A protocol for a nationwide multicentre, prospective surveillance cohort and nested-consented cohort to determine the incidence and clinical outcomes of slipped capital femoral epiphysis

**Aims**

Slipped capital femoral epiphysis (SCFE) is one of the most common hip diseases of adolescence that can cause marked disability, yet there is little robust evidence to guide treatment. Fundamental aspects of the disease, such as frequency, are unknown and consequently the desire of clinicians to undertake robust intervention studies is somewhat prohibited by a lack of fundamental knowledge.

**Methods**

The study is an anonymized nationwide comprehensive cohort study with nested consented within the mechanism of the British Orthopaedic Surgery Surveillance (BOSS) Study. All relevant hospitals treating SCFE in England, Scotland, and Wales will contribute anonymized case details. Potential missing cases will be cross-checked against two independent external sources of data (the national administrative data and independent trainee data). Patients will be invited to enrich the data collected by supplementing anonymized case data with patient-reported outcome measures. In line with recommendations of the IDEAL Collaboration, the study will primarily seek to determine incidence, describe case mix and variations in surgical interventions, and explore the relationships between baseline factors (patients and types of interventions) and two-year outcomes.

**Discussion**

This is the first disease to be investigated using the BOSS Study infrastructure. It provides a robust method to determine the disease frequency, and a large unbiased sample of cases from which treatment strategies can be investigated. It may form the basis for definitive robust intervention studies or, where these are demonstrated not to be feasible, this may be the most robust cohort study.

Cite this article: Bone Joint Open 2020;1-3:35–40.

**Keywords:** Slipped capital femoral epiphysis, Cohort study

**Strengths and Limitations**

- This large cohort seeks to define the incidence of disease, with linked national administrative data to identify any potentially missing cases.
- This study will form a large unbiased sample of cases from all relevant UK hospitals, providing results that are readily generalizable.
- The study will readily be able to determine variation in practice, and provide key information for intervention studies.
- The study is an observational cohort study of standard care. Therefore, selection bias is inherent to the study design.

**Introduction**

Slipped capital femoral epiphysis (SCFE) is the most common hip disease of adolescence. In the short-term it always requires surgery to stabilize the epiphysis onto the femoral neck, and typically results in deformity at the level of the growth plate. In the long-term, SCFE
accompanies the development of osteoarthritis, and many
patients have disability necessitating hip arthroplasty in
early adulthood. It typically presents to the clinician with
knee, thigh or hip pain, or a limp, and there is strong
evidence to suggest that obesity is the major cause.

The incidence is reported to be approximately five to
seven cases per 100,000 children aged six to 18 years, though the true incidence is unknown. Estimates are
based on hospital administrative data, in which the
validity of the diagnoses is not confirmed.

While SCFE is the most common hip disease of adoles-
cence, robust evidence to support effective management
and intervention is poor, with no clinical trials to guide
treatment decisions. Administrative data are unable to be
used to guide management, so as such databases do not
provide detail regarding the severity and type of manage-
ment strategies, nor the clinical characteristics of the
individual. Consequently, treatment strategies vary by
country, by hospital, and even by surgeon. These differ-
bences have been illustrated in surveys of the membership
of the British, Dutch, European, and North American
Paediatric Orthopaedic Societies. The uncertainty has
prompted members of the British Society of Children’s
Orthopaedic Surgery to prioritize questions pertaining
to SCFE as two of the top five research priorities across
the whole of children’s orthopaedic surgery.

The IDEAL Framework outlines a methodological
approach to research in surgery. Research relating
to SCFE has not yet reached ‘stage 2b’ within IDEAL:
“co-operative prospective evaluation of the techniques”.
The proposed study is a 2b design, focusing on identi-
fying the case mix, technical intervention variables, and
clinical outcomes. The study uses the British Orthopaedic
Surgery Surveillance (BOSS) Study, a nationwide UK
mechanism for investigating rare orthopaedic disease,
the basis for which is described separately, develops a
nationwide cohort of SCFE to determine the disease inci-
dence, case mix, risk factors, variations in surgical inter-
ventions, and to determine the safety and efficacy of
different surgical strategies.

Specific objectives
1. What is the incidence of SCFE in the UK?
2. How does incidence vary by region?
3. What is the case-mix variation (patient factors, SCFE, radi-
ological severity, and clinical stability)?
4. What is the UK variation in surgical management, and is
this related to patient, disease, or surgeon factors (e.g.
surgeon volume)?
5. What influence do patient, disease, and surgeon factors
have on radiological outcomes at two years?
6. What influence do patient, disease, and surgeon factors
have on patient-reported outcome measures (PROMs) at
two years?
7. Is there correlation between radiological measures and
PROMs at two years?
8. Does patient, disease, or radiological factors predict sub-
sequent contralateral disease?

Methods
A national prospective comprehensive surveillance
cohort study of SCFE will be formed in two parts:

Anonymized surveillance cohort. A consecutive an-
onymized comprehensive cohort encompassing all UK
cases of SCFE. Individual consent is not sought for this
element of the study. In a study of a rare disorder, in which
the number of cases is small, refusal to contribute data by
one or two individuals will result in under-ascertainment
of cases and incorrect calculation of incidence. Seeking
consent would therefore reduce case ascertainment and
introduce bias; for example, certain groups or types of
individual might be more likely to refuse consent. The
consecutive surveillance cohort is important to minimize
selection bias, in accordance with recommendations of
the IDEAL framework, and this method of case ascer-
tainment has been established in similar surveillance
programmes.

Consented cohort. An identified cohort formed from
those within the surveillance cohort that consent to the
collection of PROMs, and future data linkage.

The cohort will be collected from all UK orthopaedic
units treating children and adolescents, with sites acting
as data collection centres. All orthopaedic units treating
children have agreed to participate as part of their audit
and risk management activities, with encouragement
from the British Orthopaedic Association, and British
Society for Children’s Orthopaedic Surgery. This follows
similar methodology to the successful UK Obstetric
Surveillance Study (UKOSS).

The study is underpinned by bespoke software that
automates many aspects of the follow-up and communi-
cation with sites. The software is built around the REDCap
Electronic Data Capture platform (Vanderbilt Univer-
sity, Nashville, Tennessee, USA), with bespoke elements
adding to the functionality to facilitate the study. This is
described in detail elsewhere as the BOSS Study.

In brief, reporting clinicians upload case details
including only minimal identifiers of individuals, including
sex, and month and year of birth, with monthly
electronic prompts to clinicians inviting them to confirm
case ascertainment and to prompt follow-up. Given that
SCFE is rare, other data sources (nationwide administra-
tive data, such as hospital episode statistics) can be peri-
odically linked to the BOSS records using the minimal
identifiers, to identify potential missing cases at each site.

Individuals and their families will be informed about
the BOSS Study, and will be invited to consent to provide
patient reported outcomes to enrich the data collected.
Patients can consent on paper at participating hospitals,
or will be given a unique code allowing them to consent
and participate in the study online at the study website.
Case definition

Inclusions. Patients must fulfil all of the following criteria:
1. Skeletally immature individuals;
2. Radiological confirmation of displacement of the epiphysis relative to the metaphysis occurring at the proximal femoral physis;
3. Newly presenting to secondary/tertiary care during the study period with the above radiological changes in either hip (patients will be included if the other side has been affected outside the study period, but the opposite hip is newly affected);
4. Undergoing surgical stabilization during hospital admission; and
5. A resident within the England, Scotland, or Wales.

Exclusions. Previous attempts at stabilization of the currently affected hip.

Denominator population. The denominator population will be defined as the population of children aged six to 18 years within the geographical boundaries of England, Scotland, and Wales.

Potential missing cases may be identified from two sources; national administrative data and an independent trainee reporting system. Potential missing cases are flagged to reporting clinicians each month when prompted to upload true cases, or to click a hyperlink to identify erroneous cases.

For national administrative data, cases of SCFE routinely undergo urgent surgery; therefore, the use of the data is ideal to supplement case ascertainment. ICD-10 codes pertaining to SCFE were identified in a prior study using administrative data (Table I). Diagnostic and interventional SCFE codes will be searched within the admission codes within the hospital episode statistics database (Tables II and III).

For the National Orthopaedic Surgery Trainee Research Network, the British Orthopaedic Network Environment (BONE) will function as a reporting network to highlight potential cases. If a trainee becomes aware of a case in the hospital where they are working, they will enter the date of admission, date of surgery, sex, and hospital trust onto a secure electronic REDCap database, which is separate from the main study database. Data entered into the trainee’s system does not capture full case details and is intended to maximize recruitment to the main database only; data entered into the trainee database is not a substitute for data entered into the main study. At the end of each month, the trainee will be prompted to electronically verify that cases they have recorded truly reflect the activity they experienced over this period.

Data collected. Demographics including height and weight, disease chronicity and severity, surgical intervention (including co-interventions), and intraoperative monitoring techniques (fluoroscopy/blood flow) were collected (Tables II and III).

The healthcare team reported the following outcomes at three months and two years: complications (such as infection, fracture, avascular necrosis, and chondolysis); subsequent operative interventions; planned operative interventions; contralateral SCFE; and radiological sphe- ricity, measured using α angle (at two years only).

Consented cohort. Several PROMs were used, including the Wong-Baker Faces pain rating scale, EQ-SD-Y (EuroQol), and paediatric quality of life (PedsQL; Mapi Research Trust, Lyon, France).

The Wong-Baker Faces scale is a validated self-reported tool. It is an ordinal assessment of pain using a series of six facial expressions to illustrate the degree of pain intensity. A numerical rating is assigned to each face (with 0 being ‘no hurt’ to 10 being ‘hurts worst’). It has been validated for use among children aged over three years. It is highly correlated to the visual analogue scale (r = 0.90; p < 0.001). Test-retest reliability is excellent (r = 0.90, p < 0.001). The Wong-Baker scale is widely used in clinical practice, forming part of the Royal College of Emergency Medicine ‘composite tool for the assessment of pain in children’ produced in 2013 as part of a best practice guidelines.
Table II. Schedule of observations for the anonymized surveillance cohort.

| Detail | Admission | 3 months postoperative | 2 years postoperative | Admission for opposite sided SCFE at any stage |
|-------|-----------|------------------------|-----------------------|-----------------------------------------------|
| Surgeon case report (case details) | X | X | X | X |
| Most recently available routinely collected radiographs of relevant hip or pelvis.* (AP and lateral as per standard care; pre- and postoperative (or intraoperative if postoperative unavailable)) | X | X | X | X |

*The BOSS Study does not require that radiographs be taken for the purpose of the study. It is routine practice to undertake radiographs in the treatment and follow-up of SCFE. The BOSS Study requests the anonymized routinely collected images from the medical record for use by the study team.

Table III. Schedule of observations for the nested consented cohort.

| Questionnaire | Admission (± 2 weeks) | 3 months (± 2 weeks) | 2 years (~3 months/ + 1 month) | Admission for opposite-sided SCFE (± 2 weeks)* |
|---------------|-----------------------|---------------------|-------------------------------|-----------------------------------------------|
| Initial admission, questions for parents/guardians (case details) | X | X | X | X |
| EQ-5D-Y (proxy if aged > 4 years and < 8 years) | X | X | X | X |
| PedsQL (proxy if aged < 8 years) | X | X | X | X |
| Wong Baker Faces Pain Scale (aged 4+ years) | X | X | X | X |

*This will be collected if a patient already enrol in the study presents with a SCFE in the opposite hip.

EQ-5D-Y is the youth version of the EQ-5D-3L, which is a validated, generalized, health-related quality of life questionnaire consisting of five domains related to daily activities with a three-level answer possibility. EQ-5D-Y has been especially adapted in terms of language for children aged eight to 18 years.18,19 A proxy version is available for younger children. Its age appropriateness in terms of feasibility, reliability, and validity in children and adolescents has been established.19 There is currently ongoing work to produce EQ-5D-Y value sets for use in children and adolescents. Our interim solution is to apply adult EQ-5D value sets to the EQ-5D-Y classification.

PedsQL is a well-validated, widely-used quality of life tool for use in children.20 It provides a general measure of quality of life, in addition to three summary scores, including a total scale score, a physical health score, and a psychosocial health score.

Long-term follow-up. The strength of UK data linkage offers an efficient means for a population cohort to be tracked to ‘definitive outcomes’; requiring minimal intrusion to the patient, and minimal attrition and follow-up costs. Subsequent arthroplasty is regarded as ‘failure’ of the hip, and is therefore the definitive long-term outcome and can be ascertained via linkage to the National Joint Registry.21 Measurement is proposed after ten years, and at five yearly intervals. Consent will be broad for future linkage to healthcare and other administrative datasets, in line with recommendations of the recent Medical

Research Council report concerned with maximizing the utility of cohorts.22

All patients entered into the surveillance cohort can participate in the consented cohort. Consent can be obtained at any time in the patient’s follow-up, but questionnaires should only be completed at the time-points specified in the schedule of observations.

Sample size, statistics, and analysis. Incomplete existing data means it is not possible to accurately predict the number of cases expected. National administrative data demonstrates an incidence of approximately five to seven cases per 100,000 of children aged six to 18 years.24 If we assume this approximates to the rest of the UK and use population data from the 2001 census (9.1 million six- to 18-year-olds), this suggests there would be 615 annual new cases of SCFE ($30 in England, $5 in Scotland, and 30 in Wales). The resulting 95% Poisson confidence intervals would allow the incidence to be estimated in the range 6.43 to 7.52 cases per 100,000 of children aged six to 18 years per year.

The surveillance cohort will recruit for a period of 18 months to identify the incidence of disease. The nested consented cohort will require 300 cases to enable meaningful comparisons to be made within subgroups (approximately 60% of those thought to be eligible).

The full statistical analysis plan, including dummy tables, is available on request. Key planned analyses are defined as:
1. Incidence rates will be estimated using reported new cases of SCFE, and denominators from UK census data. Rates will be stratified by country, region, age, and sex, and 95% confidence intervals will be calculated based on an assumed Poisson distribution for counts.

2. Variations in case-mix will be reported using descriptive statistics.

3. Variations in surgical management will be reported using descriptive statistics. Surgical management decisions are likely to vary by hospital, patient, and disease. In order to better understand this process, decision trees will be constructed to characterize overall management practices and highlight variation by centre.

4. Subsequent contralateral disease in SCFE is a binary outcome; therefore, logistic regression will be used to assess the importance and quantify the effects of a range of patient, disease, and radiological risks factors on this outcome, after adjusting for known confounders; recursive partitioning will be used to understand the most likely combinations of subgroups of baseline factors in predicting contralateral SCFE. Time to contralateral SCFE will be displayed using Kaplan-Meier plots, overall and split by age group and sex.

5. Univariate and multivariate analyses including random effects will be used to explore the relationship between baseline factors and two-year outcomes. Logistic regression for binary outcomes (such as AVN), and linear regression for continuous outcomes (e.g. α angle and two-year PROMs).

6. Associations between hip shape and PROMs at two years will be quantified using Spearman’s rank r and displayed with scatterplots.

**Ethical considerations and approval**

The ethical approach for the anonymized surveillance study has broadly been described elsewhere.

Among those entering the consented study, informed written/electronic consent will be obtained from parents or legal guardians (if participants are younger than 16 years). Patients who become aged 16 years while in the study will be asked to provide a written/electronic consent to affirm their willingness to continue participation in the study.

Assent will be sought from competent minors over eight years of age, where the research team assesses competence and relevance to do so. Where possible, the minor should personally write their name and date the assent form themselves. The form is then countersigned by the parent/legal representative and the researcher taking consent. Assent forms do not substitute for the consent form. Assent should be taken where appropriate; however, the absence of assent does not exclude the patient from the study if consent has been obtained from the parent/legal representative.

This programme of work complies with the Helsinki Declaration and was reviewed and approved by the National Research Ethics Service Committee London – City and East (REC ref 15/LO/2202) and the Health Research Authority (ref 190754). The release of national administrative data for this purpose was approved by the Public Benefit and Privacy Panel (PBPP) in Scotland (ref - 1617 to 0030) and the Data Access Advisory Group (DAAG) in England (ref NIC-362142-K9C7P). There was no similar process in Wales.

**Patient and public involvement**

Representatives of Steps UK, the primary charitable support group for children and young people with limb disorders, were consulted in the development of the funding application for this programme of work. Members of this group will sit on the study management group. The National Institute for Health Research Young Person’s Advisory Group, a group of children and young people involved in improving the conduct of research in children, assisted in the development of the participant information materials.

**Discussion**

The framework proposed by the IDEAL collaboration forms the basis for the study. The evidence in the treatment of SCFE is such that the current evidence is not mature enough to support the development of randomized clinical trials. The intention of this large surveillance cohort and nested-consented cohort is to provide robust feasibility data for randomized trials, and if such trials are not feasible, then the intention is that this will form the definitive cohort.

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