Low rate of subsequent surgery and serious complications following intra-articular steroid injection for base of thumb osteoarthritis: national cohort analysis

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ABSTRACT

Objectives. Intra-articular steroid injection is commonly used to treat base of thumb osteoarthritis (BTOA), despite a lack of large scale data on safety and effectiveness. We estimate the incidence of serious complications and further procedures following BTOA injection, including the risk of post-operative serious surgical site infection for subsequent operative intervention.

Methods. Hospital Episode Statistics data linked to mortality records from 01/04/1998-31/03/2017 were used to identify all BTOA injections undertaken in adults in the National Health Service secondary care in England. Patients were followed up longitudinally until death or 31/03/2017. A multivariable regression with a Fine and Gray model adjusting for the competing risk of mortality in addition to age, sex and socioeconomic deprivation was used to identify factors associated with progression to further procedure. Secondary outcomes included serious complications after injection and subsequent surgical site infection.

Results. 19120 primary injections were performed during the 19-year period in 18356 patients. 76.5% were female; mean age 62 years (SD 10.6). 50.48% underwent further procedure; 22.40% underwent surgery. Median time to further intervention was 412 days (IQR 110-1945). Female sex was associated with increased risk of proceeding to surgery. Serious complication rate following injection was 0.04% (0.01-0.08) within 90 days. Of those proceeding to surgery, 0.16% (0.06-0.34) presented with a wound infection within 30 days and 90 days, compared to an overall post-operative wound infection rate of 0.03% (0.02-0.05).

Conclusions. Very low rates of serious complications were identified following BTOA injections performed in secondary care; only one in five patients proceeded to subsequent surgery.

Clinical trial registration: clinicaltrials.gov, https://www.clinicaltrials.gov, NCT03573765

Keywords: osteoarthritis; thumb; surgical procedures; intra-articular injection; complications/adverse events

KEY MESSAGES

- This large national cohort identified 50% of cases proceeded to further intervention after intraarticular steroid BTOA injection
- 22% proceeded to surgery at any time, mostly within a year of injection
- Very low rates of serious complications of BTOA intra-articular injection in secondary care were found
INTRODUCTION
Base of thumb osteoarthritis (BTOA) is a common hand condition presenting to primary and secondary care physicians, characterised by pain and reduced function.[1-3] Early treatment options for BTOA include intra-articular steroid injection in addition to splinting and hand therapy.[4, 5] Developing best evidence for hand arthritis is a research priority for patients with hand conditions in the UK.[6]

Systematic reviews of available randomised control trials (RCT)s and case series noted that evidence of efficacy of intra-articular steroid injections for BTOA was limited and heterogeneous.[7-10] Smaller single centre studies have estimated that following BTOA intra-articular steroid injection, only around one third proceed to surgery.[11]

Efficacy aside, research from a recent large US insurance dataset raised concerns that BTOA steroid injections predispose patients to a higher risk of post-operative complications.[12] However, previous studies in other areas of the body have found no evidence to support this finding.[13, 14]

Study into the long term course of treatment and risk of complications within routine clinical care is therefore an important addition to the literature in order to better counsel patients. Observational research offers the opportunity to follow patients for longer after an intervention than clinical trials, and enables rare complications and complications that do not present within a short time frame to be better identified.[15]

Objectives
Our primary aim was to estimate the incidence of further procedures after intra-articular steroid injection for BTOA in adults in the NHS in England. Secondary aims were to identify factors associated with proceeding to further intervention, especially surgery, serious complications and if having a BTOA injection prior to surgery affected the risk of serious surgical site infection.

METHODS
Data Source
A bespoke pseudonymized extract of individual level patient data from the NHS Digital Hospital Episode Statistics Admitted Patient Care (HES APC) dataset was made (1st April 1998 to 31st March 2017). This extract contained all episodes of NHS care associated with BTOA, defined by a validated list of codes.[16] HES APC contains all admissions, including daycase care, for all individuals, and the extract contained all episodes before and after the
‘index’ BTOA episode. The extract contained all episodes of care remunerated by the NHS in England, including independent providers (i.e. private hospitals undertaking procedures on behalf of the NHS on NHS patients). All patient episodes of care within the NHS England system are linked via a patient’s individual NHS number. This enabled linkage of all NHS funded treatments undertaken and longitudinal follow up of each patient. The HES APC extract was also linked to the ONS national mortality dataset prior to pseudonymization to identify cause and date of death.[17] The NHS covers the vast majority of healthcare provision in England, with only 11% of the population estimated to hold private healthcare insurance, and only 13% of all elective surgery being privately funded outside of the NHS.[18]

**Ethical Approval**
This study was approved by the University of Oxford Research Services Clinical Trials Research Group (project ID 12787), and the NHS Data Access Advisory Group (DAAG). It was carried out in accordance with the NHS Digital Data Sharing Agreement (DARS-NIC-29827-Q8Z7Q) and registered at clinicaltrials.gov (NCT03573765). Studies using non-identifiable records from Hospital Episode Statistics are exempt from research ethics committee approval. Patients have the right to request that their data is not released by NHS Digital for use by researchers (register a “Type 2 opt-out”).

**Population**
Patients identified as having a BTOA injection were followed up until death, or censored at the end of the study (31/03/2017) in order to maximise the longitudinal follow up possible within the dataset. Minimum follow up was one day, to capture all complications including those occurring within the first 24 hours post-operatively. Duplicate episodes can occur over the change of financial year, and these were removed.

Exposures and outcomes were defined using previously validated OPCS-4.7 classification for interventions and International Classification of Disease (ICD) version 10 codes for disease (Supplementary Table S1, available at *Rheumatology* online), defined in an initial validation study for identification of all cases of BTOA in secondary care.[19-21]

Two further clinical validation studies were undertaken within our institution to look at the patient population defined within the injection cohort, and the validity of identifying surgical subtypes in HES APC. Discussion with clinical coders, NHS digital and a sample of over 300 patients undergoing injection or surgery within one year was undertaken. The injection cohort was confirmed to include patients undergoing injection in theatre, in specialist
outpatient injection clinics run by rheumatologists and hand surgeons, and those undergoing injection in the radiology department as an outpatient procedure. The injection validation study showed we were able to identify patients who had undergone a BTOA intra-articular injection with a positive predictive value of 85.8% using our previously validated code list (Supplementary Table S1, available at *Rheumatology* online). In the second clinical validation study, the coding for BTOA surgical subtypes found a positive predictive value of 99% in our Trust within a year’s sample of 104 patients undergoing BTOA surgery, and therefore our code list was considered appropriate.

In order to further characterize the population included, factors associated with the development of BTOA were identified using OPCS and ICD-10 codes (Supplementary Table S2, available at *Rheumatology* online). A past medical history of carpal tunnel syndrome (CTS), generalized osteoarthritis (OA), knee OA, rheumatoid arthritis, hand or wrist fracture, and oophorectomy was identified if the patient had an episode including the relevant code at any time prior to or within the hospital episode for BTOA injection. To determine socioeconomic status, Index of Multiple Deprivation (IMD; a Government generated score of relative deprivation based upon geographical location within England) was used, and the Charlson Comorbidity Index (CCI) was used to determine overall combined comorbidity level of each patient at the time of injection or surgery. Ethnicity was included as defined by NHS Digital.[22-24]

A further procedure undertaken in secondary care was defined as a code for surgery after injection or a second injection in the same hand when calculating incidence rates, survival and regression analysis. In order to identify the ‘worst case scenario’ of possible patients who may go on to a procedure but have missing laterality codes, a further definition of three or more procedures per person was also included when calculating an estimate of the number of people requiring a further procedure.

To estimate the number of cases proceeding to surgery after injection, surgery was defined as any episode containing the OPCS and ICD codes in Supplementary Table S1, available at *Rheumatology* online, that occurred after injection. Laterality linked injection and surgery was again used in survival analysis and surgical intervention rates.

Serious complications after primary intra-articular injection as identified in hospital admission records were defined as severe infection (septic arthritis, wound infection leading to wound dehiscence or wound debridement) and tendon injury. As these complications were identified from HES APC, the complications required an episode of admission to hospital
including as a day case patient or requiring surgery, occurring in the same hand as the injection within 30 or 90 days of injection (see Supplementary Table S3, available at Rheumatology online). Surgical site infection after BTOA surgery for those who had a pre-operative intra-articular steroid injection was defined in the same manner, and compared with the rates seen in all post-operative BTOA surgery within the HES extract. The NHS framework of complications within 30 and 90 days was used to determine the comparative incidence rate.[25] All results with a count of less than 7 were redacted to reduce the risk of secondary disclosure of data according to the NHS digital analysis guide.[26] Cox proportional hazard analysis of the factors associated with post-operative complications was planned a priori.

**Statistical methods**

We calculated age and sex specific incidence rates of surgery using ONS mid-year population estimates.[27] All complications were calculated as a proportion of the sample with 95% confidence intervals. Incomplete records consisted of only 0.74% cases for age, sex, ethnicity and IMD deciles, and were assumed to be missing at random. We therefore did not employ any imputation, but undertook complete case analysis. Laterality code was present in 93.8%; comparison of demographics of those with and without laterality present within their records demonstrated that the patients were comparable. (Supplementary Table S4, available at Rheumatology online).

Kaplan Meier analysis was undertaken to identify the trend in time to further intervention or surgery. We identified factors associated with further intervention using a Fine and Gray model to produce both a crude and adjusted sub-hazard ratios (sHR) accounting for the competing risk of mortality.[28] Proportional hazards assumption was tested using Schoenfeld residuals. Age was categorized and the category containing the median age (60-69 years) used as the baseline category due to the non-linear relationship of age with adverse outcome that did not meet the proportional hazards assumption. Statistical analysis was undertaken using STATA version 15.1. A Poisson distribution was assumed and the delta method used to calculate confidence intervals for complications.

**RESULTS**

**Patient Demographics**

Figure 1 describes the data processing details. In the study period, 19120 primary BTOA injections (18356 patients) and 4282 operations were performed on 3863 individuals in English NHS hospitals. Median follow up time was 5.0 years (interquartile range 2.2-8.8 years). 128 (0.67%) had less than 30 days of follow up without an event due to having their
primary injection during March 2017; 351 (1.8%) patients had less than 90 days of follow up without an event, i.e. due to having primary injection between January to March 2017 (1·40%). 76.5% of patients were female, and the mean age at injection was 62y (SD 10.6). A peak of intervention was observed in women around the perimenopausal age that was not as prominent in men (Supplementary Figure S1, available at Rheumatology online). 64.7% of patients had a low level of overall comorbidity with a CCI of zero or one. 83% of patients identified themselves as being of a white background, and the sociodemographic distribution of patients undergoing primary BTOA injection was roughly even across the strata. The full demographic profile of patients undergoing primary BTOA injection, further intervention and surgical intervention are shown in Table 1.

Trends in further intervention
9651 further interventions were identified after primary BTOA injection in 6461 individuals. The median time to second procedure was 412 days (IQR 110-1945), with an incidence rate of 66.7 per 1000 person years (95% confidence interval [65.06-68.41])). 4282 surgeries were undertaken after an injection at any point giving an incidence rate of 22.3 per 1000 person years (95% CI [21.51 to 23.19]). Kaplan Meier analysis of time to further intervention and surgery are given in Figures 2a and 2b. The sunburst plot in Figure 3 illustrates the treatment paths taken in secondary care following primary BTOA injection. The central ring represents all primary intraarticular injections in the cohort, and the outer ring represents the number and type of subsequent interventions undertaken during the follow up period. The central ring shows that 49.5% of primary injections had no subsequent intervention observed. Of the 50.5% of primary injections that were observed to undergo a further intervention, 28.1% underwent a second intraarticular injection, with simple trapeziectomy being the most common surgical procedure undertaken following BTOA injection.

Factors associated with further intervention after injection
Crude univariable analysis suggested an association of increased incidence of further intervention with female sex. This was not confirmed in multivariable analysis (Figure 4) when adjusting for age, comorbidity and socioeconomic status. Compared to those in the median age category, patients who were at the extremes of the age range at the time of primary injection had a reduced risk of further intervention that persisted in adjusted analysis (adjusted subhazard ratio sHR 0.30 [0.13 to 0.68] for those age 18-29 years, adj sHR 0.44 [0.33 to 0.59] for those age 30-39 years; Supplementary Table S5, available at Rheumatology online). Increasing levels of co-morbidity was associated with reduced incidence of further intervention and there was no association seen between further intervention and socioeconomic status.
When considering the factors associated with proceeding to surgery after injection, female sex was associated with a 12% increased relative risk within multivariable analysis (adj sHR 1.12 [1.02 to 1.23]; Figure 5; Supplementary Table S6, available at *Rheumatology* online). As was seen with all further intervention, there was a reduced likelihood of progressing to surgery at the extremes of age, and with increasing comorbidity. No association was found with socioeconomic status.

**Complications after injection**

There were a very small number of cases identified as complicated by septic arthritis, neurovascular injury, need for wound debridement or tendon repair after primary injection in secondary care. As all absolute numbers were under 7, the true value must be minimised according to NHS digital analysis rules. This gives a maximum rate of 0.04% (95% confidence interval 0.01-0.08) within 30 or 90 days of injection for wound debridement or tendon repair and a rate of 0.04% (95% confidence interval 0.01-0.08) for septic arthritis or neurovascular injury at any post-operative time point within this cohort.

**Complications after subsequent surgery**

In the 4282 thumbs that underwent intra-articular injection in secondary care prior to undergoing surgery, less than 7 cases presented with serious surgical site infection within 30 or 90 days. The true value must therefore be minimised, but gives a maximum rate of surgical site infection (SSI) for those having a pre-operative injection of 0.16% (0.06-0.34). In total, 43 076 BTOA surgeries were identified in the 19 year period, of which only 0.03% presented with serious surgical site infection within 30 or 90 days respectively.

**DISCUSSION**

**Key findings**

This large national cohort study observed approximately 50% of primary intra-articular BTOA injections in secondary care proceeded to further intervention. The most common further procedure was a repeat injection. One in five patients in the cohort went on to have surgery at a median time of 412 days following injection.

Patients at the extremes of age and with greater levels of comorbidity were observed to be less likely to undergo further injection or progress to surgery. When adjusted for age, social deprivation and comorbidity, female sex was observed to be associated with increased risk of progression to surgery. A very low rate of complications was seen in secondary care following injection, with less than 4 in 10,000 patients needing hospital treatment for severe
infection, neurovascular injury, or tendon injury. Although a higher incidence of surgical site infection was seen if patients underwent a pre-operative intra-articular injection at any time prior to surgery, the incidence of serious infection remained below 2 in 1000 for complications within 90 days of surgery.

This study adds to the literature surrounding the incidence of serious complications following intra-articular steroid injections in the hand. Our data are in stark contrast to rate of post-surgical complications found in US data containing insured and Medicare (state assisted healthcare) patients, where 21% of patients sustained any form of complication after BTOA surgery.[29] In their study, undergoing steroid injection prior to surgery increased the odds of a complication by 20%, although no absolute rate of complications was reported for those patients who had pre-operative intra-articular injections. Giladi et al. used a wider definition for infection (including any diagnosis infection or prescription of antibiotics within 6 weeks of surgery) which may explain some of the disparity, since only the most serious complications seen in secondary care are included in our study. A difference in studied populations within a different healthcare system may also have an impact.

**Strengths and limitations**

Our study contains data from a national source with longitudinal follow up, enabling patients to be followed within a nationalised health system including if they move to a different healthcare provider for subsequent procedures. It includes all patients presenting to a public healthcare system that includes patients with a wide age range and range of associated comorbidities and levels of social deprivation. As England in general has a low rate of intervention undertaken in the private sector, this NHS data will capture the majority of healthcare activity to produce more generalisable results for the role of interventions for BTOA in a general population. This data identifies trends in patients who may be excluded from clinical trials, and observes patients in healthcare outside of trial centres and healthcare settings engaged in research. Results found in our study align with previous work identifying positive responses to intraarticular steroid injection for hand osteoarthritis without serious complications.[30, 31]

This study is limited to interactions within secondary care only, where patients have an injection under radiological guidance, in an injection clinic, or in theatre. The patients included are therefore only those undergoing primary injection that is registered within this system. Our validation studies showed that the HES APC dataset includes patients undergoing intra-articular injections under radiological guidance or on a specific injection list, but will not include those being undertaken in traditional secondary care outpatient clinic
settings or that had occurred previously in primary care or in interface services. This produces a selection bias in the patients included, but also indicates that patients included here are those who have been referred to secondary care. As the data does not link to primary care, we cannot fully record treatment that has gone before, and this is acknowledged as a limitation.

Similarly, our study only reports complications that are sufficiently severe to present in secondary care, and will not include for example minor infections treated with oral antibiotics in primary care. Our data define the risk of serious surgical site infection or significant tendon injury requiring intervention, and can inform the consent process regarding the most serious and most clinically important complications. It must be recognised that as the study is based within secondary care only, only complications that require an inpatient admission or intervention will therefore be included. Whilst patients could present to any secondary care provider within the NHS in England and this would be detected by linkage through their individual identifier, presentations to primary care are not included. We believe that the low rates identified here are not due to misclassification bias or underreporting, but more that they only include the most serious events. Whilst this study adds to the literature by identifying the rates of the most serious complications within a national cohort, further work is needed to identify other complications that would not require admission or further intervention, for example within primary care observational datasets.

Information regarding a patient’s comorbidities in this study are only collected from HES and are therefore may not be as rich as in primary care datasets, but contain selection bias of the most pertinent comorbidities likely to affect outcome from secondary care intervention. HES APC also does not collect data on the use of orthoses, we cannot compare the use of adjuvant splints in this population alongside intra-articular injection, which should be recognised as a limitation. However, because HES APC is an administrative dataset repurposed to enable research, we have undertaken validation studies in order to minimise misclassification of cases. HES APC data has the significant advantage of preventing inclusion bias, as data is collected outside of the main research team.

**Future work**

Further work is needed to describe the rate of minor infective complications and side effects that would not produce an admitted patient care episode, identifying the rate of complications seen in primary and intermediate care in routinely collected data. Similarly, a large cohort of patients providing additional data complications such as steroid flare and skin depigmentation following injection, and use of orthoses in secondary care would also
provide a comprehensive picture of the role of intra-articular injection for BTOA. Replication in other countries would determine if similar secondary care trends are also seen outside of a national healthcare system. This study only investigates intra-articular injections overall, and as the NHS only routinely undertakes intra-articular steroid injections, it does not compare to other agents such as hyaluronic acid that are not routinely undertaken in the NHS. A great deal of prior scientific work has focussed on comparing the efficacy of the two injections within clinical trials, and future work could compare their efficacy within routine clinical care if both agents are used in one healthcare system.[32-35] This study also does not compare between radiologically guided or blind injections, or compare patient reported outcomes following injection or surgery, and this could be further investigated. Finally, this study found that progression to surgery was more common in women, and further investigation into the reasons for difference in disease progression to surgery between the sexes would enable greater understanding of the factors associated with BTOA disease progression.

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This work used data supplied by NHS Digital copyright 2018, re-used with the permission of NHS Digital. All rights reserved.

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COMPETING INTERESTS
All authors have completed an ICJME conflict of interest form that is uploaded with the study (http://www.icmje.org/conflicts-of-interest/) no support from any organization for the submitted work; D P-A has received research grants from Amgen, Servier, UCB; departmental fees for speaker services from Amgen, departmental fees for consultancy from UCB. JL reports grants from the Medical Research Council (MR/K501256/1) and Versus Arthritis (21605),
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**DATA AVAILABILITY**

The data underlying this article were provided by NHS Digital in accordance with the NHS Digital Data Sharing Agreement (DARS-NIC-29827-Q8Z7Q). No further data can be made available from the authors due to NHS Digital restrictions. Data extracts can be applied for directly via the NHS Digital data access request service (https://digital.nhs.uk/services/data-access-request-service-dars).

**PATIENT AND PUBLIC INVOLVEMENT IN RESEARCH**

This study aimed to answer questions raised by the James Lind Alliance priority setting partnership for ‘common conditions affecting the hand and wrist’. [6] No direct patient and public involvement was undertaken.
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Table 1. Baseline characteristics of patients undergoing BTOA injection, and those undergoing further intervention post injection

| Age category | All injection patients | Any intervention after 1st injection | Surgery after 1st injection |
|--------------|------------------------|-------------------------------------|----------------------------|
|              | Freq (%)               | Freq (%)                            | Freq (%)                   |
| 18-29        | 49 (0.3)               | 7 (0.1)                             | <7*                        |
| 30-39        | 280 (1.5)              | 70 (0.7)                            | 23 (0.5)                   |
| 40-49        | 1797 (9.4)             | 804 (8.3)                           | 369 (8.6)                  |
| 50-59        | 5975 (31.3)            | 3051 (31.6)                         | 1443 (33.7)                |
| 60-69        | 6490 (34.0)            | 3534 (36.6)                         | 1618 (37.8)                |
| 70-79        | 3486 (18.3)            | 1785 (18.5)                         | 698 (16.3)                 |
| >80          | 1022 (5.4)             | 398 (4.1)                           | 123 (2.9)                  |
| Missing      | 21 (0.1)               | 2 (0.02)                            | <7*                        |
| Total        | 19 120                 | 9 651                               | 4 278                      |

**IMD decile**

| IMD decile | All injection patients | Any intervention after 1st injection | Surgery after 1st injection |
|------------|------------------------|-------------------------------------|----------------------------|
|            | Freq (%)               | Freq (%)                            | Freq (%)                   |
| Least deprived 10% | 1651 (8.6)             | 911 (9.4)                           | 397 (9.3)                  |
| Less deprived 10-20% | 1805 (9.4)             | 987 (10.2)                          | 394 (9.2)                  |
| Less deprived 20-30% | 2119 (11.1)            | 1033 (10.7)                         | 458 (10.7)                 |
| Less deprived 30-40% | 2179 (11.4)            | 1069 (11.1)                         | 468 (10.9)                 |
| Less deprived 40-50% | 2030 (10.6)            | 1001 (10.4)                         | 437 (10.2)                 |
| More deprived 10-20% | 1760 (9.2)             | 894 (9.3)                           | 394 (9.2)                  |
| More deprived 20-30% | 1902 (10.0)            | 918 (9.5)                           | 434 (10.1)                 |
| More deprived 30-40% | 1844 (9.6)             | 932 (9.7)                           | 421 (9.9)                  |
| More deprived 40-50% | 1988 (10.4)            | 1027 (10.6)                         | 466 (10.9)                 |
| Most deprived 10% | 1726 (9.0)             | 836 (8.7)                           | 381 (8.9)                  |
| Missing      | 116 (0.6)              | 43 (0.5)                            | 28 (0.7)                   |
| Total        | 19 120                 | 9 651                               | 4 278                      |

**Ethnic group**

| Ethnic group | All injection patients | Any intervention after 1st injection | Surgery after 1st injection |
|--------------|------------------------|-------------------------------------|----------------------------|
|              | Freq (%)               | Freq (%)                            | Freq (%)                   |
| Any white background | 16018 (83.8)         | 8700 (90.2)                         | 3866 (90.4)                |
| Any Asian background | 354 (1.85)            | 140 (1.5)                           | 50 (1.2)                   |
| Any Black background | 70 (0.4)              | 22 (0.2)                            | 13 (0.3)                   |
| Any mixed background | 41 (0.2)              | 9 (0.1)                             | <7*                        |
| Chinese      | 16 (0.1)               | 11 (0.1)                            | <7*                        |
| Any other ethnic group | 96 (0.5)             | 33 (0.3)                            | 11 (0.3)                   |
| Not stated   | 2233 (11.7)            | 659 (6.8)                           | 268 (6.3)                  |
| Not known    | 292 (1.0)              | 77 (0.8)                            | 28 (0.7)                   |
| Total        | 19 120                 | 9 651                               | 4 278                      |

**Charlson index**

| Charlson index | All injection patients | Any intervention after 1st injection | Surgery after 1st injection |
|---------------|------------------------|-------------------------------------|----------------------------|
| 0             | 7 881 (41.2)           | 4139 (42.9)                         | 1 966 (46.0)               |
| 1             | 4486 (23.5)            | 2474 (25.6)                         | 1 078 (25.2)               |
| 2             | 2 535 (13.3)           | 1230 (12.7)                         | 523 (12.2)                 |
| 3             | 1 538 (8.0)            | 738 (7.7)                           | 306 (7.2)                  |
| 4             | 836 (4.4)              | 361 (3.7)                           | 128 (3.0)                  |
| >=5           | 1844 (9.6)             | 709 (7.4)                           | 277 (7.4)                  |
| total         | 19 120                 | 9 651                               | 4 278                      |

**Comorbidities**

| Comorbidities | All injection patients | Any intervention after 1st injection | Surgery after 1st injection |
|---------------|------------------------|-------------------------------------|----------------------------|
| Carpal Tunnel Syndrome | 2123                  | 1107                                | 550                        |
| Knee Osteoarthritis     | 2258                  | 1155                                | 515                        |
| General Osteoarthritis  | 4102                  | 2092                                | 804                        |
| Rheumatoid Arthritis    | 142                   | 30                                  | <7*                        |
| Wrist Fracture          | 110                   | 36                                  | 17                         |
| Oophorectomy            | 661                   | 380                                 | 185                        |

*Numbers less than 7 suppressed in line with NHS Digital disclosure control guidelines - percentages of other groups rounded to prevent secondary disclosure of data [26]

IMD: Index of Multiple Deprivation
Figure 1. Data processing flow chart.
Figure 2. Kaplan-Meier plots divided by sex for risk of A) further procedure and B) surgery after primary BTOA injection.
Figure 3. Sunburst representing procedures that occurred following primary BTOA injection.
Figure 4. Forest plot of factors associated with proceeding to further intervention following BTOA injection.
Figure 5. Forest plot of factors associated with proceeding to surgery following BTOA injection.