



# Cognitive Impairment and Postoperative Outcomes in Patients Undergoing Primary Total Hip Arthroplasty a Systematic Review

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## Cognitive impairment and postoperative outcomes in patients undergoing primary total hip arthroplasty: A systematic review



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### ABSTRACT

**Study objective:** Total hip arthroplasty (THA) is a common surgical procedure in the elderly. Varying degrees of cognitive impairment (CI) are frequently seen in this patient population. To date, there has been no systematic review of the literature specifically examining the impact of CI on outcomes after elective THA. The aim of this systematic review was to identify studies that compare the postoperative outcomes of patients with and without CI after undergoing elective primary THA.

**Design:** We conducted a systematic review of prospective and retrospective studies. A systematic literature review was conducted by searching MEDLINE, PubMed, and Embase from between January 1, 1997 and January 1, 2018. A total of 234 articles were reviewed and 22 studies were selected.

**Setting:** Operating room and short-term and long-term postoperative recovery up to 2 years.

**Patients:** Patients with CI who underwent an elective primary THA that required general anesthesia with a comparator group of patients who did not have dementia.

**Interventions:** Patients who underwent elective primary total hip arthroplasty.

**Measurements:** Outcomes included post-operative delirium (POD), mortality and other complications, discharge disposition, length of stay (LOS), mortality, short-term (30 days) and long-term (1 month–2 years) complications.

**Main results:** 22 studies with 5,705,302 participants were included in the systematic review. Sample sizes varied greatly, ranging from 14 to 2,924,995 participants. There was an association between patients with CI and an increase in POD, in-hospital mortality, complications during hospitalization, non-routine disposition, LOS, mortality between 1 month to 2 years, and worse postoperative functional status.

**Conclusions:** We demonstrate that there are strong associations between patients with pre-existing CI undergoing THA and increased POD, hospital mortality, hospital complications, and hospital LOS. We report good quality evidence linking complications after THA to preexisting CI. Screening for CI can improve care and better predict the risk of developing postoperative complications such as delirium. Further investigations can address perioperative factors that can help reduce complications and show the utility of more widespread assessment of preoperative cognitive impairment.

### 1. Introduction

Total hip arthroplasty (THA) is one of the most successful orthopedic procedures designed to alleviate pain and restore function, and is a commonly performed major orthopedic procedure involving the

lower extremity [1]. However, patients undergoing THA may suffer major complications, which may be due to surgical, anesthesia or patient-related factors [2]. At the same time, the outcomes of these surgeries have improved in recent decades due to advances in preoperative medical optimization, surgical techniques, anesthetic and postoperative

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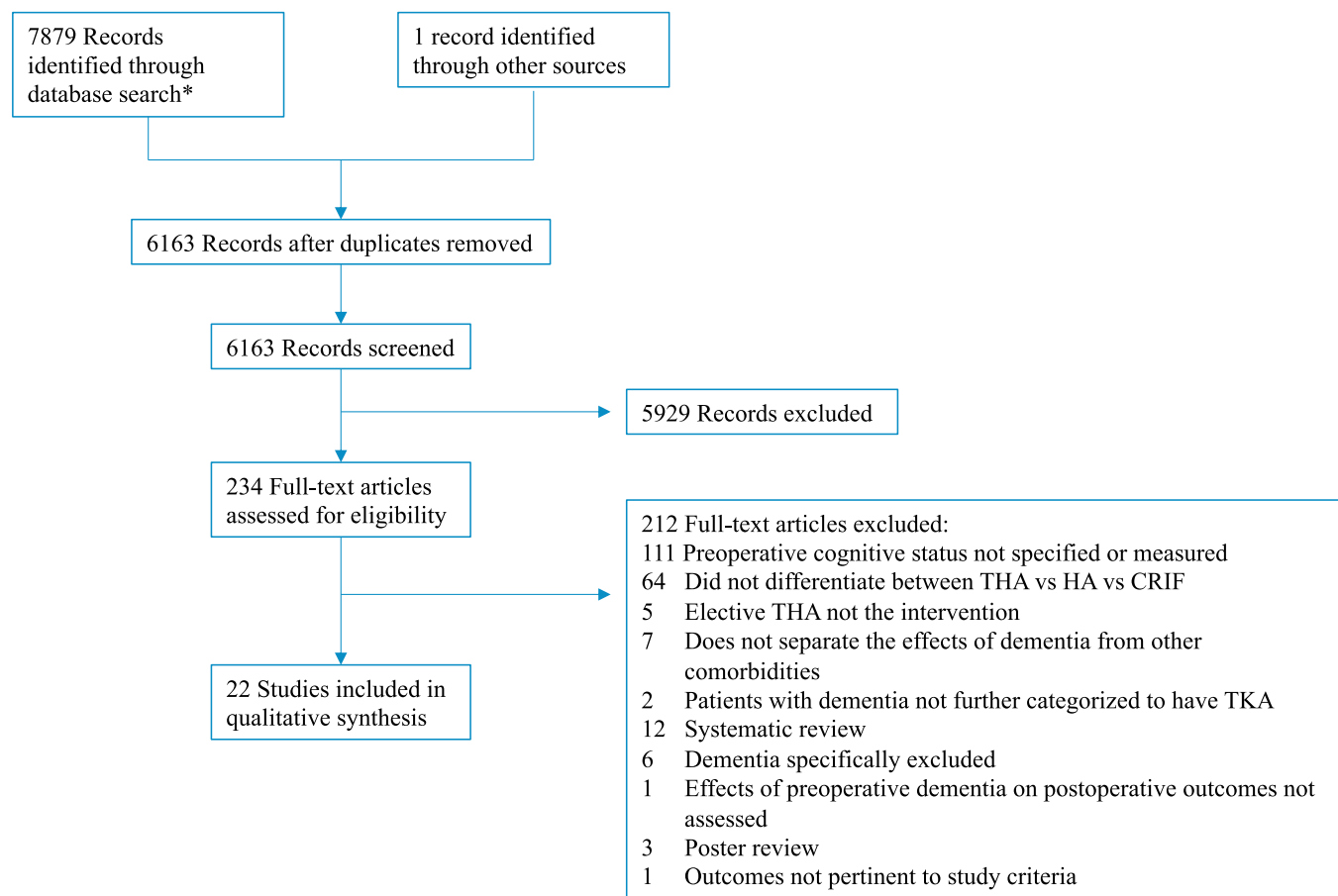


Fig. 1. Flow diagram illustrating the systematic search process to identify relevant studies for inclusion in the final review.

\*Articles were identified from PubMed/Medline (n = 4242) and Embase (n = 3637). See Appendix A for more detail.

THA, total hip arthroplasty; HA, hip arthroscopy; CRIF, closed reduction internal fixation.

care [3]. One way that outcomes have improved has been through risk stratifying patients prior to THA [4]. Previous studies have demonstrated that the presence of cognitive impairment (CI) in patients prior to surgery is associated with poor post-operative outcomes [5]. However, most surgeons and anesthesia providers do not routinely assess cognitive function in THA patients prior to surgery. Given the overall mortality associated with elective THA is estimated at 0.30% at 30-days and 0.65% at 90-days [6], there exists a need to develop strategies to further decrease major complications in patients undergoing this procedure.

To date, no systematic review has specifically evaluated post-operative outcomes of patients with CI who receive general anesthesia and undergo elective primary THA. A systematic review of prospective, retrospective, and other observational studies can help compare the postoperative outcomes of patients with and without CI after undergoing this procedure. Our hypothesis is that patients with CI will have a more complicated in-hospital course, including higher risk of post-operative delirium, longer hospital stay, and increased wait times to a health care facility. Additionally, we hypothesize that these patients will have an increased risk of mortality and complications within 30 days post-discharge and 30 days to 2 years post-discharge.

## 2. Materials and methods

### 2.1. Protocol and registration

The protocol for this systematic review was designed according to PRISMA guidelines with the assistance of the research librarian at the

Countway Library of Medicine, Boston Massachusetts. The protocol has been registered with PROSPERO (Registration Number: CRD42017072154. Website: <http://www.crd.york.ac.uk/PROSPERO>).

### 2.2. Eligibility criteria

Original studies that measured post-operative delirium (POD), postoperative mortality, quality of life in patients suffering from pre-operatively dementia or cognitive impairment following THA were considered for this review. As there was no single cognitive impairment scale that was used to measure CI, different methods ranging from using Mini-Mental Status Exam (MMSE) in combination with other assessment tools were included in the study. The other tools ranged from National Adult Reading Test (AMNART), Auditory Verbal Learning Test (AVLT), Stroop Color-Word Test (SCWT), and Controlled Word Association Test (COWAT), Mini-Cog© and clock drawing test [7]. However, we only included patients who had CI based on these tools or had a preexisting diagnosis of dementia. Only studies that included patients who underwent elective major total hip arthroplasty were deemed eligible while patients who underwent hemiarthroplasty were excluded. Review articles, published abstracts, letters to the editor, study protocols, and case reports were excluded from this systematic review.

### 2.3. Information sources and search

A literature search was conducted by searching MEDLINE, PubMed, and EMBASE using the following keywords: “Alzheimer’s”, “dementia”,

“cognition”, “cognitive defects”, “cognitive deficits”, “cognitive disorders”, “cognitive dysfunction”, “cognitive function”, “cognitive impairment”, “cognitive status”, “memory defects”, “memory deficits”, “memory disorders”, “memory dysfunction”, “memory impairment”, “mental function”, “anesthesia”, “surgery”, “surgical procedure”, “operation”, “outcomes”, “outcome assessment”, “prognosis”, and “surgical outcomes”. Appendix A provides a detailed description of the database-specific search terms and methodology used during the literature search.

All peer reviewed articles published between January 1, 1997 and January 1, 2018 and published in English were critically evaluated using standards from the PRISMA Statement. Inclusion criteria for this study consisted of (a) patients with stated cognitive impairment who received an elective primary THA that required general anesthesia, and (b) studies focused on adult patients who had a comparator group of patients who did not have dementia. To avoid reporting bias, the only studies included were peer reviewed publications designed as a prospective cohort, retrospective cohort or case-control study. We excluded studies that did not have a comparator group of patients without dementia. Furthermore, we excluded studies that did not evaluate patients for cognitive impairment or specify the patients' cognitive status. If patients had a procedure other than THA or an additional concurrent surgical intervention, those studies were also excluded. Finally, studies that did not observe the outcomes of interest were also excluded. After reviewing all of the searched articles using the parameters mentioned above, a total of 234 studies were reviewed and 22 studies were selected for analysis (Fig. 1). Other reasons for exclusion are listed in Fig. 1. In terms of outcomes measurements, we were interested in in-hospital, short- and long-term outcomes. The following outcomes were analyzed for in-hospital outcomes: post-operative delirium (POD), mortality, complications, post-discharge disposition, and length of stay (LOS). The following outcomes were evaluated for short-term outcomes (within 30 days after operation): mortality and complications. For the long-term outcomes (1 month–2 years after an operation) we assessed mortality, functional status, and complications.

#### 2.4. Study selection and data extraction

The studies were identified independently and subsequently reviewed by three authors in two different phases. During the first phase, two authors (BLE and JME) conducted, in a systematic way, the review of the articles produced by the search criteria in the databases and appraised study titles and abstracts to determine eligibility. During the second phase, the third author (OV) reviewed the full-text articles identified during the first phase and determined if the articles met the criteria and then included the ones that did. A fourth author (RDU) evaluated the validity of reasons for the excluded articles. In the second phase, the reviewer assessed the study design, duration of follow-up, and the other outcomes of interest. The third author (OV) extracted the data from the studies that met the criteria. The data included publication title, author(s), year of publication, the location of publication, study design, type of patient population, size, intervention given to the patient population, type of cognitive assessment, measure for cognitive impairment, and outcome results.

#### 2.5. Quality assessment

The quality and risk of bias of the studies were assessed by the Newcastle-Ottawa-Scale (NOS) [8]. The scale is categorized into three dimensions including selection, comparability, and study type outcome for cohort studies and exposure outcome for case control studies. The scale ranges from 0 to 9 and rates the quality of the studies (ie. good, fair, and poor) by awarding stars in each domain. For example, a “good” quality score required 3 or 4 stars in the selection category, 1 or 2 stars in comparability category, and 2 or 3 stars in outcomes category. A “fair” quality score required 2 stars in selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes. A “poor” quality score

reflected 0 or 1 star in selection, or 0 stars in comparability, or 0 or 1 star in outcomes. Finally, we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) approach to assess the strength of the body of evidence for each study [9]. The analysis of each of the studies based on the Newcastle-Ottawa Scale is shown in Table 2.

### 3. Results

#### 3.1. Study characteristics

All of the studies included in this systematic review (Fig. 1) included cohorts of patients who had a preexisting diagnosis of CI or who were found to have CI during pre-operative screening with one of the commonly used screening tools. A total of 22 studies were included. The studies included did not all examine the same postoperative outcomes. Nine of the studies were conducted in the United States, while the other studies included 2 each from Finland and Italy, and 1 study each from the Netherlands, Switzerland, Sweden, France, Taiwan, Turkey, Singapore, Spain, and Germany. All the studies were published during or after 2010. The design of the studies included 7 retrospective cohort studies, 13 prospective cohort studies, and 2 case-control studies. The studies involved a total of 5,705,302 patients undergoing primary elective THA. There were 12 studies undergoing all elective THA, while there were 2 studies of patients undergoing a THA, total knee arthroplasty (TKA) or spine procedure, 7 studies with patients undergoing either a THA or TKA, and 1 study of THA vs other hip surgeries. In terms of the retrospective studies, there were a combined total of 5,701,043 patients who underwent primary elective THA. Prospective studies had a combined total of 4259 patients who underwent an elective THA.

#### 3.2. Measures of cognitive impairment

Cognitive impairment was assessed with multiple scoring systems including the mini-mental status exam (MMSE), National Adult Reading Test (AMNART), Auditory Verbal Learning Test (AVLT), Stroop Color-Word Test (SCWT), and Controlled Word Association Test (COWAT), Mini-Cog®, clock drawing test, and Cognitive Activity Scale (CAS). Eleven of the 22 studies included patients with a preexisting diagnosis of cognitive impairment. Ten studies utilized the screening tools listed above. There was heterogeneity in the definition of CI, with studies variably using specific cutoff values or assessing cognitive impairment as a continuous linear variable. Studies included in the review are listed in Table 1.

#### 3.3. Association of cognitive impairment with in-hospital outcomes

The outcomes examined in the included studies are shown in Table 3. Nine studies assessed the impact of preoperative cognitive impairment on POD. Two of the studies were retrospective cohort studies designed with a combined total of 580 patients who underwent THA. Both studies were good quality studies based on the Newcastle Ottawa scale. The study by Mosk et al. showed that poor preoperative cognitive function predicted POD, while Enemark et al. showed that the rates of POD did not differ from patients who did not have preoperative cognitive dysfunction [7,8].

Seven of the studies were prospective cohort studies with a combined total of 1646 patients who underwent THA. All seven studies were good quality studies based on the Newcastle Ottawa Scale. Zerah et al. showed that POD was more frequent in patients with dementia with a demonstrated odds ratio of 3.12 (95% CI 1.97–4.96,  $P = 0.05$ ) higher than patients without dementia, when controlled for potential confounders [10]. Culley et al. found that 24% of patients screened positive for probable cognitive impairment using the Mini-Cog® test score cutoff of less than or equal to 2 [11]. The authors performed an

**Table 1**  
Characteristics of studies included in the systematic review.

First author, Year, Location	Design, Setting	Population	n (primary THA)	Intervention	Cognitive Assessment	Criteria for Cognitive Impairment	Associations
Mosk, 2017 (Netherlands)	Retrospective cohort study	Patients age > = 70 with hip fracture and who went through arthroplasty	566	THA	preexisting	preexisting	Patients with dementia and delirium were more often institutionalized and had a higher incidence of 6-month mortality after an episode of delirium was noted. Patients with dementia are vulnerable, due to their functional dependency and poor nutritional state. Of a total of 566 included patients, 75% were females. The median age was 84 years (interquartile range: 9). Delirium was observed in 35%. Significant risk factors for delirium were a high American Society of Anesthesiology score, delirium in medical history, functional dependency, preoperative institutionalization, low hemoglobin level, and high amount of blood transfusion. Delirium was correlated with a longer hospital stay (P = 0.001), increased association with complications (P < 0.001), institutionalization (P < 0.001), and 6-month mortality (P < 0.001). Patients with dementia (N = 168) had a higher delirium rate (57.7%, P < 0.001) but a shorter hospital stay (P < 0.001). There was no significant difference in the 6-month mortality between delirious patients with (34.0%) and without dementia (26.3%). Conclusion: Elderly patients with a hip fracture are vulnerable for delirium, especially when the patient has dementia. Patients who underwent an episode of delirium were at an increased risk for adverse outcomes
Enemark, 2017 (Switzerland)	Retrospective observational cohort study	patients with PD or dementia with Lewy bodies (DLB) and a hip fracture who were admitted from January 2013 through June 2014 (18 months) to the Department of Orthopedics, Copenhagen University Hospital, Herlev, Denmark	14	THA, intramedullary nail and hip gliding screw, and giridle stone	preexisting diagnosis of PD/DLB	preexisting	There were no significant differences in length of stay, delirium, or number of infections between the groups. Although patients with PD/DLB are significantly younger and have significantly lower degrees of co-morbidity than patients with COPD, their course and recovery after surgery are equivalent to those of patients with COPD. Patients with PD/DLB are at high risk of developing complications during hospital admission for hip fracture. The limitation of this study was grouping all the data and didn't separate from THA vs intramedullary nail and hip gliding screw, and giridlestone
Mukka, 2017 (Sweden)	prospective cohort study	188 patients treated with HA for a displaced FNF, patients were assessed for estimated preoperative and 1-year post op with regard to walking ability, cognitive status, quality of life, hip function	188	THA	preexisting	SPMSQ	Moderate to severe CI was associated with a high incidence of non-walking ability, worse quality of life, high mortality and re-operation rate after femoral neck fractures treated with HA.
Lee, 2017 (USA)	prospective cohort study	Patients age 65 years and older undergoing hip fracture repair surgery at John Hopkins Bayview Medical Center between 1999 and 2009 were eligible for this prospective cohort study.	466	THA	Baseline probable dementia was defined as either preoperatively diagnosed dementia per geriatrician or score less than 24 on the Mini-Mental State Examination.	preexisting	Delirium after hip fracture repair surgery in patients with preoperative dementia modifies the risk of mortality over the first postoperative year. Patients with delirium superimposed on dementia have a nearly two-fold greater odds of one-year mortality than those without dementia or delirium.

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Table 1 (continued)

First author, Year, Location	Design, Setting	Population	n (primary THA)	Intervention	Cognitive Assessment	Criteria for Cognitive Impairment	Associations
Zerah, 2017 (France)	prospective observational cohort study	Between 2009 and 2015, all patients (> 70 years) admitted after hip fracture surgery into a dedicated unit of peri-operative geriatric care were included: patients with dementia, without dementia, and with cognitive status not determined.	650	THA	preexisting	preexisting	In a dedicated geriatric care pathway, patients with dementia and patients with cognitive status not determined undergoing hip surgery have the same 6-month mortality and walking ability as patients without dementia.
Culley, 2017 (USA)	prospective cohort, single-site	Patients with age > = 65 without a diagnosis of dementia undergoing primary THA or TKA.	88; 123	THA; TKA	Mini-Cog	Mini-Cog < = 2	Low Mini-Cog score has a strong independent association with POD, discharge to place other than home, and longer hospital stay. No associations were found between low Mini-cog scores and in-hospital adverse events, or 30-day emergency room visit. 30-day mortality occurred too infrequently to be analyzed.
Tow, 2016 (USA)	prospective cohort, single-site	Patients age > = 60 undergoing elective spine, hip and knee surgeries with exclusion of patients with MMSE < 24 or with dementia.	42; 98; 2	THA; TKA; spine	CAS, MMSE	MMSE < 27/30	Strong evidence that MMSE > 27 and participation in greater number of cognitive activities were independently associated with decreased risk for POD.
Puustinen, 2016 (Finland)	prospective cohort, single-site	Elderly patients presenting for primary TKA or THA.	24; 28	THA; TKA	MOCA, MMSE, Mini-Cog, clock-drawing test	MOCA < 25/30, MMSE < 24/30, Mini-Cog 0 recalled words or 1-2 abnormal clock-drawing test, clock-drawing < 4/6	Low MoCA and MMSE scores are possibly associated with POD, discharge to health care facility, and decreased functionality at 3 months after surgery.
Guerini, 2010 (Italy)	case control, single-site	Patients age > = 65 with MMSE > 15 who underwent primary TKA, THA or hip fracture repair and required rehabilitation.	222; 88	THA; TKA	MMSE	none	Strong evidence that lower MMSE scores were linked to mortality at 12 months.
Jämsen, 2014 (Finland)	case control, multi-site.	Patients with a preexisting diagnosis of Alzheimer's disease who underwent elective primary TKA or THA.	445; 619	THA; TKA	preexisting diagnosis	preexisting	Patients with Alzheimer's disease had a longer peri-operative hospitalization (median 13 days vs eight days, p < 0.001) and an increased risk for hip revision with a hazard ratio (HR) of 1.76 (95% confidence interval (CI) 1.03 to 3.00). Dislocation was the leading indication for revision. There was no difference in the rates of infection, dislocation of the hip, knee revision and short-term mortality. In long-term follow-up, patients with Alzheimer's disease had a higher mortality (HR 1.43; 95% CI 1.22 to 1.70), and only one third survived ten years post-operatively. Increased age and comorbidity were associated with longer peri-operative hospitalization in patients with Alzheimer's disease. Strong evidence that low AVLT scores, but not MMSE or AMNART, predicted POD.
Jankowski, 2011 (USA)	prospective cohort, single-site	Patients age > = 65 without clinically apparent cognitive impairment (MMSE < 23 excluded) undergoing primary TKA, THA or revision TKA/THA.	134; 209	THA; TKA	MMSE, AMNART, AVLT, SCWT, COWAT	none	Strong evidence that MMSE < 24 independently predicts POD, longer hospital stay, nursing home admission, mortality at 1- and 3- month follow-up, and functional decline at 3-, 6- and 12- months.
Liang, 2015 (Taiwan)	prospective cohort, single-site	Patients age > = 60 undergoing elective spine, hip and knee surgeries.	111; 200; 150	THA; TKA; spine	MMSE	MMSE < 24/30	

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Table 1 (continued)

First author, Year, Location	Design, Setting	Population	n (primary THA)	Intervention	Cognitive Assessment	Criteria for Cognitive Impairment	Associations
Stavros, 2010 (USA)	retrospective, population-based, multi-site.	Patients with age > = 60 who had primary and revision THA or TKA without a preexisting diagnosis of dementia or MMSE < 24.	2,734,995; 4,166,329	primary/revision THA; primary/revision TKA	preexisting diagnosis	preexisting	Patients with preexisting dementia possibly at increased risk for in-hospital death.
Buller, 2014 (USA)	retrospective, population-based, multi-site.	Patients with age > = 18 who had primary TKA or THA.	2,924,442; 5,455,048	THA; TKA	preexisting diagnosis	preexisting	Preexisting dementia is possibly independently associated with in-hospital adverse events and non-routine discharge. Dementia also likely associated with in-hospital mortality and longer hospital stay. The present results show that CAM-ICU is highly sensitive and specific to identify delirium in hip fracture patients in the postoperative period. Among all of the risk factors, cognitive impairment and depressive mood were strongly associated with postoperative delirium. We suggest that a preoperative assessment of cognition and depression might be useful for identifying patients with a higher risk of post-operative delirium.
Koskdereloglu, 2017 (Turkey)	prospective cohort, single site	All patients aged 65years or older who were admitted for surgical repair of acute hip fracture were eligible for enrollment. We excluded patients with multiple fractures, severe hearing loss, visual impairment, accompanying severe dementia or Mini- Mental State Examination (MMSE) score < 15. Of the 173 patients, 44 were excluded, because 23 had severe dementia, eight had multi-trauma, four had visual impairment and three had hearing loss. In addition, three patients refused to be operated, two had aphasia and one had an intellectual disability. We also excluded 18 patients because of preoperative delirium, and two patients died in the postoperative period.	109	THA	MMSE	none	
Mariconda, 2016 (Italy)	A prospective observational cohort study.	552 patients (mean age, 78.3 years; range, 50–105) who underwent surgery for a hip fracture.	552	THA	MMSE	< 27	At both 4 months and 1-year follow-up time points, there was a significant decrease in ambulatory ability and the ADL index score and also an increase in the need for walking aids in comparison with the pre-fracture status. Ambulatory ability, but not ADL, significantly recovered between the 4-month and 1-year follow-up. One year after fracture, the pre-fracture functional status was regained by 57% of the patients, but approximately 13% of the formerly ambulating patients were unable to walk. The pre-fracture status was the most important determinant of ambulatory ability, need for walking aids, and ADL. Comorbidities, a poor cognitive status, and non-weight-bearing status after surgery were also negative predictors. Neither the fracture pattern nor its specific surgical treatment was predictive of any functional outcomes.

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Table 1 (continued)

First author, Year, Location	Design, Setting	Population	n (primary THA)	Intervention	Cognitive Assessment	Criteria for Cognitive Impairment	Associations
Tan, 2016 (Singapore)	Retrospective cohort study	68 patients who were transferred to a rehabilitation unit after hip fracture surgery	68	THA	preexisting	preexisting	Age, dementia and days from fracture to surgery are important predictors of FIM efficiency; age and FIM efficiency are important predictors of ambulation distance; and type of fracture is an important predictor of RLOS. Patients of age < 75 (OR 2.419, p = 0.002), absence of dementia (OR 2.570, p = 0.045) and those who received surgery < 3 days from fracture onset (OR 2.529, p = 0.036) achieved greater FIM efficiency. Younger patients of age < 75 (OR 23.177, p = 0.030) and those with FIM efficiency of more than 7 points per week (OR 38.963, p = 0.05) achieved greater ambulation distance at discharge. Type of hip fracture is an important predictor for RLOS, with neck of femur fracture patients having shorter RLOS (OR 7.186, p = 0.005) CPD and dementia patients over 90 years old have higher 90-day and 1-year mortality hazards postoperatively. Dementia patients are also discharged more quickly than nondementia patients.
Fansa, 2016 (USA)	Retrospective cohort study	39 patients over the age of 90 who underwent surgical repair of a hip fracture	39	THA	preexisting	preexisting	With this tool, we found more than one-third of our elderly patients with fracture were cognitively impaired at the time of admission. These patients had higher rates of in-hospital complications
Heng, 2016 (USA)	observational cohort study	513 patients over the age of 70 underwent THA	513	THA	Mini-Cog	The Mini-Cog test is a simple dementia assessment tool that consists of a clock-drawing task and three-object recall. It is scored on the basis of a simple algorithm (Fig. 1); a score of three words correctly recalled classifies the subject as non-demented; a recall of zero of three words classifies the subject as demented; and subjects with a recall of one to two are further classified by their clock draw (i.e., normal = non-demented, abnormal = demented) <sup>14</sup>	
Uriz-Otano, 2015, (Spain)	Prospective cohort study	314 older adults (> 65 years) admitted for rehabilitation after a hip operation	314	THA	MMSE	MCI was defined as scores between 16-23	Previous walking ability and the presence of complications, such as pressure ulcers or delirium, play a greater role in functional recovery than cognitive impairment.
Bliemel, 2015 (Germany)	prospective, observational cohort study	402 consecutive patients aged ≥ 60 years with	402	THA	MMSE	the results of the MMSE were categorized as 'no cognitive impairment' (27–30 points), 'mild cognitive impairment' (20–26 points), 'moderate cognitive impairment' (10–19 points), or 'severe cognitive impairment' (< 10 points) [31]	Patients with lower MMSE scores are at a higher risk for poorer functional outcomes. Perioperative care should focus on the preservation of functional abilities to protect these patients from an additional loss of independence and disadvantageous clinical course.

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Table 1 (continued)

First author, Year, Location	Design, Setting	Population	n (primary THA)	Intervention	Cognitive Assessment	Criteria for Cognitive Impairment	Associations
Bozic, 2012 (USA)	Retrospective cohort study	The Medicare 5% sample claims database was used to calculate the relative risk of periprosthetic joint infection and of ninety-day postoperative mortality as a function of baseline comorbidities in 40,919 patients who underwent primary total hip arthroplasty between 1998 and 2007	40,919	THA	preexisting	preexisting	Comorbid conditions associated with an increased adjusted risk of ninety-day postoperative mortality (in decreasing order of significance, $p < 0.05$ for all comparisons) were congestive heart failure (HR = 2.11), metastatic cancer (HR = 3.14), psychosis (HR = 1.85), renal disease (HR = 1.98), dementia (HR = 2.04), hemiplegia or paraplegia (HR = 2.62), cerebrovascular disease (HR = 1.40), and chronic

PD = preoperative dementia; DLB = dementia with Lewy bodies; ADL = activities of daily living; COPD = chronic obstructive pulmonary disease; AMNART = American National Adult Reading Test; AVLT = Auditory Verbal Learning Test; CAS = Cognitive Activity Scale, COWAT = Controlled Word Association Test, HR = hazards ratio, IADL = instrumental activities of daily living, LOS = length of stay, MMSE = mini-mental state exam, MoCA = Montreal Cognitive Assessment, OR = odds ratio, ROC = receiver operating characteristic, SCWT = Stroop Color-Word Test, TKA = total knee arthroplasty, THA = total hip arthroplasty, POD = postoperative delirium, FIM = Functional Independence Measure; RLOS = Rehabilitation Length of Stay.

age-adjusted multivariate analysis on patients with a Mini-Cog® score less than or equal to 2 and showed they were more likely to develop POD with an odds ratio of 4.52 (95% 1.30–15.68,  $P = 0.05$ ). Tow et al. measured delirium using Confusion Assessment Method (CAM) and severity Memorial Delirium Assessment Scale (MDAS) to assess for postoperative delirium [12]. The results demonstrated that MMSE scores between 24 and 27 were associated with delirium incidence. Jankowski et al. measured POD using CAM preoperatively and 3 months following surgery [7]. The authors showed that a reduced preoperative neurocognitive status predicted POD. A study by Liang et al. showed that when comparing those who developed post-operative delirium with those who did not, the former had a poorer preexisting cognitive function (59.5% vs. 37.0% of MMSE scores < 24,  $P < 0.007$ ) [13]. Koskderelioglu et al. showed that patients with cognitive impairment defined as a low MMSE score were more likely to have postoperative delirium ( $P = 0.001$ ; odds ratio 0.75, 95% CI 0.65–0.86) [14]. A study by Heng et al. showed that delirium was significantly increased in patients with an abnormal Mini-Cog® test and had an odds ratio of 3.22 (95% 1.59–6.77,  $P = 0.001$ ) [15]. Jansen et al. was the only case control study with 445 patients who underwent THA that could not confirm an association between preexisting cognitive impairment and POD [16].

Four studies investigated the impact of preoperative cognitive impairment on postoperative in-hospital mortality. Two of the studies were prospective with a combined total of 1052 patients while the remaining were retrospective. All of the prospective studies were good quality studies based on the Newcastle Ottawa Scale. Zerah showed that after adjusting for age, sex, and comorbidities, in-hospital mortality did not differ between dementia patients with a hazard ratio of 0.7 (95% CI 0.4–1.2), when compared with patients without dementia [10]. Bliemel et al. showed a similar finding, specifically, that complication rates were similar between patients with lower MMSE scores compared to those with normal MMSE scores ( $P > 0.05$ ) [18].

While the retrospective studies had a combined total of 5,659,437 patients. Stavros et al. showed that preoperative risk factors for in-hospital mortality were advanced age, presence of comorbid diseases such as dementia, and renal or cerebrovascular disease [17]. The study by Buller et al. showed that patients with a diagnosis of dementia had higher in-hospital mortality ( $P < 0.001$ ) [19].

Three studies investigated the impact of preoperative cognitive impairment on postoperative in-hospital complications. One of the studies was prospective, while the other 2 were retrospective. The prospective study had a combined total of 513 patients while the retrospective studies had a combined total of 2,924,456 patients. All studies were good quality studies based on the Newcastle Ottawa Scale. The prospective study of Heng et al. showed that their cohort's rate of in-hospital medical complications was 28.6% and that patients with cognitive impairment as diagnosed with the Mini-Cog® test had significantly higher odds of an in-hospital complication compared with patients with a normal Mini-Cog® (OR, 2.16 [95% CI 1.42–3.31];  $P < 0.001$ ) [15].

The retrospectives studies such as Buller showed that having diagnoses of depression, dementia and schizophrenia were associated with increased odds of adverse events ( $P < 0.001$ ) [19].

In contrast, Enemark et al. showed that patients with dementia, when compared to the non-dementia group exhibited no significant differences in hospital complications between the two groups [20].

Two studies investigated the impact of preoperative cognitive impairment on discharge disposition. The prospective study had a combined total of 88 patients while the second one was a retrospective study with a combined total of 2,924,442 patients. All these studies were good quality studies based on the Newcastle Ottawa scales. Cully et al. showed that patients with a Mini-Cog® less than or equal to 2, after adjusting for age and using a multivariate analysis were more likely to be discharged to a place other than home, with an odds ratio of 3.88 (95% CI 1.58–9.55,  $P < 0.05$ ) [11]. Buller et al. showed that all

**Table 2**  
Assessment of study quality using the Newcastle-Ottawa Scale.

First author, year	Selection	Comparability	Outcome	Total	Quality
Mosk, 2017	4	2	3	9	Good
Enemark, 2017	4	2	3	9	Good
Mukka, 2017	4	2	3	9	Good
Lee, 2017	4	2	3	9	Good
Zerah, 2017	4	2	3	9	Good
Culley, 2017	3	2	3	8	Good
Tow, 2016	4	2	3	9	Good
Puustinen, 2016	2	0	3	5	Poor
Guerini, 2010	4	2	3	9	Good
Jämsen, 2014	4	2	3	9	Good
Jankowski, 2011	4	2	3	9	Good
Liang, 2015	4	2	2	8	Good
Stavros, 2010	4	2	3	9	Good
Buller, 2014	4	2	3	9	Good
Koskderelioglu, 2017	4	2	3	9	Good
Mariconda, 2016	2	0	3	5	Poor
Tan, 2016	2	0	3	5	Poor
Fansa, 2016	4	2	3	9	Good
Heng, 2016	4	2	3	9	Good
Uriz-Otano, 2015	4	2	3	9	Good
Bliemel, 2015	4	2	3	9	Good
Bozic, 2011	4	2	3	9	Good

pre-existing psychiatric comorbidities including dementias were associated with higher odds of non-routine discharge ( $P < 0.001$ ) [19].

Five studies investigated the impact of preoperative cognitive impairment on hospital length of stay. Three studies were retrospective with a combined total of 619 patients, while one was prospective and the last one was a case control study with a combined total of 533 patients. All were good quality studies based on the Newcastle Ottawa Scale. In terms of retrospective studies, the study by Enemark et al. showed that there was no significant difference in length of stay between patients with dementia and patients without the diagnosis [20]. Fansa et al. showed that dementia patients stayed in-hospital postoperatively an average of 5.3 days ( $P = 0.013$ ) less than non-dementia patients [23]. Mosk et al. showed that patients with dementia has a shorter hospital stay when compared with patients without dementia with a  $P$  value  $< 0.001$  [22].

In contrast, the prospective study by Culley et al. showed that patients with a Mini-Cog© less than or equal to 2 were more likely to have longer hospital LOS when compared with patients with scores of  $> 2$  and showed a hazard ratio of 0.63 (95% CI 0.42–0.95,  $P = 0.05$ ) [11]. Jamsen et al. showed that patients with a preexisting diagnosis of Alzheimer's disease had a longer peri-operative hospitalization versus patients who did not have this diagnosis (median 13 days vs eight days,  $P < 0.001$ ) [21].

### 3.4. Association of cognitive impairment with short-term outcomes

We did not find any good quality studies that investigated the impact of preoperative cognitive impairment on mortality or complications within 30 days.

### 3.5. Association of Cognitive Impairment with long-term outcomes

Six studies investigated the impact of preoperative cognitive impairment on mortality between 1 months and 2 years postoperatively. Four of the studies are prospective studies with a combined total of 1321 patients. Lee et al. showed that patients with dementia had a higher risk of one year mortality than patients without dementia, with a hazard ratio of 1.71 (95% CI 1.06–2.77,  $P = 0.05$ ) after adjusting for many variables such as age, sex, medical comorbidity and surgery duration [24]. Guerini et al. showed that patients who were significantly older and had lower cognitive performance died at a higher rate during the 12-month period following discharge. The MMSE mean

score for patients who died was 22.3 compared to a mean score of 25.4, which was a significant finding ( $P = 0.003$ ) [25]. Jamsen et al. showed that patients with a preexisting diagnosis of dementia, in that case being Alzheimer's disease, had a higher mortality with a hazard ratio of 1.43 (95% CI 1.22–1.70,  $P = 0.05$ ) [16]. Mukka et al. showed that patients in the cognitively impaired group had a higher mortality rate when compared with the control group when they used the Kaplan–Meier estimator (log-rank test,  $P = 0.0016$ ) [27].

The two retrospective studies included a combined total of 40,958. Fansa et al. showed that patients with dementia and age over 90 years old have a higher 90 day and 1-year mortality with hazards of 88% ( $P = 0.01$ ) and 75% ( $P = 0.01$ ), respectively [23]. Bozic et al. showed that comorbid conditions such as congestive heart failure, metastatic cancer, psychosis, renal disease, hemiplegia or paraplegia, cerebrovascular disease, and chronic pulmonary disease had an increased adjusted risk of 90-day postoperative mortality [26]. Also, dementia had an increased adjusted risk of 90-day postoperative mortality with a hazard ratio of 2.04 (95% 1.55 2.69,  $P = 0.0001$ ).

Four studies investigated the impact of preoperative cognitive impairment on functionality between 1 month and two years postoperatively. Two of the 4 studies were good quality studies while the rest were poor quality based on the Newcastle Ottawa Scale. Three of the four studies are prospective studies with a combined total of 984 patients. Mukka et al. showed that the cognitively impaired group exhibited less function during walking (28% vs. 4% and with an odds ratio of 9.2 (95% CI 2.63–32.7,  $P = 0.001$ ) [27]. Mariconda et al. showed that patients with poor cognitive status with an MMSE score  $< 27$  had worse prognosis in terms of losing the ability to walk at 1 year and with an odds ratio of 0.93 (95% CI 0.88 0.98,  $P = 0.005$ ) [29]. Uriz-Otano et al. showed that patients with CI had lower rates of recovering autonomy in activities of daily living (ADLs) before the surgery and were less likely to walk when compared to patients without cognitive impairment, 50% vs 73%, respectively ( $P < 0.001$ ). This study showed that the degree of CI had an odds ratio of 1.12 (95% CI 1.04–1.22) as it predicted the functional recovery after surgery [30]. While the single retrospective study had a total of 68 patients. Tan et al. showed that patients with dementia had less function post-discharge, and dementia was an important predictor when using the Functional Independent Measure (FIM) tool. Using a univariate analysis they demonstrated that dementia (mean = 1.7  $\pm$  SD 1.3,  $P = 0.023$ ) was a factor contributing to a lower FIM score [28].

Three studies investigated the impact of preoperative cognitive impairment on complications between 1 month and two years postoperatively. Two of the studies analyzed were good quality studies while the remaining study by Puustinen et al., was poor quality based on the Newcastle Ottawa Scale [31]. All studies were prospective studies while none were retrospective with a combined total of 1119 patients. Zerah et al. showed that patients with dementia were more likely to be institutionalized after 6 months compared to patients without dementia with an odds ratio of 2.6 (95% CI 1.4–4.9,  $P = 0.003$ ) [10]. Puustinen et al. showed that patients with low preoperative MoCA, MMSE, and Mini-Cog© scores had higher long-term complications and predicted higher follow-up treatment in health-care center hospitals with an odds ratio of 0.721 with  $P = 0.043$  [31]. The Puustinen et al. study was poor quality based on the Newcastle Ottawa Scale. Jamsen et al. showed that patients with a preexisting diagnosis of Alzheimer's disease had an increased risk for hip revision in the long term, with a hazard ratio of 1.76 (95% CI 1.03–3.00,  $P = 0.05$ ) [16].

## 4. Discussion

This systematic review demonstrates that there is a fair to good quality evidence demonstrating that preoperative CI predisposes patients undergoing elective primary THA to worse in-hospital outcomes, increasing the risk for delirium, longer hospital stay and discharge to a health care facility rather than home.

**Table 3**  
Outcome measures assessed in studies meeting inclusion criteria and the strength of the body of evidence for each outcome studied.

First author, year	In-hospital					Short-term (within 30 days)		Mid-term (1 month–2 years)		
	POD	Mortality	Complications	Discharge disposition	Length of stay	Mortality	Complications	Mortality	Functionality	Complications
Mosk, 2017	X				X					
Enemark, 2017	X		X		X					
Mukka, 2017								X	X	
Lee, 2017								X		
Zerah, 2017	X	X								X
Culley, 2017	X			X	X					
Tow, 2016	X									
Puustinen, 2016										X
Guerini, 2010								X		
Jämsen, 2014					X			X		X
Jankowski, 2011	X									
Liang, 2015	X									
Stavros, 2010		X								
Buller, 2014		X	X	X						
Koskderelioglu, 2017	X									
Mariconda, 2016									X	
Tan, 2016									X	
Fansa, 2016					X			X		
Heng, 2016	X		X							
Uriz-Otano, 2015									X	
Bliemel, 2015		X								
Bozic, 2011								X		
Summary of evidence <sup>a</sup>	(4) 2b, (1) 4; consistent results	(2) 2b; inconsistent results	(2) 2b; inconsistent results	(3) 2b, (1) 4; consistent results	(3) 2b, consistent results	(2) 2b; inconsistent results	(1) 2b; inconsistent results	(1) 3b, (2) 2b; consistent results	(2) 4, (1) 2b; inconsistent results	(1) 2b
Quality of body of evidence <sup>b</sup>	Moderate	Low	Low	Moderate	Moderate	Low	Low	Low	Low	Low

<sup>a</sup> Level of evidence based on Oxford Centre for Evidence-based Medicine's "Levels of Evidence".

<sup>b</sup> Grading based on the Cincinnati Children's Hospital Medical Center Evidence Collaboration's "Grading the Body of Evidence".

This is the first systematic review to specifically assess preoperative CI as a prognostic factor for adverse postoperative outcomes in primary THA patients. While previous systematic reviews have examined outcomes in elderly patients admitted with a femoral neck fracture, these studies focused on outcomes after rehabilitation instead of immediately post-operatively [32,33]. In this review we specifically examine patient outcomes immediately after THA in the hospital setting and also include both short- and long-term outcomes rather than just the outcomes following rehabilitation facility stay. Finally, this review included a significantly larger, more diverse cohort of patients than any previous study [32].

Researchers and clinicians are increasingly advocating for the development and use of tools to identify patients with cognitive impairment (CI) who are undergoing surgery. This effort is particularly valuable in the population undergoing THA due to the large number of elderly patients [34]. Screening for CI has been shown to improve care and better predict the risk of developing postoperative complications such as delirium [35]. Post-operative outcomes such as delirium can cause delay in rehabilitation, longer hospitalization stays, increased mortality and possibly long-term cognitive impairment. However, most preoperative evaluations focus on the assessment of cardiac, pulmonary, renal and hepatic organ systems while routine assessment for possible CI is not done [36].

Although previous studies have examined the impact of cognitive impairment and delirium, no existing review has systematically assessed the impact of CI on outcomes in a large cohort of patients. For example, a review by Bin Abd Razak et al. systematically reviewed the incidence of postoperative delirium in patients undergoing total joint arthroplasty of the hip and knee with the goal of identifying the risk factors that led to higher delirium rates in this patient population [37]. However, there was no analysis of the impact of CI on postoperative outcomes. Similarly, a review by Rao et al. examined the outcomes of

patients with dementia versus patients without dementia [38]. However, that study focused on patients with diagnosed dementia, as opposed to cognitive impairment, which is both more prevalent and less clinically apparent.

This review adds to the existing literature by synthesizing the post-operative outcomes based on studies between 1997 and 2018 with patients who had CI and underwent a THA. We were able to assess various post-operative outcomes including POD, mortality, discharge disposition, LOS, as well as short- (e.g. 30 day) and long-term (e.g. 1 month–2 years) complications. For all the outcomes of interest, the majority of the studies show that pre-operative CI is associated with worse outcomes. However, there is one conflicting finding on the impact of CI on the hospital LOS. Mosk et al. showed that patients with CI had shorter length of stay while the other studies showed the opposite [22]. Potential explanations for this variation include that the patient population of the Mosk et al. study was from a skilled nursing facility and these patients were being discharged back to those facilities.

#### 4.1. Implications for clinical practice

The results of our study suggest that CI is an important and under-appreciated factor in patient recovery after elective THA [39]. Routine pre-operative screening currently focuses on organ system dysfunction that may result in immediate complications. Given the impact of CI on postoperative outcomes, patients may benefit from multidisciplinary interventions and clinical pathways to prevent unwanted complications in this population, such as POD. The ready availability of screening instruments and the clinical importance of CI on outcomes suggests that routine screening for cognitive impairment may be necessary in certain patient populations, such as those aged 65 or older and those with other significant co-existing conditions, in order to risk-stratify these patients [36]. Early identification of patients with CI would allow for focused

post-operative interventions to limit and mitigate the risk of developing or exacerbating post-operative complications such as delirium or cognitive decline. These patients could be preferentially triaged to perioperative pathways that include early geriatrician involvement, multimodal analgesia, early mobilization and frequent redirection with the goal of maintaining function, limiting delirium and improving neurocognitive recovery.

This study has additional implications for future health services research, as there is evidence that one third of patients with hip fractures have concomitant cognitive impairment, but many hip fracture trials have specifically excluded this population (38). Given the prevalence of CI and the adverse outcomes associated with the condition, future hip fracture trials are needed to identify factors associated with improved outcomes after elective THA in this higher risk population.

This review also underscores the unavoidable heterogeneity of patients with CI, given variable definitions used in the studies included. Future research is needed to formally subdivide CI, so that trials can be conducted with a more standardized patient cohort. The standardization should be both in measurement methods and the threshold values used to select the CI group to have better comparisons across studies.

#### 4.2. Strengths and limitations

This study has several strengths. First, we developed a well-defined protocol with two levels of review, created clear inclusion and exclusion criteria and a good documentation of reasons for study exclusion. We used an established systematic review methodology to evaluate the evidence. Also, we accepted a broad range of terms when it comes to the definition of CI that ensured the inclusion of all significant published literature. An additional strength is that we also included more recent literature reflecting contemporary surgical and anesthetic practices.

There are several limitations of this study. First, this systematic review is limited since it includes different subgroups of cognitively impaired patients. In addition, this review does not analyze how other covariates such as age or other comorbidities with preoperative cognitive impairment affect the outcomes of this review. Second, there was significant heterogeneity in sample size and study design. For example, the studies employed different tools to assess cognitive status, such as MMSE, Mini-Cog®, MoCA, and several others. Further, the assessment of cognitive status was different in each study as each had different scales and several had a different threshold value. Another limitation to generalizability is the study location. Only nine of the 22 studies were conducted in the US. However, the two largest studies in our review were done in the US and they include > 90% of the study participants, making this limitation of generalizability less of a concern.

#### Disclosures

None.

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None.

#### Appendix A. A detailed description of the database-specific search terms used during the literature search

##### PUBMED database:

(alzheimer's OR dementia OR cognition OR "cognitive defects" OR "cognitive deficits" OR "cognitive disorders" OR "cognitive dysfunction" OR "cognitive function" OR "cognitive impairment" OR "cognitive status" OR "memory defects" OR "memory deficits" OR "memory disorders" OR "memory dysfunction" OR "memory impairment" OR

"mental function") AND

(anesthesia OR surgery OR "surgical procedure" OR operation) AND (outcomes OR "outcome assessment" OR prognosis OR "surgical outcomes")

##### EMBASE and MEDLINE databases:

('alzheimer disease'/exp OR 'alzheimer disease' OR 'dementia'/exp OR 'dementia' OR 'cognitive defect'/exp OR 'cognitive defect' OR 'memory disorder'/exp OR 'memory disorder' OR 'mild cognitive impairment'/exp OR 'mild cognitive impairment' OR 'thinking impairment'/exp OR 'thinking impairment') AND ('anesthesiology'/exp OR 'anesthesiology' OR 'surgery'/exp OR 'surgery') AND ('outcomes research'/exp OR 'outcomes research' OR 'outcomes'/exp OR 'outcome assessment'/exp OR 'outcome assessment' OR 'prognosis'/exp OR 'prognosis') AND ('cognition'/exp OR 'cognition' OR 'mental function'/exp OR 'mental function' OR 'dementia'/exp OR 'dementia') AND [1997-2017]/py AND [humans]/lim AND [english]/lim NOT ('children' OR 'child' OR 'pediatric' OR 'adolescent')

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