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None declared.

Clinical outcomes and quality of life after Total Knee Replacement (TKR) - A systematic review protocol

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Review question / Objective: **Clinically, knee is the most common site of osteoarthritis (OA), followed by the hand and hip. The basic research question of our study: Is total knee replacement (TKR) associated with better clinical outcomes and quality of life among patients with OA knee aged 40 and above, not responding to non-surgical management, is? Based on this review question, the following objectives are proposed, 1. to refresh the evidence on clinical effectiveness of TKR and 2. to explore the determinants influencing its success. Population Patient aged >= 40 years with OA Knee of all Kellgren Lawrence grade. Intervention Total Knee Replacement (TKR) Comparator Pre-TKR Outcome Clinical effectiveness in terms of improvement in QoL.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 April 2022 and was last updated on 28 April 2022 (registration number INPLASY202240166).

INTRODUCTION

Review question / Objective: **Clinically, knee is the most common site of osteoarthritis (OA), followed by the hand and hip. The basic research question of our study: Is total knee replacement (TKR) associated with better clinical outcomes and quality of life among patients with OA knee aged 40 and above, not responding to non-surgical management, is? Based on this review question, the following objectives are proposed, 1. to refresh the evidence on clinical effectiveness of TKR**

and 2. to explore the determinants influencing its success. Population Patient aged >= 40 years with OA Knee of all Kellgren Lawrence grade. Intervention Total Knee Replacement (TKR) Comparator Pre-TKR Outcome Clinical effectiveness in terms of improvement in QoL.

Rationale: The clinical effectiveness of TKR is being published for many years from various settings with a variety of nuances. Systematic reviews of such papers of clinical effectiveness of TKR were also published from time to time and the latest review to be published on this topic was in 2015. Many of these previous studies which were included in the reviews had multiple study designs – the common comparators used were either individuals with OA knee who did not undergo surgery or the same patient prior to surgery was used as the control group (pre and post design). The current review is a part of the broader study which is set out to calculate the values of the parameters to conduct cost utility estimates of TKR in India, for which we already have costing data of treatment of OA knee before and after TKR. Therefore, as we also require clinical effectiveness estimates from studies which had employed pre and post TKR study designs only, this current review included studies with that particular design exclusively. Also we reviewed the effectiveness of TKR for different follow-up periods starting from very short-term to long-term which have never done before. This will not only provide precise data for our main cost-utility study but will also add valuable information to the existing body of TKR literature, especially as the procedure is now being offered to increasing number of sufferers of OA knee globally and in different settings with different clinical resources. Moreover, the determinants of the "success" of TKR are yet to be synthesized systematically from the existing body of evidence, inclusion of which may add value to the current review process. As India aims to achieve Universal Health Coverage, there is a need to ramp up its primary care infrastructure and also introduce public-funded health insurance and assurance schemes to finance healthcare. Pradhan Mantri Jan Arogya Yojana (PMJAY) being one of the insurance choices in the public exchange place, cost-effectiveness of important disability-alleviating procedures like TKR assumes extreme importance as this may help to allocate resources efficiently for such critical procedures within the ambit of insurance and address the issue of moral hazard effectively. With an increase in ageing population, new technological advancements, and competition for limited resources demand judicious resource allocation globally. In the present era, there are limited medical resources and therefore it is essential for the healthcare provider to know the clinical and cost-effectiveness of the treatment. This is true for TKR as it is a seminal procedure for disabling conditions like knee OA, which is on the rise across the globe. Therefore, it is imperative that a comprehensive health technology assessment is carried out for TKR in India, which becomes even more relevant given the scarcity of information in India. This systematic review attempts to establish the effectiveness of total knee replacement in terms of quality of life.

Condition being studied: Osteoarthritis (OA) is a chronic degenerative disease characterized by deterioration of the cartilage in joints and is a leading cause of disability globally. The characteristics of the knee OA comprises of muscle weakness, fatigue and increased pain in joints. When these symptoms progress, it will lead to decreased mobility, deconditioning, reduced functional capacity and mobility and overall contributes to decline in the patient's quality of life. Clinically, the knee is the most common site of OA, followed by the hand and hip. Osteoarthritis is the second most common rheumatologic problem and is the most recurrent joint disease encountered in the clinical practice in Indian and Asian populations aged 40 and above with a prevalence in the range of 22% to 39%. Knee osteoarthritis is considered to have an estimated prevalence of 3.8% radiographically confirmed symptomatic cases. The prevalence was found to be higher among

females than in males and peaked at around 50 years of age. According to the Global Burden of Disease 2010 Study hip and knee joints are commonly affected with osteoarthritis. The disease condition ranked 11th highest in terms of YLDs (Years lived with disability) and 38th highest in terms of overall disease burden calculated in terms of Disability Adjusted Life Years (DALYs) among 291 conditions. With the burden of OA being on the rise, it has significant implications on the individuals affected, the healthcare system, and also has broader socioeconomic repercussions on the society. Symptomatic knee osteoarthritis has been shown to have a significant impact on the quality of life (QoL) of the patients suffering from the condition. Health-related quality of life (HRQoL) is a multidimensional concept equipped to assess the impact of health status on areas related to the quality of life such as physical and psychosocial wellbeing, the fulfillment of life roles, and satisfaction, in contrast, to merely objective changes in health status. This metric is commonly used in clinical effectiveness and economic evaluation studies to determine how effective treatments are or how they relate to cost-effectiveness. Total knee replacement (TKR) is proven to be extremely effective in treating symptoms of OA and is also associated with high patient satisfaction and improved QoL.

METHODS

Search strategy: The outcome measures included were Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee Society Score (KSS), EQ5D,Knee Injury, and Osteoarthritis Outcome Score (KOOS), SF 36/12, Quality of life (QoL). A literature search was performed on 7/9/2021 using the PubMed database by three authors__ Dr. Jeba Malar, Ms.Amatullah Sana Qadeer, Dr. Naline Gandhi _____. No time limits were imposed on the search. The search term was formulated by three authors Dr. Jeba Malar, Ms.Amatullah Sana Qadeer, Dr. Naline Gandhi _____ after conducting a thorough literature for relevant keyword identification. The MESH terms for keywords of interest were identified and Boolean operators were used in conjunction to prepare the search parameter. The final search parameters used were: ("arthroplasty, replacement, knee"[MeSH Terms] OR ("arthroplasty"[All Fields] AND "replacement"[All Fields] AND "knee"[All Fields]) OR "knee replacement arthroplasty"[All Fields] OR ("total"[All Fields] AND "knee"[All Fields] AND "replacement"[All Fields]) OR "total knee replacement"[All Fields]) AND ("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields]).

Participant or population: Patients whose age is above >= 40 years with knee Osteoarthritis with all Kellgren -Lawrence grades will be considered. According to the WHO report, the prevalence of osteoarthritis is higher among older adults aged 40 years and above. Both male and female with knee OA will be included. Studies suggested total knee replacement to be the treatment of choice among patients diagnosed with Kellgren Lawrence grade ≥ III. However, in India moral hazard associated with TKR is high where patients with lower KL-grade OA are undergoing TKR. Hence, the review will include studies conducted on patients diagnosed with all Kellgren-Lawrence grades osteoarthritis knee.

Intervention: All approaches of Total knee replacement (TKR) such as posterior stabilizing, cruciate retaining & constraint approaches will be considered for the review. Total knee replacement is extremely effective in treating symptoms of OA and is also associated with high patient satisfaction and improved QoL. TKR is performed to improve the patient's function, correct deformity, maintain balance in mobility and alleviate the knee pain. It is a proven effective means for relieving the pain and other symptoms associated with Knee OA. It is a common surgical modality practiced in western countries like Spain, Russia, UK, USA and Australia. Despite its effectiveness, financial and resource constraints prohibit

its widespread use in developing countries like India.The review will exclude studies which assess revision TKR.

Comparator: The comparator for the intervention that is TKR would have ideally been non-surgical conservative management of OA knee of comparable severity. However, for ethical reasons, almost all the studies in this domain did not track any patient who was eligible for TKR but who was not offered TKR . Hence, in all the studies that were considered for this review, the pre-TKR status of the patients were compared to their post TKR status – thus the same individual serving as the comparator for himself or herself.

Study designs to be included: Reports of Randomized Control Studies (RCT) and observational cohort studies, will be included.

Eligibility criteria: Randomized control trial, quasi-randomized control trial considering pre-TKR and post-TKR and prospective& retrospective cohort study where pre-treatment and post-treatment effectiveness score is compared will be used for the review. Studies involving participants >/= 40 years of age will be included. The studies including both clinical effectiveness like KOOS (Knee Injury and Osteoarthritis Outcome Score), WOMAC (Western Ontario and McMaster University Osteoarthritis Index), OKS (Oxford Knee Scores), Knee Society Score (KSS) and/or patient-reported utilities such as EQ5D (Euro QoL 5 dimensional); SF-12, SF-36 will be taken into consideration. Studies assessing total knee replacement performed for causes other than age-related osteoarthritis (e.g traumatic osteoarthritis) will be excluded from the review.

Information sources: An electronic search will be done to identify the relevant studies. The studies conducted on humans, those which are published in the English language will be considered for the exercise. The following electronic database will be used for the search of studies and the appropriate MeSH terms/search strategies will be employed. a. Cochrane Central Register of Controlled Trials (CENTRAL) b. NHS Database c. MEDLINE (PubMed) d. HTAIn repository
Additional literature which was considered relevant to the review was identified through "snowballing" the bibliographies of the studies that the search process yielded.

Main outcome(s): Studies using the following five Patient Reported Outcome Measures (PROMs), either as standalone measures or in combinations, were included in the review, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score (OKS), Knee Society Score (KSS), Knee Injury, Osteoarthritis Outcome Score (KOOS) and Short Form 36/12 (SF 36/12). WOMAC measures the condition of patients with osteoarthritis knee in terms of three components, pain, stiffness and function of the knee joint. KSS and KOOS also assess the same components as WOMAC but with different scoring scales – KOOS measuring wellbeing in addition. OKS measures the individual levels of functions, activities of daily living and how patients suffering knee arthropathy have been affected by pain outcomes . SF-36 and SF-12 (which is an abbreviated version of the longer SF-36) assess purely the quality of life among patients with chronic health conditions. The studies, those used these five PROMs to measure the changes in the situation before and after TKR, were considered for the systematic review.

Additional outcome(s): Nil.

Data management: After primary and secondary screening, the studies to be included for systematic review will be finalized. The information collected will be summarized into a matrix created on MS-Excel. The matrix will include the study name, author name, objectives, population, inclusion, exclusion criteria, methodology, outcome estimation, measures of association, determinants and study findings.

Quality assessment / Risk of bias analysis: Method of quality assessment in primary studies. A narrative synthesis will be

performed initially with the included studies. Risk of bias will be assessed using Cochrane Risk of Bias tool (RoB). Based on the Cochrane Risk of Bias Tool, a five domain tool will be used to evaluate the risk of bias for randomized controlled trials (RCTs), which involves elements such as selection, performance, attrition, reporting, and others. Similarly, A Cochrane Risk of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI) involving seven domains will be used to assess risk of bias in non-randomized studies.

Strategy of data synthesis: The clinical effectiveness of and quality of life (QoL) of Knee Osteoarthritis pre and post-TKR will be obtained from a systematic literature review. Numerous. PROMs encompass several components, but for each component, different PROMs have different numbers of items, and each item uses a different measurement scale. Therefore, the review process needs harmonization of the PROMs, so that based on such standardized metrics, comparison between studies can be carried out. This process will involve aligning the directions of the scores into a uniform scale and a composite score will be calculated using a weighted mean approach by the item numbers in each PROM measures. Finally, the mean difference will be calculated as a proportion of pre-score from pre to post scores.

Subgroup analysis: NA.

Sensitivity analysis: NA.

Language: Papers published in English language were only imposed for selection of studies for the review.

Country(ies) involved: India.

Keywords: Knee osteoarthritis; pre and post Total Knee replacement; QALY.

Dissemination plans: The results of this study would be published in a peer-reviewed indexed journal. The findings from the systematic review would be communicated to the Department of Health Research as a part of the Health Technology Assessment Report on the cost-utility of total knee replacement for osteoarthritis knee patients.

Contributions of each author:

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