Epidemiological factors associated with revision of total joint replacement surgery: A nested case-control study

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Research Article

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Abstract

Background: Total Joint Replacement (TJR) is the most effective treatment for patients with end-stage joint pathologies, such as osteoarthritis (OA). However, this procedure can result in prosthesis failure, consequently requiring an early revision. These revision surgeries come at a high cost to the healthcare system and increase morbidity to patients. Therefore, it is crucial to identify factors associated with revisions to inform surgical decision-making.

Methods: This study was a nested-case control study utilizing participants recruited in the he Newfoundland Osteoarthritis Study (NFOAS), initiated in 2011. Study participants were patients who underwent TJR (hip/knee) due to various pathologies, with OA accounting for a large proportion of cases. Revision status was collected through a chart review on the Eastern Health Meditech Health Care Information System. Seventy-two variables collected by general health questionnaires and medical reports were examined for associations with revisions.

Results: A total of 1086 patients were recruited in the study; 810 patients were included (41.5% hip and 58.5% knee) in the final analysis; 30 of them underwent revision surgery. Seven factors were identified to be associated with revision status (number of live births, hysterectomy, hypertension, lateral epicondylitis, back pain that radiates to legs, more than five comorbidities, and the surgeon; all $p<0.05$). Of these variables, patients requiring revisions were more likely to have had lateral epicondylitis or their primary surgery conducted by the surgeon coded E5. In contrast, non-revision patients were associated with more live births, more than five comorbidities, hysterectomy, hypertension, or back pain that radiated to their legs.

Conclusions: Our data suggested that surgeon and patients' health factors were associated with the odds of requiring revision surgery. Therefore, patients' risk of revision surgery could theoretically be calculated prior to TJR, better informing patient treatment decisions.

Background

Total hip and knee replacement surgery resides as two of the most common inpatient surgeries conducted in Canada and worldwide(1, 2). With over 130,000 hip and knee surgeries performed in Canada during 2018–2019, the demand of these procedures increased over 20% in the past five years resulting in a 1.4 billion dollar cost nationally(3). This trend is multifactorial. Firstly, TJR has become a safe and effective treatment for highly debilitating joint pathologies such as osteoarthritis (OA). This is in part due to evolving technologies for implants, fellowship programs dedicated to hip and knee arthroplasty, and national registries providing evidence for quality improvement(4). Secondly, demographic factors such as a growing older population and increasing prevalence of obesity are risk factors that contribute to the growing incidence of OA(5).

Ideally, these arthroplasties should last 15–20 years before requiring a revision, however, early prosthetic revision is a well-recognized complication of these procedures(6, 7). An early revision can be defined as any prosthetic replacement that takes place before the estimated longevity of the prosthetic. The interval of time used to define an early revision is highly variable, depending on the joint registry or report one subscribes to. Early hip and knee revision surgery has been reported to occur in 2.2% and 1.9% of patients respectively, when early is defined as before 2-years(1). These surgeries not only represents a large expense to the healthcare system, costing 1.4–1.6 times more than the primary procedures, but also imposes increased morbidity and risk to the patients that endure them(1).

As the number of total joint replacements (TJR) performed annually continue to increase, the number of revisions required and their cost to the healthcare system will grow as well. Therefore, it is crucial that the utilization of these procedures is guided by an evidence-based approach. Identification of patient factors that contribute to the risk of requiring an early revision will allow clinicians to appropriately inform patients of risk, optimize surgical decisions, and monitor patients postoperatively. Therefore, the aim of this study was to examine the epidemiological factors of TJR revision surgery in a well-established TJR patient cohort.

Methods

Study Participants

This study was a retrospective nested case-control study conducted as part of the Newfoundland Osteoarthritis Study (NFOAS), which was initiated in 2011(8). Participants were recruited from those undergoing TJR at St. Clare's Mercy Hospital and Health Science Centre General Hospital in St. John's, Newfoundland and Labrador (NL), Canada. The study recruited 1086 patients who underwent total knee or hip replacement surgeries between November 2011 and September 2017 largely due to OA with a small number of patients due to other joint diseases. Patients of all disease aetiologies were included in the current study. Joint revision was defined as requiring a staged or full replacement of the prosthetic after undergoing total joint replacement. Revision status was collected through a chart review of patients on the Eastern Health Meditech Health Care Information System. The accuracy of revision status was valid up to and including June 7th, 2021. The study was approved by the Health Research Ethics Authority of Newfoundland and Labrador (HREB # 2011.311), and written informed consent was obtained from all participants. All methods were performed in accordance with the relevant guidelines and regulations of this authority.

When enrolled into the NFOAS, patients were requested to fill out an extensive general health questionnaire pre-surgery. The questionnaire was split into five sections which included demographics, occupation, medical history, nodal status, and family history of OA. This questionnaire included 84 questions of which some had multiple parts. Questionnaire data was self-reported and converted into electronic format from hard copy and confirmed by a second researcher. For questions regarding medical history patients were instructed to only report conditions that were given by a doctor or other health professional. Information on patients' multisite musculoskeletal pain (MSMP) was collected using a simple questionnaire where patients were asked to circle sites of pain on a manikin (**Supplementary**

Fig. 1), and the total number of pain sites was summed. Patients were considered to have MSMP if they had seven or more sites of pain, consistent with other studies(9, 10). Patients' age, height, and weight at surgery were collected from electronic medical records. In cases where TJR was indicated due to trauma, weight and height were not consistently measured pre-operatively. In these cases BMI were either left blank or a measurement close to the surgical date was reported.

Statistical Methods

Data underwent a quality control procedure prior to final analysis. Patients were excluded from analysis if they did not complete the questionnaire or surgical data (revision status, surgeon, or type of implant used) was missing or incomplete. Questions were excluded from analysis if the answer was not categorical or numerical (i.e. if the answer was a text box), as analysis of those variables was not possible. As many of the reported cancers and cardiovascular disease were reported in low numbers, two merged variables, cancer (breast cancer, colon cancer, melanoma, basal cell carcinoma, squamous cell carcinoma, and other reported cancers) and cardiovascular disease (congenital heart disease, coronary heart disease, myocardial infarction, angina, stroke, deep vein thrombosis, and varicose veins) were created. For quantifying co-morbidities all diseases reported in the general questionnaire were included in this analysis (**Supplementary Table 1**). For individual variables, patients were excluded from analysis if they left a question blank or reported the variable as unknown. Patients were also excluded from the analysis for factors that were not relevant to them (male patients were excluded from exclusively female questions such as menopause, and patients who did not suffer from back pain were excluded from the analysis of back pain that radiated to either leg).

Associations between each variable and revision status was assessed utilizing the appropriate univariable statistical test. Given some variables had one category with a large proportion of patients (reason from primary, hip prosthesis type, and knee prosthesis type), for these variables the category with highest proportion of revisions was compared to the others to give the highest probability of detecting a significant difference. When analysing the variable of surgeons who conducted the primary replacement, surgeon E6 and E5 both had high incidence of revisions and were compared separately to the other surgeons' revision proportions. Normality of distribution for continuous variables was tested with the Shapiro-Wilk test. The Mann-Whitney U test was used to compare non-normally distributed continuous variables. Chi-Squared or Fisher's exact test were used to test categorical variables. All results were analyzed using IBM SPSS Statistics Version 27 with a significance level defined as $\alpha = 0.05$. No correction for multiple comparison was used as all factors included in this analysis are not random but instead are observations in nature; thus, not using a multiple testing correction would lead to fewer interpretation errors and open up more potential for important findings(11).

Results

Descriptive Statistics

A total of 1086 patients were recruited in the study, 276 were excluded because of missing data on general questionnaire or revision status. 810 patients were included in the final analysis (41.5% hip and 58.5% knee), of which 30 (40.0% hip and 60.0% knee) were flagged for requiring a revision surgery **(Fig. 1)**. Mean time elapsed between surgeries for the revision group was 2.5 ± 2.2 years (Table 1). The primary reason for revision surgery was infection (33.3%), followed by persistent pain (26.7%), aseptic loosening (13.3%), periprosthetic fracture (6.7%), and others (20%) (Table 2). Patients not requiring revision surgery (n = 780) acted as the control group and were not found to significantly differ in age, sex, or BMI from revision patients (Table 1). While our sample was composed of slightly more female patients (56.9%), this was not statistically significant (Table 1). The majority of the patients suffered from OA (82.1%), the remaining aetiologies included fracture (9.4%), inflammatory arthritis (4.1%), osteonecrosis (4.0%), and others (0.5%) (Table 1). We found no significant difference between revision groups when comparing OA to all other aetiologies combined (Table 1).

Table 1
Overview of study sample demographics and group comparisons, n = 810.

Demographics	Revisions (n = 30)	Non-revisions (n = 780)	P-Value
Mean Age Years (± SD)	63.3 ± 9.1	65.8 ± 10.2	0.220
Sex (% for females)	56.7	56.9	0.952
Mean BMI (kg/m^2 ,±SD)	33.7 ± 6.3	32.8 ± 7.3	0.608
Mean Time Elapsed Between Surgeries (± SD)	2.5 ± 2.2	N/A	N/A
Reason For Primary			
Osteoarthritis	25	640	0.793*
Osteonecrosis	3	29	
Fracture	1	75	
Inflammatory Arthritis	1	32	
Other	0	4	

*When compared to all combined other aetiologies.

Table 2
Reasons for TJR revision surgery.

Reason For Revision	Frequency	Percentage
Infection	10	33.3%
Persistent Pain	8	26.7%
Aseptic Loosening	4	13.3%
Fracture	2	6.7%
Other	6	20.0%

Factors Associated with Revision Surgery

We tested seventy-two variables (full list of the variables is provided in **Supplementary Table 2**) for association with the requirement of patients to undergo an early revision surgery. Of these variables seven factors were found to be significantly associated with revision surgery (Tables 3). Patients having hypertension, more than five comorbidities, back pain that radiates to either leg, greater number of live births, and hysterectomy were associated with less likelihood of undergoing an early revision surgery whereas patients having lateral epicondylitis and receiving the primary surgery by surgeon E5 were associated with a higher risk of requiring revision surgery (Table 3; all $p < 0.05$).

Table 3
Factors found to be significantly associated with revision status ($p < 0.05$).

Variable	Groups Compared		OR	CI	P-value
	Revisions[1]	Non-revisions[2]			
Number of live births*	1.73 (CI 0.70–2.77)	2.90 (CI 2.70–3.11)	N/A	N/A	0.007
Hysterectomy#	17.6%	44.5%	0.269	0.076–0.948	0.029
Lateral epicondylitis ##	29.6%	9.9%	3.845	1.622–9.116	0.005
Hypertension#	37.0%	58.3%	0.420	0.190–0.931	0.028
Back Pain That Radiates to Either Leg##	16.7%	65.6%	0.105	0.023–0.486	0.001
More Than Five Comorbidities#	7.4%	24.8%	0.242	0.057–1.034	0.038
Surgeon E5[3,##]	36.0%	18.3%	2.507	1.083–5.802	0.036
Other Surgeons (Excluding F6)[4]	72.7%	81.7%	Reference		

Statistic methods included Mann-Whitney U-test (*), Chi-Squared test (#), and Fisher's exact test where appropriate (##). OR, Odd ratio; CI, 95% Confidence interval.

[1]n = 12–27, [2]n = 323–689, [3]n = 134, [4]n=573.

Given the expected association between number of live births and hysterectomy, we tested and found that a greater number of live births were significantly associated with having a hysterectomy in our data ($p = 0.001$). To elucidate any difference within the revision group (n = 30) sex, age, and BMI were compared between hip vs knee patients with no significance between joint site found. Sub-group analysis was also preformed between the top two reasons (representing 60%) for revision surgery (infection vs pain), with no significance found for sex, age, or BMI. Lastly, we found no significance for sex, age, BMI, or reason for revision surgery when comparing very early revisions (< 2 years; 56.6%) to revisions occurring at 2 years or later (43.3%).

Discussion

The literature is constantly growing on the association between patient, surgical, and healthcare factors in relation to hip and knee revisions. Since most of these studies have been conducted utilizing joint registry data, they are restricted to variables recorded in registries. These registries rarely track patient characteristics, while other studies have limited patient-focused variables in favour of surgical and prosthetic variables. Our study evaluated seventy-two variables, most of which focused on patient lifestyle and healthcare factors. This allowed for a broad analysis of the influence of patient characteristics on early TJR revisions, representing an important addition to the existing literature.

In this study, we found that the primary reason for revision surgery was prosthetic joint infection. This finding was consistent with national reports that showed over 30% of total joint revisions were due to infection(1). The demographics of our study also matched closely to what was observed in national reports. Where females represented 53.7% and 60.2% of hip and knee replacements respectively, and the median age ranged from 67–68 years(1). Surprisingly, we found BMI was not associated with revision in our study, whereas other studies have reported a relationship between elevated BMI and early revisions(2, 12, 13). One explanation for this could be that our sample population had an higher mean BMI (over 30 kg/m^2) with less variability compared to other studies(2, 12, 13). Furthermore, our study found that age was not associated with increased odds of a patient having to undergo revision surgery. Current literature is inconsistent on the impact of age on revisions status. In one Canadian report, age was found not to differ between early revisions and non-revision groups for hip and knee(1). However, two large registry studies in the UK found that younger patients were more likely to require a revision due to infection(12, 13). This may suggest a population specific association. The fact that our study population was younger than the UK studies(12, 13) might be another explanation.

Our data indicated that both the number of live births and hysterectomy were associated with reducing risk of undergoing revision surgery. Interestingly, our data also showed that the likelihood of a hysterectomy increased with more live births. This is not surprising given that emergency hysterectomies are performed to manage life-threatening hemorrhage after a caesarean or vaginal delivery. One systematic review found that multiparity accounted for 87% of emergency peripartum hysterectomies worldwide (14). Thus, our observation in the current study might represent the same potential mechanism. However, the negative association with TJR revision surgery necessitates further investigation.

Our study found that patients having hypertension, back pain that radiates to either leg, or more than five co-morbidities were less likely to undergo revision surgery. This represented an interesting finding given the overwhelming evidence that co-morbidities are a risk factor for revision surgery(1, 15). Patients with co-morbidities are complex and high-risk surgical candidates, having longer lengths of stay in hospital, higher risk of readmission, and increased risk of mortality(16). Combined with the advanced age of our study population, this may have represented a relative contraindication for revision surgery in our study and explain the reduced revision rate. However, we recognized that this is a complex variable to interpret and highly dependent on the co-morbidities incorporated into the analysis.

Back pain that radiates to either leg represents a non-specific variable for sciatica and chronic pain. Therefore, it could be postulated that these patients were managed with pharmacologic therapy for their chronic pain and were unlikely to report pain after TJR. Given pain is a clinical indication of a failed prosthetic, this may explain its association with non-revisions. Furthermore, a large meta-analysis discovered hypertension was not associated with the risk of periprosthetic joint infection(2). While our study and others report infection as the leading cause of revisions, it does not account for over 60% of indications for revision(1). Our study included all indications for revision surgery which may explain the difference.

While patient activity level was not collected in this study, lateral epicondylitis can be interpreted as a surrogate variable for activity. Patients that reported lateral epicondylitis are likely to have manually intensive occupations or increased athletic activity(17). Therefore, this finding could suggest a link between activity level and revision rates. We found that one surgeon coded E5 had a high volume (16.5%) of TJR and a statistically higher proportion of revisions compared to other surgeons. This is in contrast to previous reports that higher surgery volume contributes to lower or no difference of revision rates (3, 12, 14). This finding can likely be attributed to the individual surgeon’s practice and not a generalizable association.

Observational cohort studies such as this come with inherent bias and limitations. However, when analysing cases of TJR revisions that occur infrequently; these studies provide important insight for further research. One limitation of this study is the low power due to a limited number of revisions. Given the low rate of revision surgery, large recruitment of TJR patients is needed to obtain more revision cases. However, due to logistical reasons this typically means fewer variables are collected on patients. Additionally, hip and knee replacements were combined in our analysis to boast the quantity of revisions and while they are similar, they also have differences. For example the second common reason for hip revision is periprosthetic fracture, while for knee it is prosthetic instability(1). However, on subsequent analysis we did not find a difference in the demographics of revisions when comparing hip to knee.

In summary, to our knowledge, this is the most extensive study examining patient factors associated with revision surgery for knee or hip arthroplasty. For which we found seven out of seventy-two factors to be associated with revision status. Additionally, our case group was found to be homogenous with no distinct differences found within revision patients. It is key to note that the variables found to be non-significant also provide value to existing literature. While some of these variables may have been underpowered in our analysis, indicated by their significance reported in other studies. They still provide evidence of factors that are unlikely to be associated with early TJR revisions.

Conclusions

To conclude, our findings suggest that patients' health factors are associated with the odds of requiring revision surgery and are largely consistent with the existing literature. Therefore, patients' risk of revision surgery could theoretically be calculated prior to TJR, better informing patient treatment decisions. Given the rare occurrence of TJR revisions, retrospective studies such as this one are critical for ascertaining what patient, surgical, and healthcare factors are associated with negative outcomes. Future large-scale prospective studies are needed to determine if these factors are predictive of TJR outcomes.

Abbreviations

Total Joint Replacement (TJR)

Osteoarthritis (OA)

Newfoundland Osteoarthritis Study (NFOAS)

Newfoundland and Labrador (NL)

Multisite Musculoskeletal Pain (MSMP)

Declarations

Ethics Approval and Consent to Participate

This study was approved by the Health Research Ethics Authority of Newfoundland and Labrador (HREB # 2011.311), and written informed consent was obtained from all participants. All methods were performed in accordance with the relevant guidelines and regulations of this authority.

Consent For Publication

Not applicable.

Availability of Data and Materials

The datasets generated and analysed during the current study are not publicly available due to privacy of participants personal health information but are available from the corresponding author on reasonable request.

Competing Interest

Author PR discloses speaker paid presentations for AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, and UCB. They also disclose they are a paid consultant for AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, and UCB. They also disclose research support as a PI from AbbVie, Pfizer, Novartis, and Janssen.

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Authors RG, ML, CC, and AF declare they have no competing interests.

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Author Contributions

RG analysed and interpreted the patient data, and was a major contributor in writing the manuscript. ML had a major role in data collection and analysis. CC had a role in data analysis. AF had a role in study conception and data acquisition. PR had a role in study conception and data acquisition. GZ had a role in study conception and design, along with data analysis and interpretation. All authors read and approved the final manuscript.

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References

1. Canadian Institue for Health Information. Canadian Institute for Health Information. Early Revisions of Hip and Knee Replacements in Canada: A Quality, Productivity and Capacity Issue. Ottawa, ON: CIHI; 2020. https://secure.cihi.ca/free_products/early-revisions-hip-knee-replacements-canada-2016-2019-report-en. Accessed May 11, 2022.
2. Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD. Patient-related risk factors for periprosthetic joint infection after total joint arthroplasty: A systematic review and meta-analysis. PLoS One. 2016;11(3):1–18.
3. CIHI. Canadian Institute for Health Information. Hip and Knee Replacements in Canada: CJRR Annual Statistics Summary, 2018–2019. Ottawa, ON: CIHI; 2020. https://secure.cihi.ca/free_products/CJRR-annual-statistics-hip-knee-2018-2019-report-en. Accessed May 11, 2022.
4. Serra-Sutton V, Allepuz A, Espallargues M, Labek G, Pons JMV. Arthroplasty registers: A review of international experiences. Int J Technol Assess Health Care. 2009 Jan;25(1):63–72.
5. Vina ER, Kwoh CK. Epidemiology of osteoarthritis: Literature update. Curr Opin Rheumatol. 2018;30(2):160–7.
6. Evans JT, Evans JP, Walker RW, Blom AW, Whitehouse MR, Sayers A. How long does a hip replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. Lancet (London, England). 2019;393(10172):647–54.
7. Evans JT, Walker RW, Evans JP, Blom AW, Sayers A, Whitehouse MR. How long does a knee replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. Lancet. 2019;393(10172):655–63.
8. Zhang W, Likhodii S, Zhang Y, Aref-Eshghi E, Harper PE, Randell E, et al. Classification of osteoarthritis phenotypes by metabolomics analysis. BMJ Open. 2014 Nov 1;4(11):e006286.

9. Wolfe F, Butler SH, Fitzcharles M, Häuser W, Katz RL, Mease PJ, et al. Revised chronic widespread pain criteria: development from and integration with fibromyalgia criteria. Scand J Pain. 2020 Jan 1;20(1):77–86.
10. Liu M, Xie Z, Costello CA, Zhang W, Chen L, Qi D, et al. Metabolomic analysis coupled with extreme phenotype sampling identified that lysophosphatidylcholines are associated with multisite musculoskeletal pain. Pain. 2021 Feb 1;162(2):600–8.
11. Rothman KJ. No Adjustments Are Needed for Multiple Comparisons. Epidemiology. 1990;1(1).
12. Lenguerrand E, Whitehouse MR, Beswick AD, Kunutsor SK, Foguet P, Porter M, et al. Risk factors associated with revision for prosthetic joint infection following knee replacement: an observational cohort study from England and Wales. Lancet Infect Dis. 2019;19(6):589–600.
13. Lenguerrand E, Whitehouse MR, Beswick AD, Kunutsor SK, Burston B, Porter M, et al. Risk factors associated with revision for prosthetic joint infection after hip replacement: a prospective observational cohort study. Lancet Infect Dis. 2018;18(9):1004–14.
14. Van Den Akker T, Brobbel C, Dekkers OM, Bloemenkamp KWM. Prevalence, Indications, Risk Indicators, and Outcomes of Emergency Peripartum Hysterectomy Worldwide: A Systematic Review and Meta-analysis. Obstet Gynecol. 2016;128(6):1281–94.
15. Prokopetz JJ, Losina E, Bliss RL, Wright J, Baron JA, Katz JN. Risk factors for revision of primary total hip arthroplasty: A systematic review. BMC Musculoskelet Disord. 2012;13.
16. Podmore B, Hutchings A, Skinner JA, MacGregor AJ, Meulen J van der. Impact of comorbidities on the safety and effectiveness of hip and knee arthroplasty surgery. https://doi-org.qe2a-proxy.mun.ca/101302/0301-620X103B1BJJ-2020-0859R1. 2020 Dec 31;103-B(1):56–64.
17. Tosti R, Jennings J, Sewards JM. Lateral epicondylitis of the elbow. Am J Med. 2013;126(4).

Figures

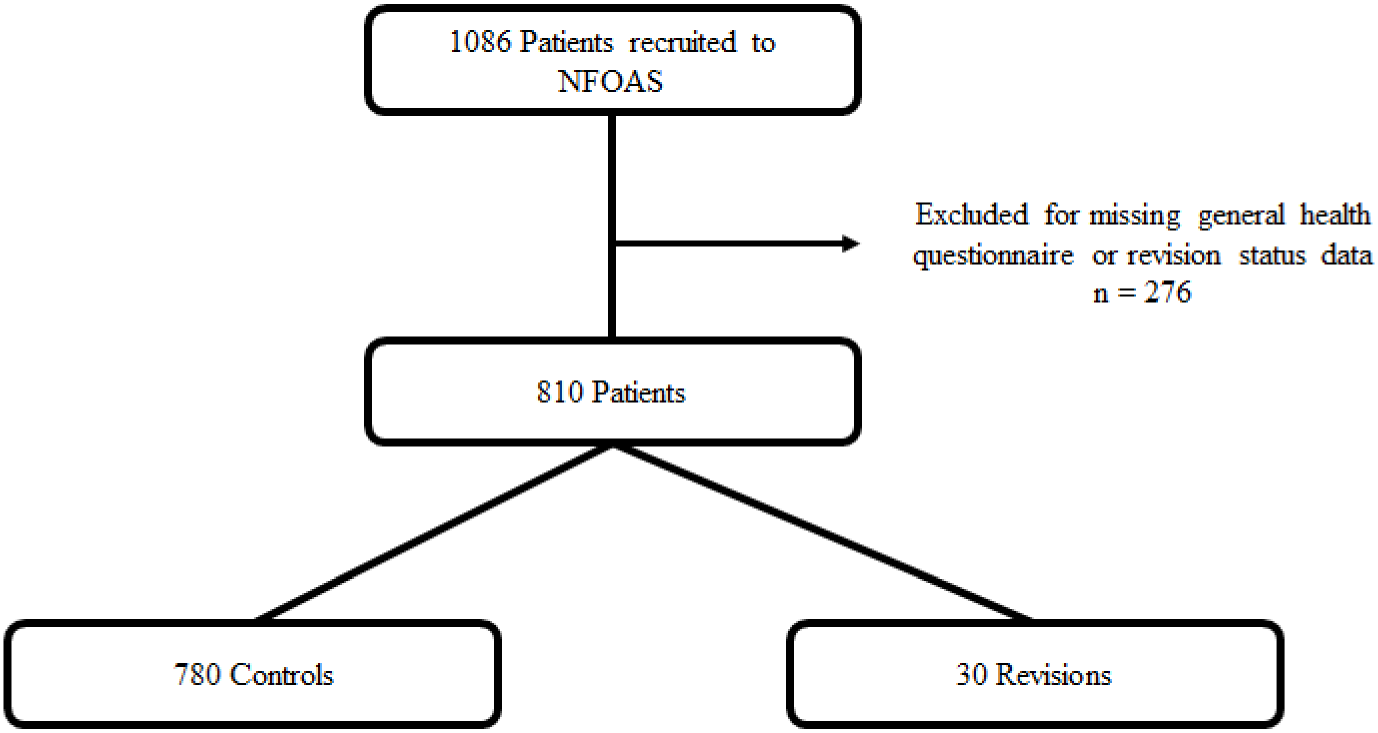

Figure 1

Flow chart for sample selection.

Supplementary Files

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