced. The patient-derived KSFS evaluates use of walking aids and supports, ability to complete standard activities of daily living and discretionary activities. The KSKS and KSFS each range from 0 (worst) to 100 (best). Both provide a validated rating of the functional outcome of the patient and knee prosthesis after TKA[33]. In addition, the Oxford Knee Score (OKS)[34] will also be used, which is a 12-item, patient-assessed questionnaire designed specifically for use in patients undergoing TKA [7]. It assesses an individual's pain and physical disability. Each item is scored from 1 (least difficulty/severity) to 5 (most difficulty/severity), and individual item scores are summed to yield an overall score ranging from 12 (no pain or limitation) to 60 (severe pain or limitation). A lower OKS indicates a better outcome. It has good reliability, construct and content validity, and sensitivity to clinically important changes over time[34,35]. It correlates strongly with pain but less with postoperative functioning[36].

HRQoL will be assessed based on the 36-Item Short Form Health Survey (SF-36)[37] to obtain a baseline score. It consists of 36 questions categorised into 8 domains (physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions). Higher scores indicate better health status and quality of life.

Days alive and out of hospital (DAOH) will also be determined for each patient at 1 month, 6 months and 12 months to assess overall impact of postoperative delirium on morbidity and mortality. DAOH will be calculated based on death date (if present) and duration of all subsequent hospitalisations until the follow-up date. This will be recorded as a percentage by dividing DAOH by total potential follow-up period, which is the time period between the operation and the respective dates of follow-up (1 month, 6 months and 12 months). %DAOH is a useful measure as it emphasises the deaths occurring early in follow-up and takes into account the severity (duration) of any hospitalisation.[38]

Postoperative risk factors

Other postoperative data will be collected as variables for risk factors.

Postoperative pain at rest will be evaluated using the pain Visual Analog Scale (VAS) during the same visit as CAM on POD 1, 2 and 3. Each patient will score pain experienced at rest on a scale, with 0 = no pain and 10 = maximum pain.

Sensory impairment will also be assessed during the postoperative interviews similar to the preoperative assessments.

The flowchart shown in Figure 4 depicts a patient's journey starting from enrolment in the PEC.

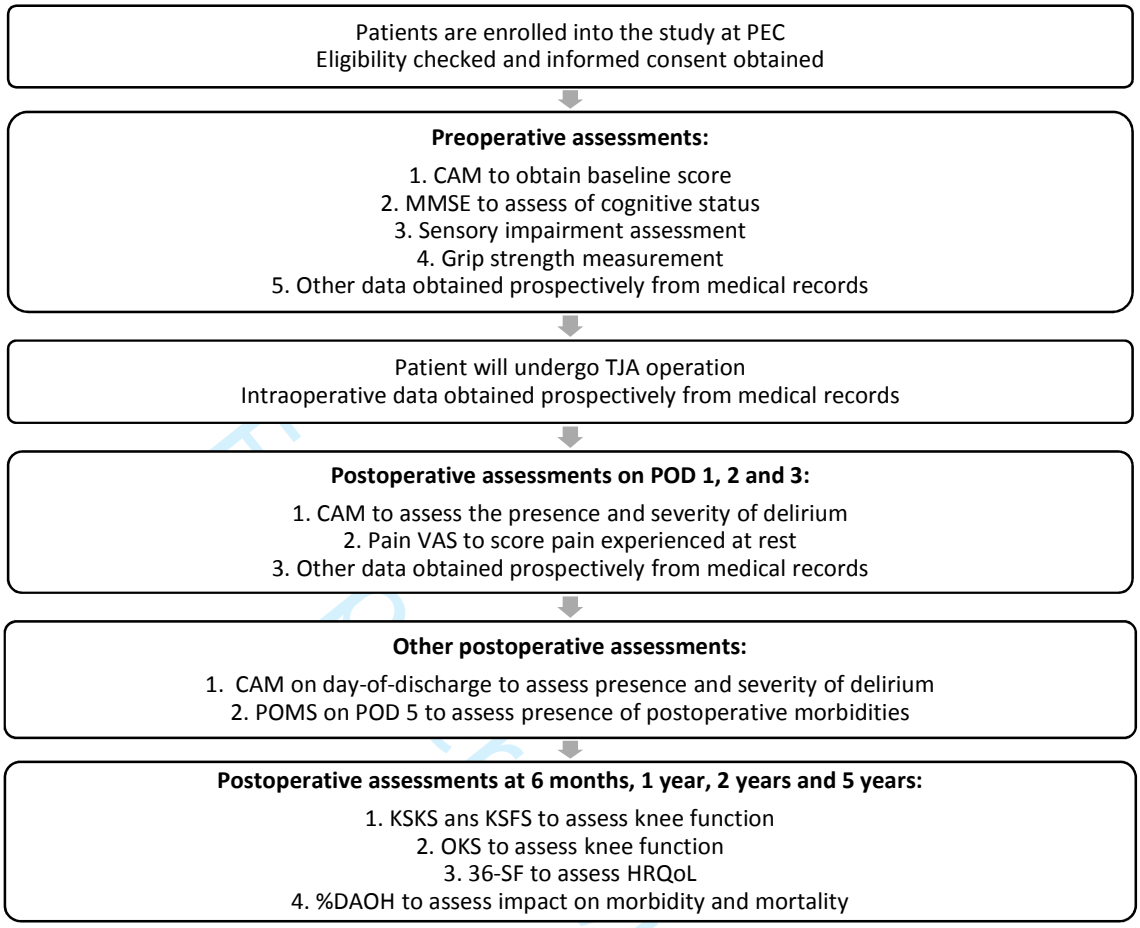

Figure 4 - Flowchart depicting a patient's timeline during the study

Data management

Patient data will be kept confidential throughout the study. All electronic study data entry, storage and analysis will be done according to institutional data security policy, using password protected data in secure systems.

The patient data collected will be de-identified and the key kept securely separated with access limited to principal investigator and co-investigators. A study-related identification number given to each patient will be used on the case report form. Research members will enter the de-identified data into the REDCap™ (Research Electronic Data Capture) tool hosted on a secure server at Singapore General Hospital[36]. The hardcopy of the research data will be securely stored within the department. The softcopy of research data will be saved in a password-protected file and will be stored in institution approved login-protected system and encrypted hard-drive. Only study members will have access to the data.

Power and sample size calculations

The sample size will be calculated based on the incidence of postoperative delirium. Based on existing literature, the estimated incidence of postoperative delirium following TJA is

around 10%. Using this estimate, a minimum sample size of 150 patients will be needed to detect the incidence with a precision of 5% and power of 80%. The sample size of 200 patients is needed to measure incidence to account for attrition.

However, this study will also be analysing the factors which may be correlated to postoperative delirium by logistic regression. A study population size of 500 will thus be targeted to be able to run a multiple logistic model while minimising the limitation of a small number of events of postoperative delirium.

Statistical analyses

The incidence of postoperative delirium following TJA using the standard formula – the number of patients diagnosed to have postoperative delirium divided by the total number of patients in the study, and the result expressed as a percentage.

Potential risk factors of postoperative delirium will also be identified by comparing the perioperative data recorded between the patients with and without postoperative delirium. Data will first be summarised using descriptive statistics including mean, standard deviation (SD), median, range and frequency tables. Univariate analyses will then be used identify the differences between the two groups. Data of continuous variables will be compared using the Student's t-test (normally distributed data) or the Wilcoxon rank sum test (not normally distributed data). Data of categorical variables will be compared by Pearson Chi-square test or Fisher's exact test.

The variables which are statistically significant or close to significant (p value <0.05 or <0.1) between the two groups of patients will then be selected for inclusion in a multivariate logistic regression model. This will determine the independent predictors of postoperative delirium. The final model will be determined by sensitivity analysis. The sensitivity analysis can help us to understand the contribution of each parameter to the model outputs, investigate which parameter will have the biggest influence and then refine the model to obtain the final model which is statistically and clinically meaningful. Odds ratio (OR) will be used to describe the relative risks of postoperative delirium.

Postoperative outcomes which are associated with the incidence of postoperative delirium will also be examined by comparing patients with and without postoperative delirium. The postoperative POMS score, incidence of PONV, LOS, incidence of 30-day readmission and %DAOH will be similarly compared using Student's t-test and Person Chi-square tests as appropriate.

For the long-term postoperative outcomes, the median postoperative SF-36, KSKS, KSFS and OKS scores at 6 months, 1 year, 2 years and 5 years will be compared to the median preoperative baseline scores using the Wilcoxon matched pairs sign rank test. The tests with a change greater than the minimally clinically important difference (MCID) will be identified. The MCID values for each test will be obtained from the pre-existing literature. These variables will then be analysed by analysis of covariance (ANCOVA) to identify predictors of the long-term postoperative test scores. All predictor variables were incorporated into the multivariate ANCOVA model. Analyses were performed separately for the various tests that demonstrated changes greater than MCID.

ETHICS AND DISSEMINATION

This study has been approved by the Singapore General Hospital Institutional Review Board (SGH IRB) (CIRB Ref: 2017/2467) and is registered on the ClinicalTrials.gov registry (Identified: NCT03260218). In the event of any important protocol modifications, all investigators, SGH IRB and trial participants will be notified.

The results of this study will be presented at international conferences and submitted to a peer-reviewed journal. The data collected will also be made available in a public data repository.

All eligible participants will be approached by the research assistant during their visit to the preoperative evaluation clinic. They will be given an explanation about the study, a patient information sheet and a consent form. They will then be given an ample time to consider if they would like to participate in the study. They will also be allowed to ask questions freely. If the participant expresses an interest to participate in the study, a written consent will be obtained. The consent forms are in English. However, participants from non-English speaking backgrounds will be provided a translator. For illiterate participants, an accompanying family member will be approached to verify and witness the consent process.

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FUNDING STATEMENT

This work was supported by the Singhealth Duke-NUS Academic Medical Centre Nurturing Clinician Scientists Scheme Award, project number 12/FY2017/P1/15-A29. This funding source, Singhealth Duke-NUS Academic Medical Centre, has no role in the design of this study and will not have a role in the analysis and interpretation of the results.

COMPETING INTEREST STATEMENT

None.

APPENDIX

1. Preoperative data collection form (DCF)
2. Postoperative data collection form
3. POMS Instrument
4. SF-36 Instrument

Appendix 1 – Preoperative DCF

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____
Date of preoperative assessment:
_____

DEMOGRAPHIC
Age: _____
Gender: Male ☐ Female ☐
Race: Chinese ☐ Malay ☐ Indian ☐ Others ☐
Language:
English ☐ Mandarin ☐ Malay ☐
Others _____
Highest education completed:
_____
Height: _____ m
Weight: _____ kg
BMI: _____

OP DETAILS
Surgeon:
_____
Type of Operation:
TKR ☐ THR ☐
Unilateral L ☐/ R ☐ OR Bilateral ☐
Primary ☐ Revision ☐
Pre-operative Dx:
_____
_____
_____
_____

Grip Strength: _____

BACKGROUND MEDICAL CONDITION
ASA: _____

Charlson Comorbidity Index
Overall score: _____

CVS	
☐	Myocardial infarction
☐	Congestive heart failure
☐	Peripheral vascular disease
CNS	
☐	Cerebrovascular disease
☐	Hemiplegia or paraplegia
☐	Dementia
Respi	
☐	Chronic pulmonary disease
MSK	
☐	Rheumatologic disease
GI	
☐	Peptic ulcer disease
☐	Mild liver disease
☐	Moderate or severe liver disease
Endocrine	
☐	Diabetes without chronic complications
☐	Diabetes with chronic

Smoking ☐
Alcoholism ☐
Diabetes:
OHGA ☐ Insulin ☐
Latest HbA1c _____
Chronic kidney disease ☐
Pre-existing dementia ☐
Other pre-existing neurological problems
☐ CVA
☐ Parkinson Disease
☐ Depression
☐ Anxiety
☐ Schizophrenia and other delusional disorders
Visual impairment ☐
Hearing impairment ☐
STOPBANG score _____
Chronic Medications
Benzodiazepine ☐
Statin ☐
Tramadol ☐ Oxynorm ☐
Anti-depressants
Tricyclics ☐ SSRI ☐ SNRI ☐ MOAI ☐
Anti-psychotics
Haloperidol ☐ Quetiapine ☐

	complications
Renal	
☐	Mild Renal disease
☐	Moderate or severe renal disease
Malignancy	
☐	Any malignancy, including leukemia and lymphoma
☐	Non-metastatic solid tumour
☐	Metastatic solid tumor
Immunological	
☐	AIDS/HIV

IntraOp

ANA Type: _____

	Yes	No
Fem N block	☐	☐
Benzo Use:	☐	☐
Atropine Use:	☐	☐
Opioid use **If yes , dose: _____**	☐	☐
Dexa use **If yes , dose: _____**	☐	☐
Promethazine use:	☐	☐
Ondansetron:	☐	☐
Blood Transfusion	☐	☐
Hypotension **If yes, duration: _____**	☐	☐

Olanzapine ☐ Clozapine ☐

Preoperative Laboratory Results

Hemoglobin _____

MCV _____

RDW _____

MCV _____

MCHC _____

Urea _____

BASELINE CAM

1. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐

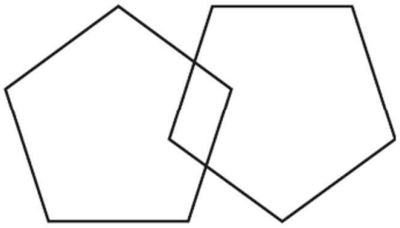
c. Uncertain _____
d. No ☐

4. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

BASELINE MINI MENTAL STATE EXAMINATION

Total score _____
Level of consciousness
Alert ☐ Drowsy ☐ Stupor ☐ Coma ☐

	Question	Score
1	What is the • year • month • day of the week • date • current time now (without looking at your watch)?	/ 5
2	What country are we in? What area/street are we in? Which part of Singapore is this place (North, south, east, west or central) Which hospital are we in? Which floor?	/ 5
3	Show the objects: ball, flag, tree Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials _____	/ 3
4	Serial 7's. 1 point for each correct answer. Stop after 5 answers. Alternatively spell "world" backward.	/ 5
5	Ask for the 3 objects repeated above. Give 1 point for each correct answer.	/ 3
6	Name a pencil and watch. Repeat the following "No ifs, ands, or buts" Follow a 3-stage command: "Take a paper in your hand, fold it in half, and put it on the floor." Read and obey the following: CLOSE YOUR EYES	/ 2 / 1 / 3 / 1 / 1

		Write a sentence. Copy the design shown 	/ 1 / 1	

Appendix 2 – Postoperative DCF

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

POD1

CAM ASSESSMENT

5. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
6. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
7. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
8. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

VISUAL/HEARING IMPAIRMENT

Visually impaired ☐

Hearing impaired ☐
If yes to above, hearing aids? ☐

PERIOPERATIVE DETAILS

Tourniquet time: _____ minutes

Intra-articular injections:
(i) Tranexamic acid ☐ Dosage:
(ii) Morphine ☐ Dosage:

	(iii) Marcaine ☐ Dosage: (iv) Adrenaline ☐ Dosage: (v) Ketorolac ☐ Dosage: (vi) Triamcinolone ☐ Dosage: (vii) Vancomycin ☐ Dosage: (viii) Normal Saline ☐ Dosage: (ix) Others: _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

POD2

CAM ASSESSMENT

9. Acute onset change in mental status from baseline?
    a. Yes ☐
    b. No ☐
    c. Uncertain _____
10. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
11. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
12. How is the patient's overall level of consciousness?
    a. Alert (normal) ☐
    b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
    c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
    d. Stupor (Difficult to arouse) ☐, fluctuating ☐
    e. Coma (Unarousable) ☐, fluctuating ☐
    f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

POD3

CAM ASSESSMENT

1. Acute onset change in mental status from baseline?
    a. Yes ☐
    b. No ☐
    c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
4. How is the patient's overall level of consciousness?
    a. Alert (normal) ☐
    b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
    c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
    d. Stupor (Difficult to arouse) ☐, fluctuating ☐
    e. Coma (Unarousable) ☐, fluctuating ☐
    f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

DAY OF DISCHARGE

POSTOPERATIVE MORBIDITY SURGERY

Morbidity Type	Criteria	Tick if present (☐)
Pulmonary	De novo requirement for supplemental oxygen or other respiratory support (e.g. mechanical ventilation or CPAP)	
Infectious	Currently on antibiotics or temperature > 38°C in the last 24h	
Renal	Presence of oliguria (< 500 ml/day), elevated serum creatinine (> 30% from preoperative value), or urinary catheter in place for a nonsurgical reason	
Gastrointestinal	Unable to tolerate an enteral diet (either by mouth or via a feeding tube) for any reason, including nausea, vomiting, and abdominal distension	
Cardiovascular	Diagnostic tests or therapy within the last 24h for any of the following: de novo myocardial infarction or ischaemia, hypotension (requiring pharmacologic therapy or fluid therapy > 200ml/h), atrial or ventricular arrhythmias, or cardiogenic pulmonary edema	
Neurologic	Presence of a de novo focal deficit, coma or confusion and delirium	
Wound complication	Wound dehiscence requiring surgical exploration or drainage of pus from the operation wound, with or without isolation of organisms	
Haematologic	Requirement for any of the following within the last 24h: packed erythrocytes, platelets, fresh-frozen plasma, or cryoprecipitate	
Pain	Surgical wound pain significant enough to require parenteral opiates or regional analgesia	

CPAP: continuous positive airway pressure

Appendix 3 – Postoperative Morbidity Survey

Morbidity type	Criteria	Source of data
Pulmonary	Has the patient developed a new requirement for oxygen or respiratory support.	Patient observation Treatment chart
Infectious	Currently on antibiotics and/or has had a temperature of >38°C in the last 24 hr.	Treatment chart Observation chart
Renal	Presence of oliguria <500 mL/24 hr; increased serum creatinine (>30% from preoperative level); urinary catheter in situ.	Fluid balance chart Biochemistry result Patient observation
Gastrointestinal	Unable to tolerate an enteral diet for any reason including nausea, vomiting, and abdominal distension (use of antiemetic).	Patient questioning Fluid balance chart Treatment chart
Cardiovascular	Diagnostic tests or therapy within the last 24 hr for any of the following: new myocardial infarction or ischemia, hypotension (requiring fluid therapy >200 mL/hr or pharmacological therapy), atrial or ventricular arrhythmias, cardiogenic pulmonary edema, thrombotic event (requiring anticoagulation).	Treatment chart Note review
Neurological	New focal neurological deficit, confusion, delirium, or coma.	Note review Patient questioning
Hematological	Requirement for any of the following within the last 24 hr: packed erythrocytes, platelets, fresh-frozen plasma, or cryoprecipitate.	Treatment chart Fluid balance chart
Wound	Wound dehiscence requiring surgical exploration or drainage of pus from the operation wound with or without isolation of organisms.	Note review Pathology result
Pain	New postoperative pain significant enough to require parenteral opioids or regional analgesia.	Treatment chart Patient questioning

Appendix 4 – 36-Item Short Form Health Survey

RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:
   - ○ 1 – Excellent
   - ○ 2 - Very good
   - ○ 3 – Good
   - ○ 4 – Fair
   - ○ 5 – Poor

2. **Compared to one year ago**, how would you rate your health in general now?
   - ○ 1 - Much better now than one year ago
   - ○ 2 - Somewhat better now than one year ago
   - ○ 3 - About the same
   - ○ 4 - Somewhat worse now than one year ago
   - ○ 5 - Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	○ 1	○ 2	○ 3
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	○ 1	○ 2	○ 3
5. Lifting or carrying groceries	○ 1	○ 2	○ 3
6. Climbing **several** flights of stairs	○ 1	○ 2	○ 3
7. Climbing **one** flight of stairs	○ 1	○ 2	○ 3
8. Bending, kneeling, or stooping	○ 1	○ 2	○ 3
9. Walking **more than a mile**	○ 1	○ 2	○ 3
10. Walking **several blocks**	○ 1	○ 2	○ 3
11. Walking **one block**	○ 1	○ 2	○ 3
12. Bathing or dressing yourself	○ 1	○ 2	○ 3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	Yes	No
13. Cut down the amount of time you spent on work or other activities	○ 1	○ 2
14. Accomplished less than you would like	○ 1	○ 2
15. Were limited in the kind of work or other activities	○ 1	○ 2
16. Had difficulty performing the work or other activities (for example, it took extra effort)	○ 1	○ 2

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	Yes	No
17. Cut down the **amount of time** you spent on work or other activities	○ 1	○ 2
18. **Accomplished less** than you would like	○ 1	○ 2
19. Didn't do work or other activities as **carefully** as usual	○ 1	○ 2

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?
    - ○ 1 - Not at all
    - ○ 2 - Slightly
    - ○ 3 - Moderately
    - ○ 4 - Quite a bit
    - ○ 5 – Extremely

21. How much **bodily** pain have you had during the **past 4 weeks**?
    - ○ 1 - None
    - ○ 2 - Very mild
    - ○ 3 - Mild
    - ○ 4 - Moderate
    - ○ 5 - Severe
    - ○ 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?
    - ○ 1 - Not at all
    - ○ 2 - A little bit

- 3 - Moderately
- 4 - Quite a bit
- 5 – Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
24. Have you been a very nervous person?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
25. Have you felt so down in the dumps that nothing could cheer you up?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
26. Have you felt calm and peaceful?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
27. Did you have a lot of energy?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
28. Have you felt downhearted and blue?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
29. Did you feel worn out?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
30. Have you been a happy person?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
31. Did you feel tired?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?
    - 1 - All of the time
    - 2 - Most of the time
    - 3 - Some of the time
    - 4 - A little of the time
    - 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false

33. I seem to get sick a little easier than other people	○ 1	○ 2	○ 3	○ 4	○ 5
34. I am as healthy as anybody I know	○ 1	○ 2	○ 3	○ 4	○ 5
35. I expect my health to get worse	○ 1	○ 2	○ 3	○ 4	○ 5
36. My health is excellent	○ 1	○ 2	○ 3	○ 4	○ 5

This tool was developed at RAND Health as part of the Medical Outcomes Study.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page Number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-13
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-13
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	13-14
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	14
		(*b*) Describe any methods used to examine subgroups and interactions	14
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	14
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	-
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	-
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	Report numbers of outcome events or summary measures over time	-
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	-

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	-
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	-
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	-
Generalisability	21	Discuss the generalisability (external validity) of the study results	-
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Protocol for a Single-Centre Prospective Observational Study of Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019426.R1
Article Type:	Protocol
Date Submitted by the Author:	02-Jan-2018
Complete List of Authors:	abdullah, hairil; Singapore General Hospital, Department of Anesthesiology Tan, Sapphire; University of Cambridge Pembroke College Lee, Si Jia; Singapore General Hospital, Department of Anaesthesiology Rahmatullah Bin Abd Razak, Hamid; Singapore General Hospital, Department of Orthopaedic Surgery Seet, Rachel; Singapore General Hospital, Department of Anaesthesiology Ying, Hao; Singapore General Hospital, Health Services Research Unit Sethi, Ervin; Singapore General Hospital, Department of Orthopaedic Surgery Sim, Eileen; Singapore General Hospital, Department of Anaesthesiology
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Geriatric medicine, Mental health, Anaesthesia
Keywords:	postoperative, delirium, total joint arthroplasty, incidence

TITLE

Protocol for a Single-Centre Prospective Observational Study of Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

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Word count: 3421

Keywords: postoperative, delirium, total joint arthroplasty, incidence

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ABSTRACT

Introduction

Postoperative delirium is a serious and common complication in older adults following Total Joint Arthroplasties (TJA). It is associated with increased risk of postoperative complications, mortality, length of hospital stay and postdischarge institutionalisation. Thus, it has a negative impact on the health-related quality of life of the patient and poses a large economic burden. This study aims to characterise the incidence of postoperative delirium following TJA in the South East Asian population, and investigate any risk factors or associated outcomes.

Methods and analysis

This is a single-centre prospective observational study, recruiting patients between 65 and 90 years old undergoing elective Total Knee Arthroplasty or Total Hip Arthroplasty. Exclusion criteria included patients with clinically diagnosed dementia. Preoperative and intraoperative data will be obtained prospectively. The primary outcome will be the presence of postoperative delirium assessed using the Confusion Assessment Method on postoperative day 1, 2, 3 and day-of-discharge. Other secondary outcomes assessed postoperatively will include hospital outcomes, pain at rest, knee and hip function, health-related quality of life and POMS-defined morbidity. Data will be analysed to calculate the incidence of postoperative delirium. Potential risk factors and any associated outcomes of postoperative delirium will also be determined.

Ethics and dissemination

This study has been approved by the Singapore General Hospital Institutional Review Board (SGH IRB) (CIRB Ref: 2017/2467) and is registered on the ClinicalTrials.gov registry (Identified: NCT03260218). An informed consent form will be signed by all participants before recruitment and translators will be made available to non-English speaking participants. The results of this study will be presented at international conferences and submitted to a peer-reviewed journal. The data collected will also be made available in a public data repository.

STRENGTHS AND LIMITATIONS

Strengths

1. This study is the first to evaluate the incidence of postoperative delirium in the elderly above 65 years old following TKA and THA in Singapore.
2. Association of variables to occurrence of postoperative delirium that have not been well studied such as hand grip strength, STOP-Bang score and long-term outcomes including knee function and HRQoL will be analysed.
3. The Confusion Assessment Method (CAM) will be used, which is a gold standard measure for detection of delirium.

Limitations

1. The study is conducted in a single centre in Singapore which may limit the generalisability of the results of the study.
2. Delirium will be only assessed once a day, and the presence of delirium may be missed due to the fluctuating nature of the condition.

INTRODUCTION

Delirium is a neurocognitive disorder characterised by a disturbance in attention, level of consciousness and cognition, in which symptoms are acute in onset and may fluctuate in severity throughout the day[1]. Delirium is a common perioperative complication in older adults following total joint arthroplasty (TJA). The incidence of postoperative delirium following TJA may be as high as 17%[2], although there is no data from the South-East Asian population, exposing a knowledge gap.

Patients with delirium after any surgery have an increased risk of major postoperative complications and increased mortality[3,4]. They also experience significantly longer hospital stay and are at increased risk of subsequent postdischarge institutionalisation[4–6], which increases total procedural cost[7]. With the demand of total hip arthroplasty (THA) expected to rise by almost 2-fold and that for total knee arthroplasty (TKA) by almost 7-fold by 2030[8], postoperative delirium is likely to become a significant health and economic burden. However, the impact of delirium on outcomes after TJA have not been well reported, identifying a potential knowledge gap. Furthermore, due to these various negative outcomes of postoperative delirium, it is important to characterise the risk factors associated with postoperative delirium. Older age has been reported as one of the most important risk factor for developing postoperative delirium[9,10]. According to an existing study, the average age of the population undergoing TJA is 71 years, and majority of patients are 65 years or older (81.3% for TKR and 69.5% for THR)[7]. Thus, the population under study particularly at risk to postoperative delirium. Other important predisposing risk factors include pre-existing cognitive impairment, poor physical status, alcohol abuse [5,9,10]. While these are common risk factors for the TJA population, few studies have investigated if these risk factors also predispose to postoperative delirium following TJA specifically. There is a need to investigate the presence of other risk factors particular to TJA, especially if any are modifiable. As most of such operations are elective, there may be an opportunity to address the modifiable risk factors to optimise the patient prior to the surgery or to implement perioperative management strategies to mitigate the negative outcomes of postoperative delirium.

Given the limited knowledge on the incidence, risk factors and outcomes of postoperative delirium in the South East Asian population, together with the increasing number of older adults undergoing TJA, this study's primary aim is to characterise the incidence of delirium among older adults undergoing elective TJA. Our secondary aim is to identify risk factors of postoperative delirium following elective TJA among the elderly, including demography, comorbidities, clinical laboratory data and drugs used in the perioperative period. Our final aim is to investigate the impact of postoperative delirium on the immediate and longer term postoperative recovery after TJA. Identifying such risk factors and associated clinical or functional outcomes may be important in guiding perioperative care of prospective patients undergoing TJA.

METHODS AND ANALYSIS

Study design

Institutional Review Board approval was obtained (Singhealth CIRB 2017/2467) prior to starting the study. This is a single centre, prospective observational study conducted at a tertiary public hospital in Singapore (Singapore General Hospital (SGH)). SGH is the largest hospital in Singapore with 1,597 beds in 2013[11]. 1,500 TKA surgeries were performed in SGH in 2007, accounting for 65% of all TKA surgeries in Singapore[12].

Study population

Patients aged between 65 and 90 undergoing elective total joint (hip or knee) replacement surgery in Singapore General Hospital will be screened for eligibility. A minimum age of 65 years old was chosen to be recruited based on the original study which developed and validated CAM[13]. Exclusion criteria includes patients who are unable to give their own consent for the surgery and anaesthesia. Patients with clinically diagnosed dementia will also be excluded from the study as they are deemed not to have capacity for consent.

All eligible patients will be identified from the appointment list of attendees of the preoperative evaluation clinic (PEC) at SGH where the patients attend for preoperative assessment and counselling by the anaesthetists. Patients between 65 and 90 years old undergoing TKA or THA will be approached and invited to enrol into the study. Informed consent will be obtained then.

Preoperative data

We will collect the patients' baseline characteristics preoperatively. This will allow for the identification of risk factors or correction of confounding factors during analysis of the results.

Data on cognitive status

Before the operation, each patient will be interviewed to assess their baseline cognitive status. The Mini–Mental State Examination (MMSE) will be used, which is a 11-question screening tool used to evaluate the cognitive aspects of mental function[14]. It measures domains of cognitive function including memory, attention, language, praxis and visuospatial ability. A score of 0-30 can be obtained with higher values denoting better cognitive function. A score of <24 suggests cognitive impairment. The test was adapted for use in Singapore, and the changes and reasons for the changes shown in the table in Supplementary file 1. In addition, the test will be administered in English, Chinese or Malay, according to the language the participant is most well-versed in. The Chinese version of MMSE that will be used was previously validated in Shanghai[15] and in Singapore[16]. The Malay version of MMSE that will be used was developed by translation from the English version. The Chinese and Malay versions of MMSE have similar test questions and are scored the same way as the English version, but there some differences shown in Supplementary file 2. However, a recent study in Singapore has shown that there were significant ethnic differences in unadjusted MMSE scores using the different versions of MMSE. These differences were not eliminated after accounting for known correlates of MMSE performance such as

socioeconomic status, comorbid illnesses, functional health status, and health-related behaviours[17].

The Confusion Assessment Method (CAM) will also be performed prior to the operation to obtain the patient's baseline score. CAM is a screening instrument for delirium intended for use by non-psychiatrically-trained clinicians based on the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III-R criteria[18]. It involves an interview whereby delirium can be diagnosed using the CAM algorithm based on 4 criteria – (1) acute onset or fluctuating course, (2) inattention, (3) disorganised thinking and (4) altered level of consciousness, as can be seen in Figure 1. Delirium is said to be present if criteria 1 and 2 and either of 3 or 4 are present. CAM has a sensitivity of 94-100%, specificity of 90-95%, and high inter-observer reliability[13]. This enables a new case of delirium in the postoperative period to be detected.

Other data

Sensory impairment will be assessed during the preoperative interviews. Patients will be asked to wear their visual or hearing aids during these interviews. A patient will be considered to have visual or hearing impairment if the research member conducting the interview is unable to perform the interview normally due to the sensory impairment, such as raising his/her voice for a patient with impaired hearing. The preoperative MMSE assessment provides a useful tool in assessing for visual impairment as it has several vision-dependent items (naming objects, following a written command, instructions to handle a piece of paper, writing a sentence, copying a diagram)[19].

The grip strength of each patient will also be measured using the JAMAR® Plus+ Digital Hand Dynamometer (Sammons Preston Inc, Bolingbrook, IL). Hand dynamometry has acceptable reliability and validity for measurement of grip strength[20], which can serve as an indicator of muscle function and physical fitness. The normative value of hand grip strength for elderly in Singapore has recently been published, decreasing from 18.6kg and 29.3kg for females and males respectively in the 65-69 age group to 12.4kg and 18.5kg in the 85+ age group[21].

The patient baseline characteristics will be obtained from the medical records. All perioperative data will be prospectively entered into the REDCap™ database. This will include data regarding patient's demographics, smoking history, alcohol history, pre-existing medical conditions, preoperative medications.

Each patient will also be rated preoperatively by an anaesthesiologist in the PEC based on the American Society of Anaesthesiologists (ASA) physical status classification[22]. It is a scale from 1 to 5, where 1 represents a completely healthy fit patient and 5 representing a moribund patient who is not expected to live 24 hours with or without surgery. For our analysis, we will be calculating each patient's perioperative risk based on the Charlson Comorbidity Index (CCI)[23]. 19 different comorbid medical conditions are assigned weights of 1, 2, 3 and 6 according to the degree to which they predicted mortality, and the sum of these values gives the final score. It is a valid method of estimating risk of mortality resulting from comorbidities[24]. The STOP-Bang score will also be calculated for each patient. The STOP-Bang questionnaire was a good screening tool for diagnosing obstructive sleep apnoea, with a sensitivity of 89.0% and accuracy of 79.1%[25]. Preoperative laboratory results, including data about haemoglobin or creatinine level, will also be collected.

Preoperative baseline functional scores for TKA (Oxford Knee Score, Knee Society Functional Score and Knee Society Knee Score) and for THA (Harris Hip Score and Parker Mobility Score) will be obtained from the patient by trained staff at the Orthopaedic Diagnostic Centre (ODC). These assessments will be further discussed in the "Postoperative data" section.

The preoperative data collection form (DCF) can be seen in Supplementary file 3.

Intraoperative data

Data regarding the surgery will be collected. Intraoperative data includes type of arthroplasty performed (TKA or THA), type of anaesthesia (spinal, general or other anaesthesia), use of femoral nerve block, intraoperative drug use, tourniquet time, intra-articular injections and blood transfusion (number of pints transfused). Occurrence of hypotension, which is defined as a mean arterial pressure <60mmHg, and its duration will also be recorded.

Postoperative data

Primary outcome

The primary outcome will be the presence of postoperative delirium following TJA. Each patient will be assessed for delirium on postoperative day (POD) 1, 2 and 3 in the wards at 7am as well as the day of discharge. Delirium will not be evaluated on POD 0 due to difficulty in differentiating delirium from the effects of residual anaesthesia.

CAM will be used to detect postoperative delirium and delirium severity. Delirium is said to be present if the patient meets the CAM criteria for any of the postoperative assessments. Patients assessed to have delirium will be referred to the psychiatrists for a formal diagnosis based on the DSM-V criteria and for further management.

Short-term secondary outcomes

Postoperative complications will be assessed by the Postoperative Morbidity Survey (POMS). This is a 9-point survey that can be easily used by clinicians to characterise short-term postoperative morbidity in their respective settings[26]. It is designed to only identify morbidity of a type and severity that could prolong length of stay (LOS). Using POMS, postoperative morbidity outcomes can be dichotomised into 2 categories – the absence and presence of morbidity. The POMS instrument can be seen in Supplementary file 4 attached. POMS will be assessed on POD 3, 5, 8 and 15, as recommended by the original literature[26]. It has also been reported to have good inter-rater reliability and acceptability to patients[27].

Other postoperative outcomes that will be obtained include postoperative nausea and vomiting (PONV), LOS and 30-day readmission rates. 30-day readmission is defined as readmission within 30 days of initial admission. The reason for readmission will also be obtained.

Long-term secondary outcomes

Longer-term outcomes such as functional and health-related quality-of-life (HRQoL) outcomes will also be recorded by the ODC total joint registry at 6 months, 1 year, 2 years

and 5 years postoperatively. The ODC tracks clinical outcome measures during pre- and postoperative functional assessments of the patients in SGH. Their total joint registry contains data about outcomes from knee and hip arthroplasties.

For patients undergoing TKA, knee function will be measured using the new Knee Society Knee Score (KSKS) and Function Score (KSFS)[28]. The physician-derived KSKS measures alignment, stability, joint motion and symptoms experienced. The patient-derived KSFS evaluates use of walking aids and supports, ability to complete standard activities of daily living and discretionary activities. The KSKS and KSFS each range from 0 (worst) to 100 (best). Both provide a validated rating of the functional outcome of the patient and knee prosthesis after TKA[29]. In addition, the Oxford Knee Score (OKS)[30] will also be used, which is a 12-item, patient-assessed questionnaire designed specifically for use in patients undergoing TKA [7]. It assesses an individual's pain and physical disability. Each item is scored from 1 (least difficulty/severity) to 5 (most difficulty/severity), and individual item scores are summed to yield an overall score ranging from 12 (no pain or limitation) to 60 (severe pain or limitation). A lower OKS indicates a better outcome. It has good reliability, construct and content validity, and sensitivity to clinically important changes over time[30,31]. It correlates strongly with pain but less with postoperative functioning[32].

For patients undergoing THA, hip function will be measured using the Harris Hip Score (HHS)[33]. The HHS is a clinician-based tool to assess the outcomes of hip surgery such as THA. It contains 4 subscales – pain severity, function, absence of deformity and range of motion. The total score ranges from 0 (worst) and 100 (best). It showed high validity and reliability when used to study the clinical outcome of THA[34]. Hip function will also be measured using the Parker Mobility Score (PMS)[35]. A score of 1 represents a patient who does not require a walking aid and has no restriction in walking distance, while a score of 10 represents a patient who is mostly bedbound. It is reliable and a valid predictor of in-hospital and long-term outcomes[35–37]. Outcomes for THA will only be recorded at 6 months and 2 years, unlike the other long-term secondary outcomes.

HRQoL will be assessed based on the 36-Item Short Form Health Survey (SF-36)[38] to obtain a baseline score. It consists of 36 questions categorised into 8 domains (physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions). This instrument is shown in Supplementary file 5. Higher scores indicate better health status and quality of life.

Days alive and out of hospital (DAOH) will also be determined for each patient at 1 month, 6 months and 12 months to assess overall impact of postoperative delirium on morbidity and mortality. DAOH will be calculated based on death date (if present) and duration of all subsequent hospitalisations until the follow-up date. This will be recorded as a percentage by dividing DAOH by total potential follow-up period, which is the time period between the operation and the respective dates of follow-up (1 month, 6 months and 12 months). %DAOH is a useful measure as it emphasises the deaths occurring early in follow-up and takes into account the severity (duration) of any hospitalisation.[39]

Postoperative risk factors

Other postoperative data will be collected as variables for risk factors.

Postoperative pain at rest will be evaluated using the pain Visual Analog Scale (VAS) during the same visit as CAM on POD 1, 2 and 3. Each patient will score pain experienced at rest on a scale, with 0 = no pain and 10 = maximum pain.

Sensory impairment will also be assessed during the postoperative interviews similar to the preoperative assessments.

The postoperative DCF can be seen in Supplementary file 6.

The flowchart shown in Figure 2 depicts a patient's journey starting from enrolment in the PEC.

Data management

Patient data will be kept confidential throughout the study. All electronic study data entry, storage and analysis will be done according to institutional data security policy, using password protected data in secure systems.

The patient data collected will be de-identified and the key kept securely separated with access limited to principal investigator and co-investigators. A study-related identification number given to each patient will be used on the case report form. Research members will enter the de-identified data into the REDCap™ (Research Electronic Data Capture) tool hosted on a secure server at Singapore General Hospital[36]. The hardcopy of the research data will be securely stored within the department. The softcopy of research data will be saved in a password-protected file and will be stored in institution approved login-protected system and encrypted hard-drive. Only study members will have access to the data.

Power and sample size calculations

The primary aim of the study is to characterise the incidence of postoperative delirium following TJA, which is estimated at around 10% based on existing literature[2]. Using this estimate, 150 patients are enough to detect the incidence with a precision of 5% and confidence level of 95%.

However, this study will also aim to detect potential factors which may be correlated to postoperative delirium by logistic regression. Thus, we will target to recruit 500 patients such that we are able to investigate the risk factors and associated outcomes of postoperative delirium using multiple logistic models while minimising the limitation of a small number of events of postoperative delirium.

Statistical analyses

The incidence of postoperative delirium following TJA using the standard formula – the number of patients diagnosed to have postoperative delirium divided by the total number of patients in the study, and the result expressed as a percentage.

Potential risk factors of postoperative delirium will also be identified by comparing the perioperative data recorded between the patients with and without postoperative delirium. Data will first be summarised using descriptive statistics including mean, standard deviation

(SD), median, range and frequency tables. Univariate analyses will then be used identify the differences between the two groups. Data of continuous variables will be compared using the Student's t-test (normally distributed data) or the Wilcoxon rank sum test (not normally distributed data). Data of categorical variables will be compared by Pearson Chi-square test or Fisher's exact test.

The variables which are statistically significant or close to significant (p value <0.05 or <0.1) between the two groups of patients will then be selected for inclusion in a multivariate logistic regression model. This will determine the independent predictors of postoperative delirium. The final model will be determined by sensitivity analysis. The sensitivity analysis can help us to understand the contribution of each parameter to the model outputs, investigate which parameter will have the biggest influence and then refine the model to obtain the final model which is statistically and clinically meaningful. Odds ratio (OR) will be used to describe the correlation of them with postoperative delirium.

Postoperative outcomes which are associated with the incidence of postoperative delirium will also be examined by comparing patients with and without postoperative delirium. The postoperative POMS score, incidence of PONV, LOS, incidence of 30-day readmission and %DAOH will be similarly compared using Student's t-test and Pearson Chi-square tests as appropriate.

For the long-term postoperative outcomes, the median postoperative SF-36 for each domain, KSKS, KSFS, OKS, HHS and PMS scores applicable at 6 months, 1 year, 2 years and 5 years will be compared to the median preoperative baseline scores using the Wilcoxon matched pairs sign rank test. The tests with a change greater than the minimally clinically important difference (MCID) will be identified. The MCID values for each test will be obtained from the pre-existing literature. These variables will then be analysed by analysis of covariance (ANCOVA) to identify predictors of the long-term postoperative test scores. All predictor variables will be incorporated into the multivariate ANCOVA model. Analyses will be performed separately for the various tests that demonstrated changes greater than MCID.

ETHICS AND DISSEMINATION

This study has been approved by the Singapore General Hospital Institutional Review Board (SGH IRB) (CIRB Ref: 2017/2467) and is registered on the ClinicalTrials.gov registry (Identified: NCT03260218). In the event of any important protocol modifications, all investigators, SGH IRB and trial participants will be notified.

The results of this study will be presented at international conferences and submitted to a peer-reviewed journal. The data collected will also be made available in a public data repository.

All eligible participants will be approached by the research assistant during their visit to the preoperative evaluation clinic. They will be given an explanation about the study, a patient information sheet and a consent form. They will then be given an ample time to consider if they would like to participate in the study. They will also be allowed to ask questions freely. If the participant expresses an interest to participate in the study, a written consent will be obtained. The consent forms are in English. However, participants from non-English speaking backgrounds will be provided a translator. For illiterate participants, an accompanying family member will be approached to verify and witness the consent process.

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FUNDING STATEMENT

This work was supported by the Singhealth Duke-NUS Academic Medical Centre Nurturing Clinician Scientists Scheme Award, project number 12/FY2017/P1/15-A29. This funding source, Singhealth Duke-NUS Academic Medical Centre, has no role in the design of this study and will not have a role in the analysis and interpretation of the results.

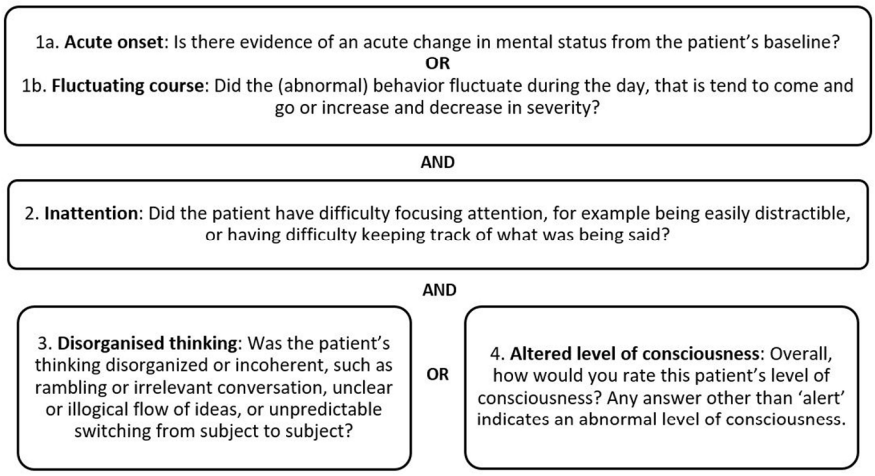
COMPETING INTEREST STATEMENT

None.

FIGURE LEGENDS

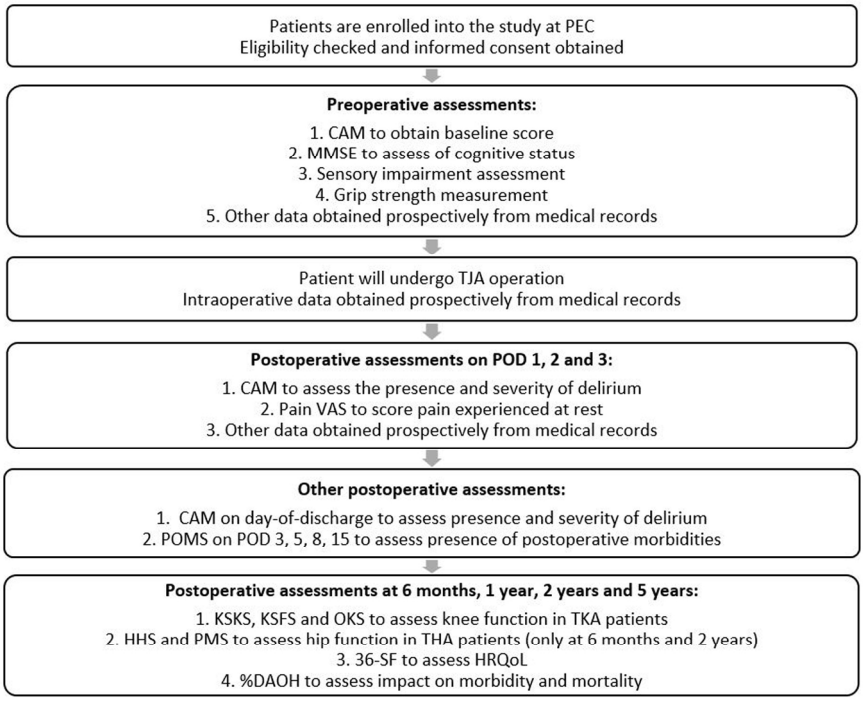
Figure 1. CAM criteria: at least one criteria on each of the 3 rows must be met for a positive result.

Figure 2. Flowchart depicting a patient's timeline during the study.



CAM criteria: at least one criteria on each of the 3 rows must be met for a positive result

240x129mm (300 x 300 DPI)



Caption : Flowchart depicting a patient's timeline during the study

180x140mm (300 x 300 DPI)

Item no.	Original version	Adapted version	Reasons
1	"What is the season?"	Without looking at your watch, what time is it?"	There are no seasons in Singapore.
2a	"What county are we in?";	"What area/street are we in?";	Singapore is a city country; "Singapore" would only the only correct answer.
2b	"What town/city are we in?"	"Which part of Singapore (North/South/East/West) are we in?"	Singapore is a city country; "Singapore" would only the only correct answer.

Item no.	English version	Chinese version	Malay version
4	Spell the word “WORLD” backwards	请把这句话倒说一遍 – “天上有月亮“	Terbalikkan ejaan “DUNIA”
7	Repeat the following – “no ifs, ands, or buts”	请清除的重复一遍 – “四十四只石狮子“	Ulangan perkataan – “da dahulu, kini dan selamanya”

Preoperative DCF

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of preoperative assessment:

_____

DEMOGRAPHIC

Age: _____

Gender: Male ☐ Female ☐

Race: Chinese ☐ Malay ☐ Indian ☐ Others ☐

Language:

English ☐ Mandarin ☐ Malay ☐

Others _____

Highest education completed:

_____

Height: _____ m

Weight: _____ kg

BMI: _____

OP DETAILS

Surgeon:

_____

Type of Operation:

TKR ☐ THR ☐

Unilateral L ☐/ R ☐ OR Bilateral ☐

Primary ☐ Revision ☐

Pre-operative Dx:

_____

_____

_____

_____

Grip Strength: _____

BACKGROUND MEDICAL CONDITION

ASA: _____

Charlson Comorbidity Index

Overall score: _____

CVS	
☐	Myocardial infarction
☐	Congestive heart failure
☐	Peripheral vascular disease
CNS	
☐	Cerebrovascular disease
☐	Hemiplegia or paraplegia
☐	Dementia
Respi	
☐	Chronic pulmonary disease
MSK	
☐	Rheumatologic disease
GI	
☐	Peptic ulcer disease
☐	Mild liver disease
☐	Moderate or severe liver disease
Endocrine	
☐	Diabetes without chronic complications

Smoking ☐

Alcoholism ☐

Diabetes:

OHGA ☐ Insulin ☐

Latest HbA1c _____

Chronic kidney disease ☐

Pre-existing dementia ☐

Other pre-existing neurological problems

☐ CVA

☐ Parkinson Disease

☐ Depression

☐ Anxiety

☐ Schizophrenia and other delusional disorders

Visual impairment ☐

Hearing impairment ☐

STOPBANG score _____

Chronic Medications

Benzodiazepine ☐

Statin ☐

Tramadol ☐ Oxynorm ☐

Anti-depressants

Tricyclics ☐ SSRI ☐ SNRI ☐

MOAI ☐

Anti-psychotics

☐	Diabetes with chronic complications
Renal	
☐	Mild Renal disease
☐	Moderate or severe renal disease
Malignancy	
☐	Any malignancy, including leukemia and lymphoma
☐	Non-metastatic solid tumour
☐	Metastatic solid tumor
Immunological	
☐	AIDS/HIV

IntraOp

ANA Type: _____

	Yes	No
Fem N block	☐	☐
Benzo Use:	☐	☐
Atropine Use:	☐	☐
Opioid use **If yes , dose: _____**	☐	☐
Dexa use **If yes , dose: _____**	☐	☐
Promethazine use:	☐	☐
Ondansetron:	☐	☐
Blood Transfusion	☐	☐
Hypotension **If yes, duration: _____**	☐	☐

Haloperidol ☐ Quetiapine ☐
Olanzapine ☐ Clozapine ☐

Preoperative Laboratory Results
Hemoglobin _____
MCV _____
RDW _____
MCV _____
MCHC _____
Urea _____

BASELINE CAM

1. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐

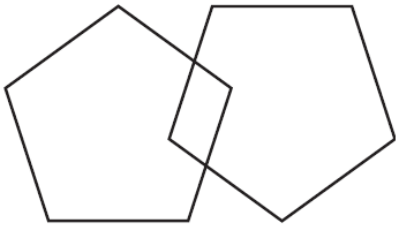
b. Yes – marked form ☐, fluctuating ☐
c. Uncertain _____
d. No ☐

4. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

BASELINE MINI MENTAL STATE EXAMINATION

Total score _____
Level of consciousness
Alert ☐ Drowsy ☐ Stupor ☐ Coma ☐

	Question	Score
1	What is the • year • month • day of the week • date • current time now (without looking at your watch)?	/ 5
2	What country are we in? What area/street are we in? Which part of Singapore is this place (North, south, east, west or central) Which hospital are we in? Which floor?	/ 5
3	Show the objects: ball, flag, tree Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials _____	/ 3
4	Serial 7's. 1 point for each correct answer. Stop after 5 answers. Alternatively spell "world" backward.	/ 5
5	Ask for the 3 objects repeated above. Give 1 point for each correct answer.	/ 3
6	Name a pencil and watch. Repeat the following "No ifs, ands, or buts" Follow a 3-stage command: "Take a paper in your hand, fold it in half, and put it on the floor." Read and obey the following: CLOSE YOUR EYES	/ 2 / 1 / 3 / 1 / 1

	Write a sentence.	/ 1
	Copy the design shown 	/ 1

Postoperative Morbidity Survey

Morbidity type	Criteria	Source of data
Pulmonary	Has the patient developed a new requirement for oxygen or respiratory support.	Patient observation Treatment chart
Infectious	Currently on antibiotics and/or has had a temperature of >38°C in the last 24 hr.	Treatment chart Observation chart
Renal	Presence of oliguria <500 mL/24 hr; increased serum creatinine (>30% from preoperative level); urinary catheter in situ.	Fluid balance chart Biochemistry result Patient observation
Gastrointestinal	Unable to tolerate an enteral diet for any reason including nausea, vomiting, and abdominal distension (use of antiemetic).	Patient questioning Fluid balance chart Treatment chart
Cardiovascular	Diagnostic tests or therapy within the last 24 hr for any of the following: new myocardial infarction or ischemia, hypotension (requiring fluid therapy >200 mL/hr or pharmacological therapy), atrial or ventricular arrhythmias, cardiogenic pulmonary edema, thrombotic event (requiring anticoagulation).	Treatment chart Note review
Neurological	New focal neurological deficit, confusion, delirium, or coma.	Note review Patient questioning
Hematological	Requirement for any of the following within the last 24 hr: packed erythrocytes, platelets, fresh-frozen plasma, or cryoprecipitate.	Treatment chart Fluid balance chart
Wound	Wound dehiscence requiring surgical exploration or drainage of pus from the operation wound with or without isolation of organisms.	Note review Pathology result
Pain	New postoperative pain significant enough to require parenteral opioids or regional analgesia.	Treatment chart Patient questioning

36-Item Short Form Health Survey

RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:
   - ○ 1 – Excellent
   - ○ 2 - Very good
   - ○ 3 – Good
   - ○ 4 – Fair
   - ○ 5 – Poor

2. **Compared to one year ago**, how would you rate your health in general now?
   - ○ 1 - Much better now than one year ago
   - ○ 2 - Somewhat better now than one year ago
   - ○ 3 - About the same
   - ○ 4 - Somewhat worse now than one year ago
   - ○ 5 - Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	○ 1	○ 2	○ 3
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	○ 1	○ 2	○ 3
5. Lifting or carrying groceries	○ 1	○ 2	○ 3
6. Climbing **several** flights of stairs	○ 1	○ 2	○ 3
7. Climbing **one** flight of stairs	○ 1	○ 2	○ 3
8. Bending, kneeling, or stooping	○ 1	○ 2	○ 3
9. Walking **more than a mile**	○ 1	○ 2	○ 3
10. Walking **several blocks**	○ 1	○ 2	○ 3
11. Walking **one block**	○ 1	○ 2	○ 3
12. Bathing or dressing yourself	○ 1	○ 2	○ 3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	Yes	No
13. Cut down the amount of time you spent on work or other activities	○ 1	○ 2
14. Accomplished less than you would like	○ 1	○ 2
15. Were limited in the kind of work or other activities	○ 1	○ 2
16. Had difficulty performing the work or other activities (for example, it took extra effort)	○ 1	○ 2

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	Yes	No
17. Cut down the **amount of time** you spent on work or other activities	○ 1	○ 2
18. **Accomplished less** than you would like	○ 1	○ 2
19. Didn't do work or other activities as **carefully** as usual	○ 1	○ 2

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?
    - ○ 1 - Not at all
    - ○ 2 - Slightly
    - ○ 3 - Moderately
    - ○ 4 - Quite a bit
    - ○ 5 – Extremely

21. How much **bodily** pain have you had during the **past 4 weeks**?
    - ○ 1 - None
    - ○ 2 - Very mild
    - ○ 3 - Mild
    - ○ 4 - Moderate
    - ○ 5 - Severe
    - ○ 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?
    - ○ 1 - Not at all

- ○ 2 - A little bit
- ○ 3 - Moderately
- ○ 4 - Quite a bit
- ○ 5 – Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
24. Have you been a very nervous person?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
25. Have you felt so down in the dumps that nothing could cheer you up?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
26. Have you felt calm and peaceful?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
27. Did you have a lot of energy?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
28. Have you felt downhearted and blue?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
29. Did you feel worn out?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
30. Have you been a happy person?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
31. Did you feel tired?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?
    - ○ 1 - All of the time
    - ○ 2 - Most of the time
    - ○ 3 - Some of the time
    - ○ 4 - A little of the time
    - ○ 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	○ 1	○ 2	○ 3	○ 4	○ 5
34. I am as healthy as anybody I know	○ 1	○ 2	○ 3	○ 4	○ 5
35. I expect my health to get worse	○ 1	○ 2	○ 3	○ 4	○ 5
36. My health is excellent	○ 1	○ 2	○ 3	○ 4	○ 5

This tool was developed at RAND Health as part of the Medical Outcomes Study.

Postoperative DCF

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians	
Serial No: _____ Date of surgery: _____ Type of surgery: _____ Date of assessment: _____	**POD1**

CAM ASSESSMENT

1. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
4. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

VISUAL/HEARING IMPAIRMENT	**PERIOPERATIVE DETAILS**
Visually impaired ☐ Hearing impaired ☐ If yes to above, hearing aids? ☐	Tourniquet time: _____ minutes Intra-articular injections: (i) Tranexamic acid ☐ Dosage: (ii) Morphine ☐ Dosage:

	(iii) Marcaine ☐ Dosage: (iv) Adrenaline ☐ Dosage: (v) Ketorolac ☐ Dosage: (vi) Triamcinolone ☐ Dosage: (vii) Vancomycin ☐ Dosage: (viii) Normal Saline ☐ Dosage: (ix) Others: _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

POD2

CAM ASSESSMENT

5. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
6. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
7. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
8. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

POD3

CAM ASSESSMENT

1. Acute onset change in mental status from baseline?
    a. Yes ☐
    b. No ☐
    c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
4. How is the patient's overall level of consciousness?
    a. Alert (normal) ☐
    b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
    c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
    d. Stupor (Difficult to arouse) ☐, fluctuating ☐
    e. Coma (Unarousable) ☐, fluctuating ☐
    f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No:
_____

Date of surgery:
_____

Type of surgery:
_____

Date of assessment:
_____

DAY OF DISCHARGE

POSTOPERATIVE MORBIDITY SURGERY

Morbidity Type	Criteria	Tick if present ( )
Pulmonary	De novo requirement for supplemental oxygen or other respiratory support (e.g. mechanical ventilation or CPAP)	
Infectious	Currently on antibiotics or temperature > 38°C in the last 24h	
Renal	Presence of oliguria (< 500 ml/day), elevated serum creatinine (> 30% from preoperative value), or urinary catheter in place for a nonsurgical reason	
Gastrointestinal	Unable to tolerate an enteral diet (either by mouth or via a feeding tube) for any reason, including nausea, vomiting, and abdominal distension	
Cardiovascular	Diagnostic tests or therapy within the last 24h for any of the following: de novo myocardial infarction or ischaemia, hypotension (requiring pharmacologic therapy or fluid therapy > 200ml/h), atrial or ventricular arrhythmias, or cardiogenic pulmonary edema	
Neurologic	Presence of a de novo focal deficit, coma or confusion and delirium	
Wound complication	Wound dehiscence requiring surgical exploration or drainage of pus from the operation wound, with or without isolation of organisms	
Haematologic	Requirement for any of the following within the last 24h: packed erythrocytes, platelets, fresh-frozen plasma, or cryoprecipitate	
Pain	Surgical wound pain significant enough to require parenteral opiates or regional analgesia	

CPAP: continuous positive airway pressure

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page Number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-13
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-13
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	13-14
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	14
		(*b*) Describe any methods used to examine subgroups and interactions	14
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	14
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	-
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	-
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	Report numbers of outcome events or summary measures over time	-
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	-

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	-
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	-
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	-
Generalisability	21	Discuss the generalisability (external validity) of the study results	-
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Protocol for a Single-Centre Prospective Observational Study of Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019426.R2
Article Type:	Protocol
Date Submitted by the Author:	26-Jan-2018
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Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Geriatric medicine, Mental health, Anaesthesia
Keywords:	postoperative, delirium, total joint arthroplasty, incidence

TITLE

Protocol for a Single-Centre Prospective Observational Study of Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

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Word count: 3421

Keywords: postoperative, delirium, total joint arthroplasty, incidence

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ABSTRACT

Introduction

Postoperative delirium is a serious and common complication in older adults following Total Joint Arthroplasties (TJA). It is associated with increased risk of postoperative complications, mortality, length of hospital stay and postdischarge institutionalisation. Thus, it has a negative impact on the health-related quality of life of the patient and poses a large economic burden. This study aims to characterise the incidence of postoperative delirium following TJA in the South East Asian population, and investigate any risk factors or associated outcomes.

Methods and analysis

This is a single-centre prospective observational study, recruiting patients between 65 and 90 years old undergoing elective Total Knee Arthroplasty or Total Hip Arthroplasty. Exclusion criteria included patients with clinically diagnosed dementia. Preoperative and intraoperative data will be obtained prospectively. The primary outcome will be the presence of postoperative delirium assessed using the Confusion Assessment Method on postoperative day 1, 2, 3 and day-of-discharge. Other secondary outcomes assessed postoperatively will include hospital outcomes, pain at rest, knee and hip function, health-related quality of life and POMS-defined morbidity. Data will be analysed to calculate the incidence of postoperative delirium. Potential risk factors and any associated outcomes of postoperative delirium will also be determined.

Ethics and dissemination

This study has been approved by the Singapore General Hospital Institutional Review Board (SGH IRB) (CIRB Ref: 2017/2467) and is registered on the ClinicalTrials.gov registry (Identified: NCT03260218). An informed consent form will be signed by all participants before recruitment and translators will be made available to non-English speaking participants. The results of this study will be presented at international conferences and submitted to a peer-reviewed journal. The data collected will also be made available in a public data repository.

STRENGTHS AND LIMITATIONS

Strengths

1. This study is the first to evaluate the incidence of postoperative delirium in the elderly above 65 years old following TKA and THA in Singapore.
2. Association of variables to occurrence of postoperative delirium that have not been well studied such as hand grip strength, STOP-Bang score and long-term outcomes including knee function and HRQoL will be analysed.
3. The Confusion Assessment Method (CAM) will be used, which is a gold standard measure for detection of delirium.

Limitations

1. The study is conducted in a single centre in Singapore which may limit the generalisability of the results of the study.
2. Delirium will be only assessed once a day, and the presence of delirium may be missed due to the fluctuating nature of the condition.

INTRODUCTION

Delirium is a neurocognitive disorder characterised by a disturbance in attention, level of consciousness and cognition, in which symptoms are acute in onset and may fluctuate in severity throughout the day[1]. Delirium is a common perioperative complication in older adults following total joint arthroplasty (TJA). The incidence of postoperative delirium following TJA may be as high as 17%[2], although there is no data from the South-East Asian population, exposing a knowledge gap.

Patients with delirium after any surgery have an increased risk of major postoperative complications and increased mortality[3,4]. They also experience significantly longer hospital stay and are at increased risk of subsequent postdischarge institutionalisation[4–6], which increases total procedural cost[7]. With the demand of total hip arthroplasty (THA) expected to rise by almost 2-fold and that for total knee arthroplasty (TKA) by almost 7-fold by 2030[8], postoperative delirium is likely to become a significant health and economic burden. However, the impact of delirium on outcomes after TJA have not been well reported, identifying a potential knowledge gap. Furthermore, due to these various negative outcomes of postoperative delirium, it is important to characterise the risk factors associated with postoperative delirium. Older age has been reported as one of the most important risk factor for developing postoperative delirium[9,10]. According to an existing study, the average age of the population undergoing TJA is 71 years, and majority of patients are 65 years or older (81.3% for TKR and 69.5% for THR)[7]. Thus, the population under study particularly at risk to postoperative delirium. Other important predisposing risk factors include pre-existing cognitive impairment, poor physical status, alcohol abuse [5,9,10]. While these are common risk factors for the TJA population, few studies have investigated if these risk factors also predispose to postoperative delirium following TJA specifically. There is a need to investigate the presence of other risk factors particular to TJA, especially if any are modifiable. As most of such operations are elective, there may be an opportunity to address the modifiable risk factors to optimise the patient prior to the surgery or to implement perioperative management strategies to mitigate the negative outcomes of postoperative delirium.

Given the limited knowledge on the incidence, risk factors and outcomes of postoperative delirium in the South East Asian population, together with the increasing number of older adults undergoing TJA, this study's primary aim is to characterise the incidence of delirium among older adults undergoing elective TJA. Our secondary aim is to identify risk factors of postoperative delirium following elective TJA among the elderly, including demography, comorbidities, clinical laboratory data and drugs used in the perioperative period. Our final aim is to investigate the impact of postoperative delirium on the immediate and longer term postoperative recovery after TJA. Identifying such risk factors and associated clinical or functional outcomes may be important in guiding perioperative care of prospective patients undergoing TJA.

METHODS AND ANALYSIS

Study design

Institutional Review Board approval was obtained (Singhealth CIRB 2017/2467) prior to starting the study. This is a single centre, prospective observational study conducted at a tertiary public hospital in Singapore (Singapore General Hospital (SGH)). SGH is the largest hospital in Singapore with 1,597 beds in 2013[11]. 1,500 TKA surgeries were performed in SGH in 2007, accounting for 65% of all TKA surgeries in Singapore[12].

Study population

Patients aged between 65 and 90 undergoing elective total joint (hip or knee) replacement surgery in Singapore General Hospital will be screened for eligibility. A minimum age of 65 years old was chosen to be recruited based on the original study which developed and validated CAM[13]. Exclusion criteria includes patients who are unable to give their own consent for the surgery and anaesthesia. Patients with clinically diagnosed dementia will also be excluded from the study as they are deemed not to have capacity for consent.

All eligible patients will be identified from the appointment list of attendees of the preoperative evaluation clinic (PEC) at SGH where the patients attend for preoperative assessment and counselling by the anaesthetists. Patients between 65 and 90 years old undergoing TKA or THA will be approached and invited to enrol into the study. Informed consent will be obtained then.

Preoperative data

We will collect the patients' baseline characteristics preoperatively. This will allow for the identification of risk factors or correction of confounding factors during analysis of the results.

Data on cognitive status

Before the operation, each patient will be interviewed to assess their baseline cognitive status. The Mini–Mental State Examination (MMSE) will be used, which is a 11-question screening tool used to evaluate the cognitive aspects of mental function[14]. It measures domains of cognitive function including memory, attention, language, praxis and visuospatial ability. A score of 0-30 can be obtained with higher values denoting better cognitive function. A score of <24 suggests cognitive impairment. The test was adapted for use in Singapore, and the changes and reasons for the changes shown in the table in Supplementary file 1. In addition, the test will be administered in English, Chinese or Malay, according to the language the participant is most well-versed in. The Chinese version of MMSE that will be used was previously validated in Shanghai[15] and in Singapore[16]. The Malay version of MMSE that will be used was developed by translation from the English version. The Chinese and Malay versions of MMSE have similar test questions and are scored the same way as the English version, but there some differences shown in Supplementary file 2. However, a recent study in Singapore has shown that there were significant ethnic differences in unadjusted MMSE scores using the different versions of MMSE. These differences were not eliminated after accounting for known correlates of MMSE performance such as

socioeconomic status, comorbid illnesses, functional health status, and health-related behaviours[17].

The Confusion Assessment Method (CAM) will also be performed prior to the operation to obtain the patient's baseline score. CAM is a screening instrument for delirium intended for use by non-psychiatrically-trained clinicians based on the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III-R criteria[18]. It involves an interview whereby delirium can be diagnosed using the CAM algorithm based on 4 criteria – (1) acute onset or fluctuating course, (2) inattention, (3) disorganised thinking and (4) altered level of consciousness, as can be seen in Figure 1. Delirium is said to be present if criteria 1 and 2 and either of 3 or 4 are present. CAM has a sensitivity of 94-100%, specificity of 90-95%, and high inter-observer reliability[13]. This enables a new case of delirium in the postoperative period to be detected.

Other data

Sensory impairment will be assessed during the preoperative interviews. Patients will be asked to wear their visual or hearing aids during these interviews. A patient will be considered to have visual or hearing impairment if the research member conducting the interview is unable to perform the interview normally due to the sensory impairment, such as raising his/her voice for a patient with impaired hearing. The preoperative MMSE assessment provides a useful tool in assessing for visual impairment as it has several vision-dependent items (naming objects, following a written command, instructions to handle a piece of paper, writing a sentence, copying a diagram)[19].

The grip strength of each patient will also be measured using the JAMAR® Plus+ Digital Hand Dynamometer (Sammons Preston Inc, Bolingbrook, IL). Hand dynamometry has acceptable reliability and validity for measurement of grip strength[20], which can serve as an indicator of muscle function and physical fitness. The normative value of hand grip strength for elderly in Singapore has recently been published, decreasing from 18.6kg and 29.3kg for females and males respectively in the 65-69 age group to 12.4kg and 18.5kg in the 85+ age group[21].

The patient baseline characteristics will be obtained from the medical records. All perioperative data will be prospectively entered into the REDCap™ database. This will include data regarding patient's demographics, smoking history, alcohol history, pre-existing medical conditions, preoperative medications.

Each patient will also be rated preoperatively by an anaesthesiologist in the PEC based on the American Society of Anaesthesiologists (ASA) physical status classification[22]. It is a scale from 1 to 5, where 1 represents a completely healthy fit patient and 5 representing a moribund patient who is not expected to live 24 hours with or without surgery. For our analysis, we will be calculating each patient's perioperative risk based on the Charlson Comorbidity Index (ChCI)[23]. 19 different comorbid medical conditions are assigned weights of 1, 2, 3 and 6 according to the degree to which they predicted mortality, and the sum of these values gives the final score. It is a valid method of estimating risk of mortality resulting from comorbidities[24]. The STOP-Bang score will also be calculated for each patient. The STOP-Bang questionnaire was a good screening tool for diagnosing obstructive sleep apnoea, with a sensitivity of 89.0% and accuracy of 79.1%[25]. Preoperative laboratory results, including data about haemoglobin or creatinine level, will also be collected.

Preoperative baseline functional scores for TKA (Oxford Knee Score, Knee Society Functional Score and Knee Society Knee Score) and for THA (Harris Hip Score and Parker Mobility Score) will be obtained from the patient by trained staff at the Orthopaedic Diagnostic Centre (ODC). These assessments will be further discussed in the "Postoperative data" section.

The preoperative data collection form (DCF) can be seen in Supplementary file 3.

Intraoperative data

Data regarding the surgery will be collected. Intraoperative data includes type of arthroplasty performed (TKA or THA), type of anaesthesia (spinal, general or other anaesthesia), use of femoral nerve block, intraoperative drug use, tourniquet time, intra-articular injections and blood transfusion (number of pints transfused). Occurrence of hypotension, which is defined as a mean arterial pressure <60mmHg, and its duration will also be recorded.

Postoperative data

Primary outcome

The primary outcome will be the presence of postoperative delirium following TJA. Each patient will be assessed for delirium on postoperative day (POD) 1, 2 and 3 in the wards at 7am as well as the day of discharge. Delirium will not be evaluated on POD 0 due to difficulty in differentiating delirium from the effects of residual anaesthesia.

CAM will be used to detect postoperative delirium and delirium severity. Delirium is said to be present if the patient meets the CAM criteria for any of the postoperative assessments. Patients assessed to have delirium will be referred to the psychiatrists for a formal diagnosis based on the DSM-V criteria and for further management.

Short-term secondary outcomes

Postoperative complications will be assessed by the Postoperative Morbidity Survey (POMS). This is a 9-point survey that can be easily used by clinicians to characterise short-term postoperative morbidity in their respective settings[26]. It is designed to only identify morbidity of a type and severity that could prolong length of stay (LOS). Using POMS, postoperative morbidity outcomes can be dichotomised into 2 categories – the absence and presence of morbidity. The POMS instrument can be seen in Supplementary file 4 attached. POMS will be assessed on POD 3, 5, 8 and 15, as recommended by the original literature[26]. It has also been reported to have good inter-rater reliability and acceptability to patients[27].

In addition, the Comprehensive Complication Index (CoCI) will also be used to assess postoperative complications, which is based on the widely established Clavien-Dindo classification. The score is the sum of all complications attributable to a single procedure, weighted according to their respective severities. The index thus integrates the severity of all major and minor postoperative complications in a patient, minimising the risk of ignoring minor complications. The score ranges from 0 (no complications) to 100 (death)[28]. The CoCI will be assessed on the day of discharge and POD 30. It is more sensitive than other existing traditional endpoints to detect treatment effects on postoperative morbidity[28].

Other postoperative outcomes that will be obtained include postoperative nausea and vomiting (PONV), LOS and 30-day readmission rates. 30-day readmission is defined as readmission within 30 days of initial admission. The reason for readmission will also be obtained.

Long-term secondary outcomes

Longer-term outcomes such as functional and health-related quality-of-life (HRQoL) outcomes will also be recorded by the ODC total joint registry at 6 months, 1 year, 2 years and 5 years postoperatively. The ODC tracks clinical outcome measures during pre- and postoperative functional assessments of the patients in SGH. Their total joint registry contains data about outcomes from knee and hip arthroplasties.

For patients undergoing TKA, knee function will be measured using the new Knee Society Knee Score (KSKS) and Function Score (KSFS)[29]. The physician-derived KSKS measures alignment, stability, joint motion and symptoms experienced. The patient-derived KSFS evaluates use of walking aids and supports, ability to complete standard activities of daily living and discretionary activities. The KSKS and KSFS each range from 0 (worst) to 100 (best). Both provide a validated rating of the functional outcome of the patient and knee prosthesis after TKA[30]. In addition, the Oxford Knee Score (OKS)[31] will also be used, which is a 12-item, patient-assessed questionnaire designed specifically for use in patients undergoing TKA [7]. It assesses an individual's pain and physical disability. Each item is scored from 1 (least difficulty/severity) to 5 (most difficulty/severity), and individual item scores are summed to yield an overall score ranging from 12 (no pain or limitation) to 60 (severe pain or limitation). A lower OKS indicates a better outcome. It has good reliability, construct and content validity, and sensitivity to clinically important changes over time[31,32]. It correlates strongly with pain but less with postoperative functioning[33].

For patients undergoing THA, hip function will be measured using the Harris Hip Score (HHS)[34]. The HHS is a clinician-based tool to assess the outcomes of hip surgery such as THA. It contains 4 subscales – pain severity, function, absence of deformity and range of motion. The total score ranges from 0 (worst) and 100 (best). It showed high validity and reliability when used to study the clinical outcome of THA[35]. Hip function will also be measured using the Parker Mobility Score (PMS)[36]. A score of 1 represents a patient who does not require a walking aid and has no restriction in walking distance, while a score of 10 represents a patient who is mostly bedbound. It is reliable and a valid predictor of in-hospital and long-term outcomes[36–38]. Outcomes for THA will only be recorded at 6 months and 2 years, unlike the other long-term secondary outcomes.

HRQoL will be assessed based on the 36-Item Short Form Health Survey (SF-36)[39] to obtain a baseline score. It consists of 36 questions categorised into 8 domains (physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions). This instrument is shown in Supplementary file 5. Higher scores indicate better health status and quality of life.

Days alive and out of hospital (DAOH) will also be determined for each patient at 1 month, 6 months and 12 months to assess overall impact of postoperative delirium on morbidity and mortality. DAOH will be calculated based on death date (if present) and duration of all subsequent hospitalisations until the follow-up date. This will be recorded as a percentage

by dividing DAOH by total potential follow-up period, which is the time period between the operation and the respective dates of follow-up (1 month, 6 months and 12 months). %DAOH is a useful measure as it emphasises the deaths occurring early in follow-up and takes into account the severity (duration) of any hospitalisation.[40]

Postoperative risk factors

Other postoperative data will be collected as variables for risk factors.

Postoperative pain at rest will be evaluated using the pain Visual Analog Scale (VAS) during the same visit as CAM on POD 1, 2 and 3. Each patient will score pain experienced at rest on a scale, with 0 = no pain and 10 = maximum pain.

Sensory impairment will also be assessed during the postoperative interviews similar to the preoperative assessments.

The postoperative DCF can be seen in Supplementary file 6.

The flowchart shown in Figure 2 depicts a patient's journey starting from enrolment in the PEC.

Data management

Patient data will be kept confidential throughout the study. All electronic study data entry, storage and analysis will be done according to institutional data security policy, using password protected data in secure systems.

The patient data collected will be de-identified and the key kept securely separated with access limited to principal investigator and co-investigators. A study-related identification number given to each patient will be used on the case report form. Research members will enter the de-identified data into the REDCap™ (Research Electronic Data Capture) tool hosted on a secure server at Singapore General Hospital[36]. The hardcopy of the research data will be securely stored within the department. The softcopy of research data will be saved in a password-protected file and will be stored in institution approved login-protected system and encrypted hard-drive. Only study members will have access to the data.

Power and sample size calculations

The primary aim of the study is to characterise the incidence of postoperative delirium following TJA, which is estimated at around 10% based on existing literature[2]. Using this estimate, 150 patients are enough to detect the incidence with a precision of 5% and confidence level of 95%.

However, this study will also aim to detect potential factors which may be correlated to postoperative delirium by logistic regression. Thus, we will target to recruit 500 patients such that we are able to investigate the risk factors and associated outcomes of postoperative delirium using multiple logistic models while minimising the limitation of a small number of events of postoperative delirium.

Statistical analyses

The incidence of postoperative delirium following TJA using the standard formula – the number of patients diagnosed to have postoperative delirium divided by the total number of patients in the study, and the result expressed as a percentage.

Potential risk factors of postoperative delirium will also be identified by comparing the perioperative data recorded between the patients with and without postoperative delirium. Data will first be summarised using descriptive statistics including mean, standard deviation (SD), median, range and frequency tables. Univariate analyses will then be used identify the differences between the two groups. Data of continuous variables will be compared using the Student's t-test (normally distributed data) or the Wilcoxon rank sum test (not normally distributed data). Data of categorical variables will be compared by Pearson Chi-square test or Fisher's exact test.

The variables which are statistically significant or close to significant (p value <0.05 or <0.1) between the two groups of patients will then be selected for inclusion in a multivariate logistic regression model. This will determine the independent predictors of postoperative delirium. The final model will be determined by sensitivity analysis. The sensitivity analysis can help us to understand the contribution of each parameter to the model outputs, investigate which parameter will have the biggest influence and then refine the model to obtain the final model which is statistically and clinically meaningful. Odds ratio (OR) will be used to describe the correlation of them with postoperative delirium.

Postoperative outcomes which are associated with the incidence of postoperative delirium will also be examined by comparing patients with and without postoperative delirium. The postoperative POMS score, CoCI score, incidence of PONV, LOS, incidence of 30-day readmission and %DAOH will be similarly compared using Student's t-test and Pearson Chi-square tests as appropriate.

For the long-term postoperative outcomes, the median postoperative SF-36 for each domain, KSKS, KSFS, OKS, HHS and PMS scores applicable at 6 months, 1 year, 2 years and 5 years will be compared to the median preoperative baseline scores using the Wilcoxon matched pairs sign rank test. The tests with a change greater than the minimally clinically important difference (MCID) will be identified. The MCID values for each test will be obtained from the pre-existing literature. These variables will then be analysed by analysis of covariance (ANCOVA) to identify predictors of the long-term postoperative test scores. All predictor variables will be incorporated into the multivariate ANCOVA model. Analyses will be performed separately for the various tests that demonstrated changes greater than MCID.

ETHICS AND DISSEMINATION

This study has been approved by the Singapore General Hospital Institutional Review Board (SGH IRB) (CIRB Ref: 2017/2467) and is registered on the ClinicalTrials.gov registry (Identified: NCT03260218). In the event of any important protocol modifications, all investigators, SGH IRB and trial participants will be notified.

The results of this study will be presented at international conferences and submitted to a peer-reviewed journal. The data collected will also be made available in a public data repository.

All eligible participants will be approached by the research assistant during their visit to the preoperative evaluation clinic. They will be given an explanation about the study, a patient information sheet and a consent form. They will then be given an ample time to consider if they would like to participate in the study. They will also be allowed to ask questions freely. If the participant expresses an interest to participate in the study, a written consent will be obtained. The consent forms are in English. However, participants from non-English speaking backgrounds will be provided a translator. For illiterate participants, an accompanying family member will be approached to verify and witness the consent process.

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FUNDING STATEMENT

This work was supported by the Singhealth Duke-NUS Academic Medical Centre Nurturing Clinician Scientists Scheme Award, project number 12/FY2017/P1/15-A29. This funding source, Singhealth Duke-NUS Academic Medical Centre, has no role in the design of this study and will not have a role in the analysis and interpretation of the results.

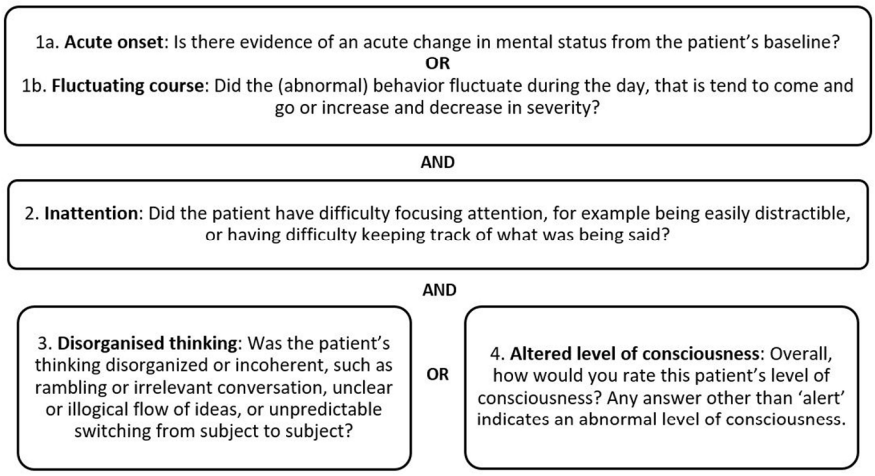
COMPETING INTEREST STATEMENT

None.

FIGURE LEGENDS

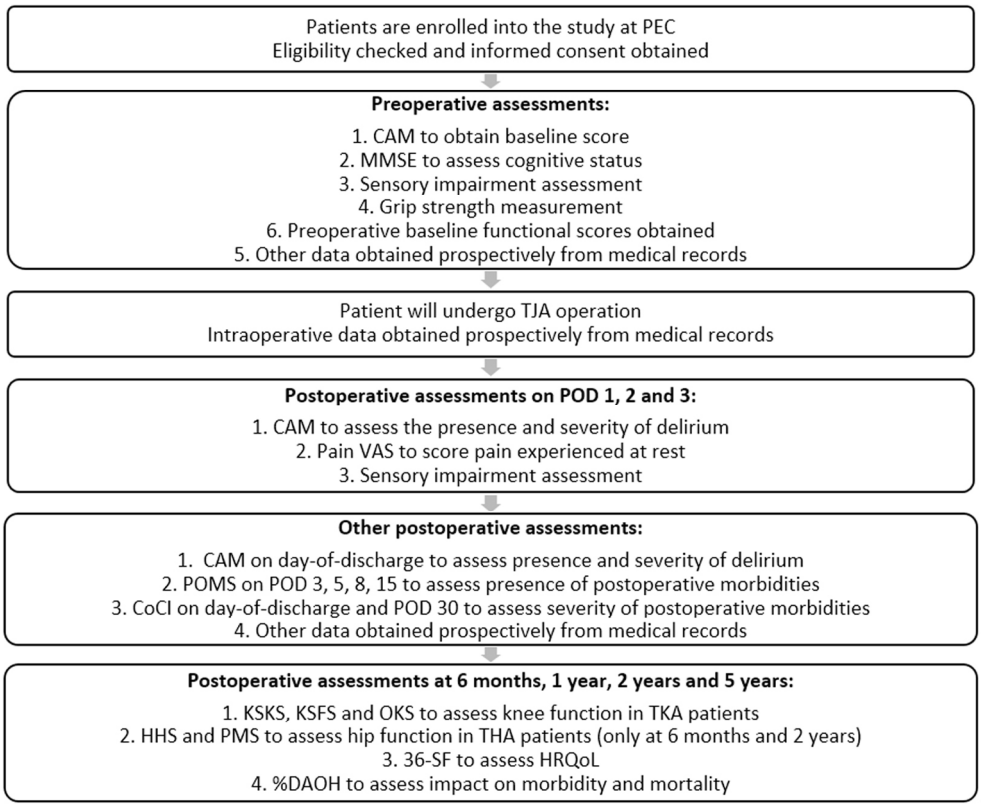
Figure 1. CAM criteria: at least one criteria on each of the 3 rows must be met for a positive result.

Figure 2. Flowchart depicting a patient's timeline during the study.



CAM criteria: at least one criteria on each of the 3 rows must be met for a positive result

240x129mm (300 x 300 DPI)



Flowchart depicting a patient's timeline during the study

140x117mm (300 x 300 DPI)

Item no.	Original version	Adapted version	Reasons
1	"What is the season?"	Without looking at your watch, what time is it?"	There are no seasons in Singapore.
2a	"What county are we in?";	"What area/street are we in?";	Singapore is a city country; "Singapore" would only the only correct answer.
2b	"What town/city are we in?"	"Which part of Singapore (North/South/East/West) are we in?"	Singapore is a city country; "Singapore" would only the only correct answer.

Item no.	English version	Chinese version	Malay version
4	Spell the word “WORLD” backwards	请把这句话倒说一遍 – “天上有月亮“	Terbalikkan ejaan “DUNIA”
7	Repeat the following – “no ifs, ands, or buts”	请清除的重复一遍 – “四十四只石狮子“	Ulangan perkataan – “da dahulu, kini dan selamanya”

Preoperative DCF

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of preoperative assessment:

_____

DEMOGRAPHIC

Age: _____

Gender: Male ☐ Female ☐

Race: Chinese ☐ Malay ☐ Indian ☐ Others ☐

Language:

English ☐ Mandarin ☐ Malay ☐

Others _____

Highest education completed:

_____

Height: _____ m

Weight: _____ kg

BMI: _____

OP DETAILS

Surgeon:

_____

Type of Operation:

TKR ☐ THR ☐

Unilateral L ☐/ R ☐ OR Bilateral ☐

Primary ☐ Revision ☐

Pre-operative Dx:

_____

_____

_____

_____

Grip Strength: _____

BACKGROUND MEDICAL CONDITION

ASA: _____

Charlson Comorbidity Index

Overall score: _____

CVS	
☐	Myocardial infarction
☐	Congestive heart failure
☐	Peripheral vascular disease
CNS	
☐	Cerebrovascular disease
☐	Hemiplegia or paraplegia
☐	Dementia
Respi	
☐	Chronic pulmonary disease
MSK	
☐	Rheumatologic disease
GI	
☐	Peptic ulcer disease
☐	Mild liver disease
☐	Moderate or severe liver disease
Endocrine	
☐	Diabetes without chronic complications

Smoking ☐

Alcoholism ☐

Diabetes:

OHGA ☐ Insulin ☐

Latest HbA1c _____

Chronic kidney disease ☐

Pre-existing dementia ☐

Other pre-existing neurological problems

☐ CVA

☐ Parkinson Disease

☐ Depression

☐ Anxiety

☐ Schizophrenia and other delusional disorders

Visual impairment ☐

Hearing impairment ☐

STOPBANG score _____

Chronic Medications

Benzodiazepine ☐

Statin ☐

Tramadol ☐ Oxynorm ☐

Anti-depressants

Tricyclics ☐ SSRI ☐ SNRI ☐

MOAI ☐

Anti-psychotics

☐	Diabetes with chronic complications
Renal	
☐	Mild Renal disease
☐	Moderate or severe renal disease
Malignancy	
☐	Any malignancy, including leukemia and lymphoma
☐	Non-metastatic solid tumour
☐	Metastatic solid tumor
Immunological	
☐	AIDS/HIV

IntraOp

ANA Type: _____

	Yes	No
Fem N block	☐	☐
Benzo Use:	☐	☐
Atropine Use:	☐	☐
Opioid use **If yes , dose: _____**	☐	☐
Dexa use **If yes , dose: _____**	☐	☐
Promethazine use:	☐	☐
Ondansetron:	☐	☐
Blood Transfusion	☐	☐
Hypotension **If yes, duration: _____**	☐	☐

Haloperidol ☐ Quetiapine ☐
Olanzapine ☐ Clozapine ☐

Preoperative Laboratory Results
Hemoglobin _____
MCV _____
RDW _____
MCV _____
MCHC _____
Urea _____

BASELINE CAM

1. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐

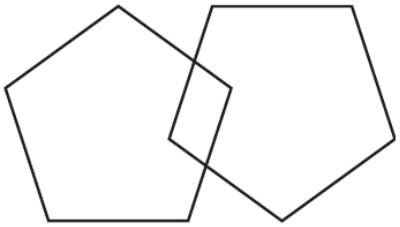
b. Yes – marked form ☐, fluctuating ☐
c. Uncertain _____
d. No ☐

4. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

BASELINE MINI MENTAL STATE EXAMINATION

Total score _____
Level of consciousness
Alert ☐ Drowsy ☐ Stupor ☐ Coma ☐

	Question	Score
1	What is the • year • month • day of the week • date • current time now (without looking at your watch)?	/ 5
2	What country are we in? What area/street are we in? Which part of Singapore is this place (North, south, east, west or central) Which hospital are we in? Which floor?	/ 5
3	Show the objects: ball, flag, tree Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials _____	/ 3
4	Serial 7's. 1 point for each correct answer. Stop after 5 answers. Alternatively spell "world" backward.	/ 5
5	Ask for the 3 objects repeated above. Give 1 point for each correct answer.	/ 3
6	Name a pencil and watch. Repeat the following "No ifs, ands, or buts" Follow a 3-stage command: "Take a paper in your hand, fold it in half, and put it on the floor." Read and obey the following: CLOSE YOUR EYES	/ 2 / 1 / 3 / 1 / 1

	Write a sentence.	/ 1
	Copy the design shown 	/ 1

Postoperative Morbidity Survey

Morbidity type	Criteria	Source of data
Pulmonary	Has the patient developed a new requirement for oxygen or respiratory support.	Patient observation Treatment chart
Infectious	Currently on antibiotics and/or has had a temperature of >38°C in the last 24 hr.	Treatment chart Observation chart
Renal	Presence of oliguria <500 mL/24 hr; increased serum creatinine (>30% from preoperative level); urinary catheter in situ.	Fluid balance chart Biochemistry result Patient observation
Gastrointestinal	Unable to tolerate an enteral diet for any reason including nausea, vomiting, and abdominal distension (use of antiemetic).	Patient questioning Fluid balance chart Treatment chart
Cardiovascular	Diagnostic tests or therapy within the last 24 hr for any of the following: new myocardial infarction or ischemia, hypotension (requiring fluid therapy >200 mL/hr or pharmacological therapy), atrial or ventricular arrhythmias, cardiogenic pulmonary edema, thrombotic event (requiring anticoagulation).	Treatment chart Note review
Neurological	New focal neurological deficit, confusion, delirium, or coma.	Note review Patient questioning
Hematological	Requirement for any of the following within the last 24 hr: packed erythrocytes, platelets, fresh-frozen plasma, or cryoprecipitate.	Treatment chart Fluid balance chart
Wound	Wound dehiscence requiring surgical exploration or drainage of pus from the operation wound with or without isolation of organisms.	Note review Pathology result
Pain	New postoperative pain significant enough to require parenteral opioids or regional analgesia.	Treatment chart Patient questioning

36-Item Short Form Health Survey

RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:
   - ○ 1 – Excellent
   - ○ 2 - Very good
   - ○ 3 – Good
   - ○ 4 – Fair
   - ○ 5 – Poor

2. **Compared to one year ago**, how would you rate your health in general now?
   - ○ 1 - Much better now than one year ago
   - ○ 2 - Somewhat better now than one year ago
   - ○ 3 - About the same
   - ○ 4 - Somewhat worse now than one year ago
   - ○ 5 - Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	○ 1	○ 2	○ 3
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	○ 1	○ 2	○ 3
5. Lifting or carrying groceries	○ 1	○ 2	○ 3
6. Climbing **several** flights of stairs	○ 1	○ 2	○ 3
7. Climbing **one** flight of stairs	○ 1	○ 2	○ 3
8. Bending, kneeling, or stooping	○ 1	○ 2	○ 3
9. Walking **more than a mile**	○ 1	○ 2	○ 3
10. Walking **several blocks**	○ 1	○ 2	○ 3
11. Walking **one block**	○ 1	○ 2	○ 3
12. Bathing or dressing yourself	○ 1	○ 2	○ 3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	Yes	No
13. Cut down the amount of time you spent on work or other activities	○ 1	○ 2
14. Accomplished less than you would like	○ 1	○ 2
15. Were limited in the kind of work or other activities	○ 1	○ 2
16. Had difficulty performing the work or other activities (for example, it took extra effort)	○ 1	○ 2

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	Yes	No
17. Cut down the **amount of time** you spent on work or other activities	○ 1	○ 2
18. **Accomplished less** than you would like	○ 1	○ 2
19. Didn't do work or other activities as **carefully** as usual	○ 1	○ 2

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?
    - ○ 1 - Not at all
    - ○ 2 - Slightly
    - ○ 3 - Moderately
    - ○ 4 - Quite a bit
    - ○ 5 – Extremely

21. How much **bodily** pain have you had during the **past 4 weeks**?
    - ○ 1 - None
    - ○ 2 - Very mild
    - ○ 3 - Mild
    - ○ 4 - Moderate
    - ○ 5 - Severe
    - ○ 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?
    - ○ 1 - Not at all

- ○ 2 - A little bit
- ○ 3 - Moderately
- ○ 4 - Quite a bit
- ○ 5 – Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
24. Have you been a very nervous person?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
25. Have you felt so down in the dumps that nothing could cheer you up?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
26. Have you felt calm and peaceful?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
27. Did you have a lot of energy?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
28. Have you felt downhearted and blue?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
29. Did you feel worn out?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
30. Have you been a happy person?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
31. Did you feel tired?	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?
    - ○ 1 - All of the time
    - ○ 2 - Most of the time
    - ○ 3 - Some of the time
    - ○ 4 - A little of the time
    - ○ 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	○ 1	○ 2	○ 3	○ 4	○ 5
34. I am as healthy as anybody I know	○ 1	○ 2	○ 3	○ 4	○ 5
35. I expect my health to get worse	○ 1	○ 2	○ 3	○ 4	○ 5
36. My health is excellent	○ 1	○ 2	○ 3	○ 4	○ 5

This tool was developed at RAND Health as part of the Medical Outcomes Study.

Postoperative DCF

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians	
Serial No: _____ Date of surgery: _____ Type of surgery: _____ Date of assessment: _____	**POD1**

CAM ASSESSMENT

1. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
4. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

VISUAL/HEARING IMPAIRMENT	**PERIOPERATIVE DETAILS**
Visually impaired ☐ Hearing impaired ☐ If yes to above, hearing aids? ☐	Tourniquet time: _____ minutes Intra-articular injections: (i) Tranexamic acid ☐ Dosage: (ii) Morphine ☐ Dosage:

	(iii) Marcaine ☐ Dosage: (iv) Adrenaline ☐ Dosage: (v) Ketorolac ☐ Dosage: (vi) Triamcinolone ☐ Dosage: (vii) Vancomycin ☐ Dosage: (viii) Normal Saline ☐ Dosage: (ix) Others: _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

POD2

CAM ASSESSMENT

5. Acute onset change in mental status from baseline?
   a. Yes ☐
   b. No ☐
   c. Uncertain _____
6. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
7. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
   a. Yes – mild form ☐, fluctuating ☐
   b. Yes – marked form ☐, fluctuating ☐
   c. Uncertain _____
   d. No ☐
8. How is the patient's overall level of consciousness?
   a. Alert (normal) ☐
   b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
   c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
   d. Stupor (Difficult to arouse) ☐, fluctuating ☐
   e. Coma (Unarousable) ☐, fluctuating ☐
   f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No: _____

Date of surgery: _____

Type of surgery: _____

Date of assessment: _____

POD3

CAM ASSESSMENT

1. Acute onset change in mental status from baseline?
    a. Yes ☐
    b. No ☐
    c. Uncertain _____
2. Does the patient have difficulty focusing attention, is easily distracted, or has difficulty keeping track of what was being said?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
3. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
    a. Yes – mild form ☐, fluctuating ☐
    b. Yes – marked form ☐, fluctuating ☐
    c. Uncertain _____
    d. No ☐
4. How is the patient's overall level of consciousness?
    a. Alert (normal) ☐
    b. Vigilant (hyperalert, overly sensitive to environmental stimuli, startled easily) ☐, fluctuating ☐
    c. Lethargic (Drowsy, easily aroused) ☐, fluctuating ☐
    d. Stupor (Difficult to arouse) ☐, fluctuating ☐
    e. Coma (Unarousable) ☐, fluctuating ☐
    f. Uncertain _____

PAIN ASSESSMENT

VAS score at time of assessment (0 – 10): _____

Postoperative Delirium Following Total Joint Arthroplasties among South East Asians

Serial No:
_____

Date of surgery:
_____

Type of surgery:
_____

Date of assessment:
_____

DAY OF DISCHARGE

POSTOPERATIVE MORBIDITY SURGERY

Morbidity Type	Criteria	Tick if present ( )
Pulmonary	De novo requirement for supplemental oxygen or other respiratory support (e.g. mechanical ventilation or CPAP)	
Infectious	Currently on antibiotics or temperature > 38°C in the last 24h	
Renal	Presence of oliguria (< 500 ml/day), elevated serum creatinine (> 30% from preoperative value), or urinary catheter in place for a nonsurgical reason	
Gastrointestinal	Unable to tolerate an enteral diet (either by mouth or via a feeding tube) for any reason, including nausea, vomiting, and abdominal distension	
Cardiovascular	Diagnostic tests or therapy within the last 24h for any of the following: de novo myocardial infarction or ischaemia, hypotension (requiring pharmacologic therapy or fluid therapy > 200ml/h), atrial or ventricular arrhythmias, or cardiogenic pulmonary edema	
Neurologic	Presence of a de novo focal deficit, coma or confusion and delirium	
Wound complication	Wound dehiscence requiring surgical exploration or drainage of pus from the operation wound, with or without isolation of organisms	
Haematologic	Requirement for any of the following within the last 24h: packed erythrocytes, platelets, fresh-frozen plasma, or cryoprecipitate	
Pain	Surgical wound pain significant enough to require parenteral opiates or regional analgesia	

CPAP: continuous positive airway pressure

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page Number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-13
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-13
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-13
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	13-14
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	14
		(*b*) Describe any methods used to examine subgroups and interactions	14
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	14
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	-
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	-
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	Report numbers of outcome events or summary measures over time	-
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	-

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	-
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	-
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	-
Generalisability	21	Discuss the generalisability (external validity) of the study results	-
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.