**\*\*\*\*\*\*\*\*\*\*\*\*THIS FILE IS NOT MEANT TO BE FOR PUBLICATION\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\***

STROBE Statement—checklist of items that should be included in reports of observational studies

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|  | Item No. | Recommendation | | Page  No. | | Relevant text from manuscript | | |
| **Title and abstract** | 1 | (*a*) Indicate the study’s design with a commonly used term in the title or the abstract | | 2 | | Using a historical cohort designwe recruited149 patients with a mean (and standard deviation) age of 19.7 (3.8) years with osteonecrosis following an open or closed reduction (1995-2005); and included 32 age-matched patients without osteonecrosis for cross-sectional comparison. | | |
| (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | | 2 | | We determined the association between the patient-reported outcomes and radiographic severity of osteonecrosis using mixed-effects regression analysis adjusted for age and acetabular dysplasia at study assessment, and number of prior operations.  Affected patients demonstrated minimal physical disability, a normal quality of life but reduced hip function. | | |
| Introduction | | |  | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | | 3 | | In previous research we determined the meaning of these four patterns of anatomical abnormality in terms of patient-based outcomes  However, none of these grades of osteonecrosis was associated with physical disability or with a reduced quality of life. We concluded that the good results were largely explained by the young patient age of 14 years. We suggested that the patients’ function would decline with increasing age, and that another study involving older patients would be needed to substantiate this hypothesis.  Further longitudinal evaluation of our existing cohort, combined with novel cross-sectional investigation of older patients treated for DDH in childhood, would for the first time, capture functional outcomes in the transition to adulthood. | | |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses 4 | | 3 | | The aims of the present study were therefore to ascertain the patient-reported outcomes hip function, physical function, and health status in adolescents and young adults with osteonecrosis secondary to DDH; and how patients with osteonecrosis change over time in terms of these outcomes. | | |
| Methods | | |  | | | |
| Study design | 4 | Present key elements of study design early in the paper | | 3 | | Further longitudinal evaluation of our existing cohort, combined with novel cross-sectional investigation | | |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | | 4 | | One researcher (A.M.) used clinical coding and the database from our previous study [12] to identify eligible patients treated in two tertiary centres from 1995 to 2005 | | |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants | | 5 | | ‘Eligible for this study were patients treated in two tertiary centres from 1995 to 2005with a diagnosis of DDH who had received a closed or open reduction with or without osteotomy and who were older than 14 years of age at the time of study assessment. We excluded patients with co-morbidities that exclude the diagnosis of DDH.’  ‘Of 311 eligible patients identified, 160 (51%) had evidence of osteonecrosis as per clinical records and radiography (Fig. 1). These included 72 patients studied in 2011 [12] when we had measured their hip function, physical function, and health status’ | | |
| (*b*)*Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed  *Case-control study*—For matched studies, give matching criteria and the number of controls per case | |  | |  | | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | | 8 | | We determined the relationship between osteonecrosis and hip function, physical function and health status with linear mixed-effects regression models [26] in order to account for within-subject correlation among 37 patients with bilateral osteonecrosis. We decided a priori to adjust all analyses for the total number of operations (with the exception of implant removal) any hip had undergone prior to the study assessment [12]; the degree of acetabular dysplasia at the most recent radiograph [27]; and the age at study assessment [12]. | | |
| Data sources/ measurement | 8\* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | | *7* | | We graded the presence of osteonecrosis according to Bucholz-Ogden  We quantified acetabular dysplasia by means of the centre-edge angle of Wiberg and the acetabular angle of Sharp. We evaluated the presence of osteoarthrosis according to Kellgren-Lawrence.  The orthopaedic resident (A.M.) examined all patients according to the Children’s Hospital Oakland Hip Evaluation Scale (CHOHES), Activity Scales for Kids (ASK) and Health Utilities Index Mark 3 (HUI-3) | | |
| Bias | 9 | Describe any efforts to address potential sources of bias | | 7 | | They first reviewed all radiographic classifications schemes and agreed on definitions and landmarks. They then evaluated all radiographs independently and their inter-rater reliability was established. | | |
| Study size | 10 | Explain how the study size was arrived at 9 | | 8 | | We estimated the sample size according to Cohen [32] based on the primary outcome, hip function. Established CHOHES scores [12] of 88, 88, 80 and 78 for Bucholz grades I-IV respectively (SD = 10) gave effect sizes (Cohen’s *d*) between 0.2 and 0.8. With α= 0.5 and β= 0.20, we estimated at least 15 patients were needed for each Bucholz-Ogden grade examined. In order to adjust for three variables, at least 105 patients with osteonecrosis were required (15 further patients for each additional variable) | | |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses.  If applicable, describe which groupings were chosen and why | We summarised scores and patient characteristics with means and standard deviations, or medians and inter-quartile range in non-normally distributed data. | | | |  | | |
| Statistical methods | 12 | 1. Describe all statistical methods, including those used to control for confounding | | | We determined the relationship between osteonecrosis and hip function, physical function and health status with linear mixed-effects regression models [26] in order to account for within-subject correlation among 37 patients with bilateral osteonecrosis. We decided a priori to adjust all analyses for the total number of operations (with the exception of implant removal) any hip had undergone prior to the study assessment [12]; the degree of acetabular dysplasia at the most recent radiograph [27]; and the age at study assessment [12]. We fitted models for each outcome measure (hip function, physical function, health status) using a backwards stepwise approach [28]. We used Akaike’s Information Criterion (AIC) [29] to assess goodness of fit. We reported least squared means for adjusted outcome scores. | | |  | | |
| 1. Describe any methods used to examine subgroups and interactions | | | Subgroup analyses showed hip function differed in those with osteonecrosis grades III/IV when compared with no osteonecrosis (p < 0.01) but not when compared with grades I/II (p = 0.05). | | |  | | |
| (*c*) Explain how missing data were addressed |  | | | |  | | |
| (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed  *Case-control study*—If applicable, explain how matching of cases and controls was addressed  *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy |  | | | |  | | |
| (*e*) Describe any sensitivity analyses |  | | | |  | | |
| Results | | | | | | | | | |
| Participants | 13\* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined  for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 5 Of 311 eligible patients identified, 160 (51%) had evidence of osteonecrosis as per clinical records and radiography (Fig. 1). These included 72 patients studied in 2011 [12] when we had measured their hip function, physical function, and health status | | | |  | | |
| (b) Give reasons for non-participation at each stage 6 | 23 could not be recruited (Fig.1). In 18 of the remaining patients we could not ascertain the effects of the osteonecrosis on patient-reported outcomes as 16 had undergone hip arthroplasties and 2 had undergone hip arthrodesis.  Of the remaining patients, five had undergone total hip replacements; one patient lived abroad; one was pregnant; one had a mental health condition preventing participation; five could not be contacted; and five declined participation). | | | |  | | |
| (c) Consider use of a flow diagram |  | | | |  | | |
| Descriptive data | 14\* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 6 Of 311 eligible patients identified, 160 (51%) had evidence of osteonecrosis as per clinical records and radiography (Fig. 1). These included 72 patients studied in 2011 [12] when we had measured their hip function, physical function, and health status.  Of 160 patients, 23 could not be recruited (Fig.1). In 18 of the remaining patients we could not ascertain the effects of the osteonecrosis on patient-reported outcomes as 16 had undergone hip arthroplasties and 2 had undergone hip arthrodesis. Thus, 117 patients (149 hips) with DDH and osteonecrosis at a mean age of 19.6 ± 3.8 years completed patient reported outcomes to measure the effects of osteonecrosis. These included 54/72 patients (75%) who had taken part in our earlier study [12] and who we could re-examine after a mean period (and standard deviation) of 8.4 ± 0.7 years or at a mean patient age (and standard deviation) of 21.9 ± 2.6 years (of the remaining patients, five had undergone total hip replacements; one patient lived abroad; one was pregnant; one had a mental health condition preventing participation; five could not be contacted; and five declined participation). From 151 patients with DDH but without osteonecrosis, we recruited an age-matched convenience sample of 32 patients (37 hips). In total, we studied 149 patients (186 hips) at a mean age (and standard deviation) of 19.6 ± 3.8 (range, 14 to 26) years.  In those with and without osteonecrosis, 86% and 97% of patients were female, respectively. This was not significant (p=0.18). In patients with osteonecrosis 36% of had undergone one operation, 36% two operations, and 28% three or more operations. This compared to 59%, 29% and 4% respectively, in patients without osteonecrosis. | | | |  | | |
| (b) Indicate number of participants with missing data for each variable of interest |  | | | |  | | |
| (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) |  | | | |  | | |
| Outcome data | 15\* | *Cohort study*—Report numbers of outcome events or summary measures over time |  | | | |  | | |
| *Case-control study—*Report numbers in each exposure category, or summary measures of exposure |  | | | |  | | |
| *Cross-sectional study—*Report numbers of outcome events or summary measures | *10* | | | |  | | |
| Main results | 16 | 1. Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 10 In patients with osteonecrosis, the median hip function summary score was 80 (interquartile range, 70 to 90); the median physical function score was 91 (interquartile range, 80 to 100); and the median health status score was 0.95 (interquartile range, 0.80, 0.97) These scores did not differ (p>0.05) from patients without osteonecrosis (Fig. 2).  The adjusted mean differences in hip function, physical function and health status scores in patients with and without osteonecrosis were -4.7 (95% confidence interval, -10.3 to 0.8);  -1.03 (95% confidence interval, -9.3 to 7.2); and 0.10 (95% confidence interval -1.1 to 1.2), respectively. | | | |  | | |
| (*b*) Report category boundaries when continuous variables were categorized |  | | | |  | | |
| (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |  | | | |  | | |

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| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11 | In 54/72 patients (75%) with longitudinal data for outcome scores available, the mean within patient changes in hip function, physical function and health status from baseline to current assessment were 7.18 (95% confidence interval, -2.11 to 12.26), -2.11 (95% confidence interval, -15.47 to 11.25), and -0.03 (95% confidence interval, -0.11 to 0.05), respectively. |
| Discussion | | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 13 | This study confirmed that, at a mean age of 21 years, it ranged from 86/100 points to 77/100 points. Aguilar et al. [35], using the CHOHES, found a mean score of 88/100 points in children without any hip problems. This would indicate that the hip function of our young adult patients was reduced in those with osteonecrosis grades III and IV by a degree that was clinically important. However, these differences were no longer seen in the adjusted analysis – scores were above 88/100 points and almost identical across all four grades of osteonecrosis. This suggests that the effects of the osteonecrosis alone did not explain the reduced hip function in grades III and IV. |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 15 | It is unknown how the remaining 13 patients not included in this follow up study faired over those eight years – this limits our conclusions about how patients change over time.  We note other potential limitations of this study. The participants of this study may have been too young to discern the ultimate effects of osteonecrosis on patient-reported outcomes. However, we selected this age group deliberately to gather insight into patients transitioning from paediatric to adult health care services, when activities and demands change after leaving school [38] often heralding the onset of functional impairments |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 16 | We demonstrated that at a mean age of 21 years, patients with and without osteonecrosis, on the whole, reported high scores in patient-reported outcomes. There are outliers with poor functional scores, but it would appear that factors other than osteonecrosis contribute to this disability. |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 16 | Clinicians could use this information when counselling the carers of affected children early when a diagnosis of osteonecrosis is made. It may also aid in determining the need (or frequency) for orthopaedic follow up appointments after skeletal maturity. |
| Other information | |  | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 17 | This study was funded by grants from Orthopaedic Research UK; NIHR; and Great Ormond Street Hospital Children’s Charity. All funders were involved in all aspects of the research including collection and analysis of data collected and funding full time staff members. |

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.