Hip Dysplasia and Femoroacetabular Impingement

Studies in newborns and young adults with focus on Radiology and Clinical Epidemiology

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Pour Noélie, Léa & François

Scientific environment

This work has been performed within the paediatric sections of the Departments of Radiology and of Orthopaedic Surgery, Haukeland University Hospital, Bergen, Norway, and the Department of Clinical Medicine, University of Bergen.

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1. List of abbreviations

AA	Acetabular roof angle of Tönnis
AAP	American Academy of Pediatrics
ADR	Acetabular depth-width ratio
AMH	Anne-Marte Haukom
AP	Anteroposterior
AVN	Avascular necrosis of the femoral head
BBC	Bergen Birth Cohort
BMI	Body mass index
CDH	Congential dysplasia of the hip
CE	Centre-edge angle
CI	Confidence interval
CT	Computer tomography
DDH	Developmental dysplasia of the hip
EQ-5D	The EuroQol Quality of life scale in five dimensions
F	Female
FAI	Femoroacetabular impingement
FHC	Femoral head coverage
FHEI	Femoral head extrusion index
FOI	Foramen obturator index
GEE	Generalised estimating equations
HUS	Haukeland University hospital
ICC	Intra-class correlation coefficient
IPW	Inverse probability weights
IØE	Ingvild Øvstebø Engesæter
JSW	Joint space width
KR	Karen Rosendahl
LBE	Lars Birger Engesæter
LBL	Lene Bjerke Laborie

LoA	Limits of agreement
M	Male
mm	millimetre
MRI	Magnetic resonance imaging
n	Number
OA	Osteoarthritis
OR	Odds ratio
PAO	Periacetabular osteotomy
PPV	Positive predictive value
PRR	Prevalence rate ratio
ROM	Range of motion
SCFE	Slipped capital femoral epiphysis
SD	Standard deviation
SHT	Sigrun Helen Tufta
TGL	Trude Gundersen Lehmann
THR	Total hip replacement
TI	Triangular index
US	Ultrasound
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

2. List of publications

This thesis is based on the following papers, referred to by their roman numerals:

I **Selective ultrasound screening for developmental hip dysplasia: Effect on management and late detected cases. A prospective survey during 1991-2006.** Laborie LB, Markestad TJ, Davidsen H, Brurås KR, Aukland SM, Bjørlykke JA, Reigstad H, Indrekvam K, Lehmann TG, Engesæter IØ, Engesæter LB, Rosendahl K. *Submitted* 2013.

II **Screening strategies for hip dysplasia: Long-term outcome of a randomized controlled trial.** Laborie LB, Engesæter IØ, Lehmann TG, Eastwood DM, Engesæter LB, Rosendahl K. *Pediatrics* 2013; 132(3). (DOI: 10.1542/peds.2013-0911).

III **Radiographic measurements of hip dysplasia at skeletal maturity- new reference intervals based on 2,038 19-year-old Norwegians.** Laborie LB, Engesæter IØ, Lehmann TG, Sera F, Dezateux C, Engesæter LB, Rosendahl K. *Skeletal Radiol.* 2013; 42(7): 925-35.

IV **Prevalence of radiographic findings thought to be associated with femoroacetabular impingement in a population-based cohort of 2081 healthy young adults.** Laborie LB, Lehmann TG, Engesæter IØ, Eastwood DM, Engesæter LB, Rosendahl K. *Radiology* 2011; 260(2): 494-502.

V **Is a Positive Femoroacetabular Impingement Test a Common Finding in Healthy Young Adults?** Laborie LB, Lehmann TG, Engesæter IØ, Engesæter LB, Rosendahl K. *Clin.Orthop Relat Res.* 2013; 471(7): 2267-77.

VI **The alpha angle in cam-type femoroacetabular impingement – new reference intervals based on 2038 healthy young adults.** Laborie LB, Lehmann TG, Engesæter IØ, Sera F, Engesæter LB, Rosendahl K. *Submitted* 2013.

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3. Abstract

This thesis focuses on two important pathological entities of the hip joint: *Hip Dysplasia*, including developmental dysplasia of the hip (DDH) in childhood and acetabular dysplasia in young adulthood, and *Femoroacetabular Impingement (FAI)* in young adults. DDH is the most common hip disease in childhood. The diagnosis of DDH in newborns involves clinical assessment of neonatal hip instability, often accompanied by ultrasound (US) assessment of both the joint instability and of the dysplastic acetabulum. Different screening policies for DDH in newborns exist, without international consensus. Undiagnosed and untreated DDH in childhood might lead to residual acetabular dysplasia in young adults, as diagnosed on radiographs, and might also give symptoms of hip pain, limping and restricted hip motion. Severe cases might evolve into early degenerative change, i.e. osteoarthritis of the hip and eventually require a total hip replacement. The diagnosis of femoroacetabular Impingement (FAI) in the adult hip is based on clinical and radiographic criteria. FAI often presents with hip pain and restricted hip range of motion. Radiologically, two subtypes of FAI are recognised. The cam-type with the pathoanatomical mechanism located on the femoral side, and the pincer-type on the acetabular side. Both types cause damage of the labrum lining the acetabulum.

The overall aim of this thesis was to investigate radiological, epidemiological and clinical aspects related to hip dysplasia and FAI, based on two population-based cohorts of newborns and young adults. We aimed to report on the effect of 16 years with a selective US screening programme for DDH in newborns (paper I), to investigate the radiological long-term outcome in young adulthood of different newborn screening strategies for DDH (paper II), to present gender-specific reference intervals for common radiographic measurements for acetabular dysplasia and early degenerative change in young adults (paper III), to report on qualitative (paper IV) and quantitative (paper VI) radiographic findings related to FAI in an unselected young population, and to report on the prevalence of the clinical test for FAI and its associations with radiological and clinical findings (paper V).

Paper I is an observational study based on prospectively collected data from a regional selective US screening programme for DDH including all babies born at the maternity unit of Haukeland University Hospital during 1991-2006. In addition to routine clinical screening of all newborns (n=81564), a hip US was performed in those considered to be at increased risk of DDH (14.1%). This approach resulted in acceptable rates of early treatment (3.0% of 81564 newborns) and of US follow-up consultations (3.3%), and in low rates of late detected subluxations and dislocations (0.32 per 1000), of children in need of surgical treatment (0.38 per 1000) and of avascular necrosis (AVN) as a complication to treatment (0.27%). We conclude this type of selective US screening appears to be a reasonable approach.

The papers II-VI are based on the '1989 Bergen Birth Cohort' (n=2038). This cohort includes all babies from the hospital's catchment area who were born in our institution during 1989 and enrolled in a large randomised controlled hip trial as newborns, and who also later attended a follow-up study ('1989 Hip Project') during 2007-2009. The results from the original trial led to the decision of a selective US screening strategy in our institution from 1990 and onwards, as reported in paper I. Paper II is a follow-up study of the initial hip trial from 1989, carried out in 2007-09. It evaluates the radiological long-term outcome in the 2038 young adults of the '1989 Bergen Birth Cohort', who were subject to one of three different screening strategies for DDH as newborns. Although the initial trial showed that both selective and universal US screenings tend to reduce the rates of late detected cases in infants and young children when compared to an expert clinical programme alone, we were unable to demonstrate any additional reduction in the rates of radiographic findings associated with acetabular dysplasia or degenerative change in young adulthood. Increased treatment rates following US screening were not associated with AVN, a serious but rare complication to abduction treatment. The studies in papers III-VI have a cross-sectional design and are based on the young adults of the '1989 Bergen Birth Cohort'. Paper III presents gender-specific reference intervals for the most common radiographic measurements for acetabular dysplasia and degenerative change of the hip joint used in young adults, which were similar to or wider than

existing values in the literature. Paper IV reports on different radiographic cam- and pincer-type findings thought to be associated with FAI, all qualitatively assessed. Overall, these findings seem to be quite common, especially in young males, with a high degree of coexistence among them. Paper V reports on the prevalence of a positive clinical test for FAI in young healthy adults, and examines its associations with clinical and radiographic findings related to FAI. This test was performed in the second half of those who met for follow-up (n=1170). Based on at least one affected hip, 7.3% males and 4.8% females had a positive impingement test. A positive test was associated with increased physical exercise and radiographic signs of cam-type FAI in males, hip pain in females, and decreased hip range of motion in both genders. Paper VI presents gender-specific reference intervals for the alpha angle on the frog-leg and anteroposterior (AP) views, the most used quantitative radiographic measurement used to diagnose cam-type FAI. The reference intervals presented for the alpha angle in this cross-sectional study are wide, especially for the AP view, with significantly higher mean values for males than females on both views. Higher alpha angles were associated with the presence of qualitative radiographic cam-type findings on both views.

In brief, the works of this thesis suggest that: Selective US screening for DDH is a reasonable approach (paper I). We could not demonstrate any additional reduction in the rates of radiographic findings associated with acetabular dysplasia or degenerative change in young adults subjected to neither universal nor selective US screening as newborns, compared to those who received clinical screening alone (paper II). Gender-specific reference intervals for radiographic measurements for acetabular dysplasia in young adults are similar or wider than existing values (paper III). Qualitative radiographic findings thought to be associated with cam- and pincer-type FAI, as well as the coexistence between them, seem to be quite common (paper IV). A positive test for FAI in healthy young adults is not uncommon, especially not in males (paper V). Higher mean alpha values with wider reference intervals are seen in males than in females on both frog-leg and AP views, with wider reference intervals for the AP view (paper VI).

4. Background

4.1 General introduction

The anatomical and structural development, function and long-term outcome of the hip joint can be compromised by several pathological changes. Hip dysplasia and femoroacetabular impingement (FAI) are two important pathological entities that affect the hip joint. They are both commonly accepted contributing factors to the development of early degenerative change and osteoarthritis (OA). Both conditions involve a suboptimal relationship between the cup-shaped acetabulum (socket) and the ball-shaped femoral head, leading to impaired function of the ball-and-socket-type hip joint. In this work the term ‘hip dysplasia’ encompasses ‘developmental dysplasia of the hip’ (DDH) in childhood and ‘acetabular dysplasia’ in young adults.

Assessment of the medical history, a detailed clinical examination and a thorough radiological work-up are all important elements in the diagnoses of both hip dysplasia and FAI. DDH in newborns consists of a poorly developed (i.e. dysplastic) acetabulum, and/or an unstable femoral head moving outside its confined place within the acetabular cup. The diagnosis of DDH is challenging. This is mainly due to the pathomechanical definition (dysplasia and/or hip instability), and the method of ascertainment (clinical examination and/or ultrasound (US)). Different screening or assessment policies for DDH in newborns exist, and the topic is debated. A routine clinical screening is usually performed in all newborns, often accompanied by a hip US offered to those at high risk for DDH (selective US strategy), or to all newborns (universal US strategy). The assessment of long-term outcome of different DDH screening strategies in newborns has been lacking. Uncomplicated, early detected cases of DDH are treated successfully with an abduction splint during the first months of life, while more complicated and most late detected cases (>1 month of life) of DDH are in need of longer treatment duration and sometimes surgical treatment.

Undiagnosed and untreated DDH in childhood can presumably manifest later as residual acetabular dysplasia in young adults, detected radiographically as a poorly developed acetabulum with a shallow acetabular cup. Common symptoms in adulthood include hip pain, limping and restricted motion, although some subjects are asymptomatic. Severe cases might evolve all the way to early degenerative change and osteoarthritis (OA) of the hip and eventually require a total hip replacement with lifelong implications.

The diagnosis of FAI is equally challenging, based on clinical and radiological findings. The key symptoms are hip pain and restricted hip range of motion. Radiologically, pathomechanical changes on the femoral (cam-type) or acetabular (pincer-type) side can be detected. Increased epidemiological knowledge of both radiological and clinical data related to FAI in a healthy young population is important, in order to better understand at what point normal anatomical variants should rather be considered pathological deformities that might be in need of treatment. For clarity, the alpha angle measured on US in DDH (paper I) is distinct from the alpha angle measured on radiographs in FAI (papers V and VI).

The works in this thesis are based on two main data sets. First, data regarding all newborns offered a selective hip US at birth was prospectively collected during 1991-2006, and reported as an observational study (paper I). Second, the ‘1989 Hip Project’ was carried out as a long-term follow-up of a part of a large randomised controlled trial (RCT) from 1988-90. The ‘1989 Bergen Birth Cohort’ includes young adults born in 1989 who took part in the RCT and later attended the ‘1989 Hip Project’ (n=2038). Papers II-VI are based on the ‘1989 Bergen Birth Cohort’. One long-term follow-up study of the ‘1989 Bergen Birth Cohort’ (paper II) and several population-based cross-sectional studies of the ‘1989 Bergen Birth Cohort’ at skeletal maturity, related to hip dysplasia (paper III) and FAI (paper IV-VI) were performed.

4.2 Hip dysplasia in newborns and young adults

4.2.1 General aspects

Hip dysplasia is a challenging pathological entity that encompasses a broad spectrum of disease. In this work the term 'hip dysplasia' includes 'developmental dysplasia of the hip' (DDH) in childhood and 'acetabular dysplasia' in young adults.

DDH: a brief historical perspective

Already in ancient times, Hippocrates (approximately 460-370 BC) noted the condition of DDH and mentioned a possible congenital association. The notion of heredity was introduced by Ambroise Paré in 1578. In 1784 Camper stated that the condition was more common in girls. Paletta presented the first autopsy descriptions of a dislocated hip in 1820, demonstrated in a two weeks old boy. The following decades, important knowledge on the topic emerged. Dupuytren made a large and important contribution to the field through his investigations as an orthopaedic surgeon with particular interest in children, and presented a study of dislocated hip joints in Paris in 1826. The first successful closed reduction of a dislocated hip joint reportedly took place in 1836, performed by Pravaz in a seven year old boy. Following this, the treatment options were refined and further developed to include different traction techniques as described by Sayre in 1876, and later also open reduction of the femoral head, first successfully performed by Poggi in 1888 and Hoffa in 1890[134]. Although Roser reported in 1879 that a dislocated hip could be diagnosed and reduced in the newborn child, a late onset of treatment (after one year of age) was often preferred the following decades. During the first decades of the 20th century, both Froelich of Nancy and later Peltesohn advocated diagnostics at birth followed by early onset of treatment, preferably as close to birth as possible. This was reinforced by several others the following decades. In Italy, early treatment was established by Putti in the early 1920's. Le Damany reported on a systematic method for detecting dislocated hips in newborns and described the 'signe de ressault'[190]. In 1937, Italian orthopaedic surgeon Ortolani described a clinical test for diagnosing a

dislocated hip[245]. He also described a sound, a 'clunk', detectable when a dislocated hip was successfully reduced back into the acetabulum during a positive test. Ortolani recommended that both the diagnosis and appropriate treatment should be initiated as early as possible, and mentioned the use of an abduction pillow. The Frejka's pillow splint, a specially developed abduction treatment device, was proposed to all babies with known risk factors of DDH some years later[100]. The Ortolani manoeuvre has become a hallmark in the clinical diagnosis of DDH, accompanied by another clinical test, the Barlow test, described by Barlow in 1962[19]. This test, which aims to identify unstable, dislocatable hips, builds on work by Coleman in 1956[59] and Palmén in 1961[246]. Palmén established the first clinical screening for DDH in Sweden in 1950, followed by Walther and Moe in Bergen, Norway in 1953[348], and by Coleman[59] in the United States. Since the 1950's, the clinical screening has played a crucial role in the diagnosis of DDH in newborns. From the 1980's, ultrasound (US) has become equally very important as a complementary diagnostic tool for this purpose, and will be described more in detail.

Development and Anatomy of the normal hip joint

In the unborn child, the two first months after gestation represent the embryonic period, dominated by tissue differentiation. The remaining time until birth corresponds to the foetal period, dominated by growth and maturation. The limb buds appear in the embryo in the fourth gestational week, and the acetabulum and the femoral head arise from the same unit of primitive mesenchyme cells[309,349]. At eight weeks of gestation a cleft develops and separates what will become a spherical femoral head and a cup-shaped acetabulum[62,349]. The hip joint and main structures, including the ligamentum teres, become fully developed by the eleventh week. Ligamentum teres is a fibrous ligament through which the femoral head will receive its main blood supply. Normal development in intrauterine life depends on balanced interactions between the triradiate and the acetabular cartilages, and the femoral head[62]. At time of birth, most of the acetabulum is cartilaginous. The femoral head is firmly held in place deep within acetabulum, as the surface tension of the synovial

fluid of the capsule joint causes a tight fit which is very difficult to disrupt in normal hips[263,351]. The fibro-cartilaginous rim (the labrum) surrounding the bony acetabulum continues to grow postnatally, adding depth to the cup-shaped acetabular socket[61]. It is commonly thought that the principal stimulus for the cup-shaped growth of the acetabulum is the presence and interaction of a spherical femoral head well-centred within it[133,262,351]. The acetabular depth will continue to increase throughout development, due to interstitial growth of the acetabular cartilage, appositional growth in the periphery of it, and periosteal formation of new bone at the acetabular margin[133,262,351]. During puberty and adolescence, the depth of the acetabular socket further increases, as three secondary ossification centres will develop[262].

A normal adult hip joint with a well-centred femoral head is the result of well-balanced interaction and growth between the acetabulum and the femoral head[61] (fig. 1). The hip joint is surrounded by a capsule and ligaments. The labrum, lining the acetabulum, may be affected in both hip dysplasia and FAI in young adults.

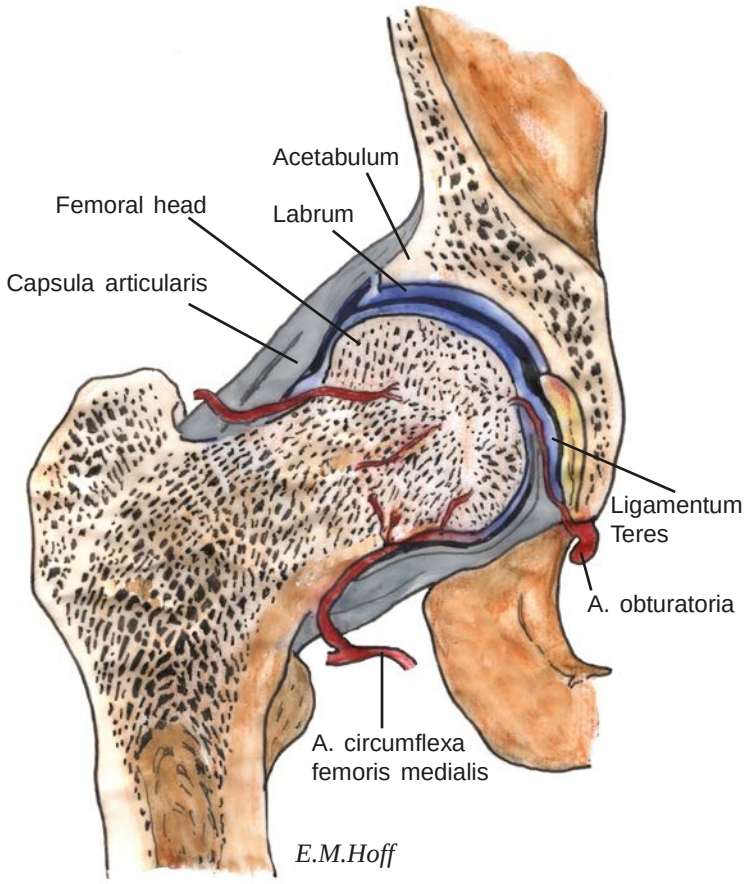


Fig. 1: Normal anatomy of the adult hip joint

Several conditions can affect the hip at different stages of development and growth. DDH is the most important diagnosis during the first years of life. Perthes' disease and slipped capital femoral epiphysis (SCFE) are two important diagnoses later in childhood and early adolescence. Perthes' disease is an aseptic avascular necrosis of the femoral head and has its peak around five to six years of age, predominantly in boys[312]. SCFE represents a condition where the femoral head slips in relation to the femoral neck in the area of the physis, during early adolescence, more often in boys[193].

Definition of DDH and Natural course of disease

DDH as a pathological entity reflects a disturbed relation between the acetabulum and the femoral head, and encompasses a spectrum of abnormal features related to both morphology and instability. The term ranges from mild acetabular dysplasia in a stable, concentric hip to more severe cases of a dysplastic acetabulum with a decentred, dislocated hip[12]. The definition of DDH varies throughout the vast amount of existing literature on the field[27,74].

The morphological component, i.e. acetabular *dysplasia*, refers to an abnormality of the hip bones, usually a poorly developed roof of the acetabular fossa resulting in a shallow acetabulum[119,120,351]. While reviewing the terminology related to clinical hip *instability*, it is useful to keep in mind both the position of the femoral head in relation to the acetabulum and the notion of time, as there is some inconsistency in the existing literature. The clinical aspect of the definition of DDH encompasses unstable (subluxatable or dislocatable), subluxated and dislocated hips[12]. In the newborn hip, the femoral head can abandon its concentric position within the acetabulum and move outwards, to become partially outside (subluxated) or totally outside (dislocated, or sometimes called luxated) the acetabular fossa. During the first weeks of life, the ligamentous laxity of the hip joint may be sufficient to allow for the hip to subluxate or dislocate, and reduce itself back into the acetabulum spontaneously[12]. This unstable position in between a stable and a subluxated or dislocated hip corresponds to a subluxatable or dislocatable hip, respectively[12,74,351]. After the first weeks, the

ligamentous laxity no more allows the dynamic outward-sliding of the femoral head. The pathological aspect thus refers solely to the position of the femoral head in relation to the acetabulum, i.e. subluxated or dislocated, without a dynamic component. A dislocated (i.e. decentred) hip in the newborn child presents with the femoral head located outside of the acetabular cup, without any contact between the two[12,61]. A dislocated femoral head typically moves superiorly, laterally and posteriorly out of the acetabulum[61]. In its most severe form, it is irreducible and cannot manually be repositioned back into the acetabulum, due to an inverted labrum, muscular contractions and constriction of the hip capsule[61]. The contracted adductor muscles contribute to limited abduction of the hip, and an adductor tenotomy might be necessary. In most cases, however, a successful reduction can be performed manually.

In order to ensure normal joint development, the femoral head must be concentrically located deep within the acetabulum. If subluxation or dislocation persists beyond the period of spontaneous reduction, structural anatomic changes might start to develop in the hip joint, as the remodelling and deepening of the acetabulum require a deeply reduced femoral head within it[12]. Originally, the term congenital dysplasia of the hip (CDH) was used. As it was considered confusing and imprecise, it was replaced by the more accurate acronym 'developmental dysplasia of the hip' (DDH)[12,175]. The change from 'congenital' into 'developmental' emphasises the notion of time and the potentially progressive nature of a disease which might not be detectable clinically at birth[61,292].

Another important notion related to the definition of DDH is the *age* of the child at time of diagnosis. 'Late' represents 'late presentation' or 'late detection', and refers directly to the time of diagnosis in relation to birth. The severity ranges from acetabular dysplasia alone, through acetabular dysplasia with a subluxated or dislocated head[142,281]. There is no clear definition of 'late diagnosis', as reflected in the literature[297]. Most authors choose at the latest six to eight weeks of age as the limit for early versus late diagnosis. In the works of this thesis, the term 'late cases of DDH' is used from one month of age, in accordance with others[28,30,80,142,281]. Late

diagnosed DDH have also been defined by sonographic appearance (i.e. by US) of the hips at six month of age[107].

Residual acetabular dysplasia can be seen during adolescence and in young adulthood. It can be visualised on plain radiographs as a poorly developed acetabulum with an insufficient coverage of the femoral head. Possible clinical symptoms, although not always present, are hip pain, limping and restricted hip motion. Acetabular dysplasia with a centred femoral head in late adolescence and young adulthood is thought to be preceded by DDH in infancy, although this remains to be confirmed[74]. Last, extensive literature focuses on the eventual development of osteoarthritis (OA) following untreated or unsuccessfully treated DDH and/or acetabular dysplasia[350,352].

Aetiology and Risk factors

The causes of DDH are not entirely understood. DDH is seen more often in children with certain identified risk factors, although 40% of children with confirmed DDH do not have any known risk factors detected at all[296,307].

Two components of possible *genetic mechanisms* underlying DDH have been proposed; primary acetabular dysplasia and connective tissue laxity. This hypothesis was supported by Wynne-Davies, who suggested two DDH phenotypes - an "acetabular dysplasia" type and a "joint laxity" type[363]. The degree of interaction between these two components needs further investigation. In an evidence synthesis for the American Academy of Pediatrics' (AAP) clinical practice guideline for the early detection of DDH, odds ratios (OR) for DDH given different risk factors were investigated. The OR of 1.7 for DDH among those with a positive family history was, however, not statistically significant (95% CI 0.05-55)[194]. Rosendahl et al reported an increased risk of DDH associated with having a first-grade relative (sibling or parent) with DDH[283].

The *environmental* risk factors are often classified into two groups: associations with limited resistance of the hip to dislocation (connective tissue laxity, shallow acetabulum) or associations with external constraints and thus limited foetal mobility

(breech presentation, oligohydramnios, high birth weight, primipara, tight clothing)[12,50,79,140]. The female gender has an increased risk for DDH, and this has been associated with a transient increase in ligamentous laxity, caused by the maternal hormone relaxin[363]. The risk of DDH after breech presentation has been estimated as high as 12% in girls and 2.6% in boys[61], with the highest risk for those with extended knees[50,79]. Breech presentations occur in approximately 2-4% of vaginal deliveries in the general population[352]. Postural deformities such as torticollis, calcaneus valgus, and talipes equinovarus (clubfoot), presumably associated to limited mobility, have all been proposed to indicate an increased risk of DDH[12,251]. The left hip is involved three times more often than the right hip, presumably due to the left occiput anterior position of most non-breech babies[61]. Also postnatal positioning plays a role[12]. In societies where swaddling, i.e. forceful adduction and extension of the newborn hips, is used, the incidence of DDH is higher[60,109,180]. On the other hand, the practice of carrying the baby astride the mother's waist with the hips in a naturally abducted and flexed position appears to lower the incidence of DDH[12]. DDH can also occur due to teratological or neuromuscular causes, which are not discussed here.

The main risk factors appear to be female gender[16,50], a positive family history[283,294,362] and breech presentation at birth[50,283,367]. Given female gender, family history and breech presentation, separately, the ORs were calculated as 4.1, 1.7 and 5.5 respectively in the AAP synthesis[194].

Epidemiology

The reported *prevalence* of DDH varies widely. Definition of disease, method of ascertainment, screening strategy and time of diagnosis, as well as ethnicity, gender and age are all influencing factors[12,61]. Some authors report on the incidence rather than the prevalence of DDH[27]. It should be kept in mind that prevalence and incidence are distinct epidemiological measurements. The prevalence of a disease indicates the total number of cases of disease within a population at a given moment, i.e. a proportion of subjects with the disease, and thus how widespread it is in a society. The incidence of a disease measures the rate of occurrence of new cases, and

thus the risk of developing the disease, within a defined time interval. The literature reporting incidences or prevalences for DDH can historically be divided into three different periods, as described by Bialik[27]: The pre-screening period (1920s to 1950s), the period of clinical screening only (1950s to 1980s), and from the 1980s and onwards, after different US techniques had become readily available.

A comprehensive review estimated the median prevalence of clinically diagnosed and persistent hip dysplasia (i.e. dislocation in one or both hips) as 1.3 per 1000 live births (range 0.84 to 1.5) in an unscreened population[191]. This estimate was based on studies on 44 unscreened populations living in the USA, Canada, Australia, the UK and Scandinavia, predominantly of northwest European ancestry. The prevalence of neonatal hip instability, i.e. dislocatable and dislocated hips as assessed clinically by the Barlow-Ortolani manoeuvre, has been estimated at higher numbers, at 1.6-28.5 per 1000[191]. This is in keeping with the fact that neonatal hip instability might be transient and only detectable the first few weeks of life. In a study of 9289 newborns, Barlow demonstrated that over 60% of the newborns with unstable hips recovered spontaneously within the first week of life, and 88% within the first two months of life[19]. These results also demonstrate that the *age* at the time of diagnosis is important when determining the prevalence of DDH. The remaining 12% of newborns with unstable hips in Barlow's series failed to recover spontaneously, corresponding to a rate of true congenital dislocation of 1.55 per 1000 births[19]. In Norway, the prevalence of clinically assessed dislocatable or dislocated hips has been reported at around 10-20 per 1000 live births[140,143,269,282].

Girls are in general more affected than boys. Neonatal hip instability is about 3-4 times more common in girls than in boys[30,43] and about 5 times more common in girls for cases presenting in later childhood[31,80]. Similarly, DDH detected on US is also more common in girls, affecting 5.7% of all girls compared with 1.2% of boys[283]. Several population-based studies with universal US screening have shown that 2-4% of all newborns have morphologically mild or severely dysplastic hips, 13-25% have

immature and 75-85% normal hips[27,72,77,90,184,283]. DDH affects both hips in approximately 30-40% of the cases[30,80].

Ethnic variation also influences the prevalence of DDH. Whereas high prevalences of clinically assessed dislocation and subluxation have been reported in unscreened populations in Turkey, Japan, Saudi Arabia, and in the Navajo Indian and the Sami populations, the prevalence is much lower in the African population[109,177,180,191,277,288,365].

The reported prevalence of *late detected cases* with subluxated or dislocated hips varies wildly. It has been estimated ranging from 0 to 200 per 1000 in unscreened populations[27]. In Norway, rates of 2.6 and of 3-5 per 1000 have been reported[142,281]. After screening programmes became available, prevalences have ranged from 0.1 to 3 per 1000 after clinical screening alone[27,29,81,212,281], from 0.2 to 0.7 per 1000 when selective US is added to the clinical screening[35,52,142,207,253,281], and from 0.13 to 0.3 per 1000 in universally screened populations[142,281]. Rates of late detected cases including sonographic dysplasia have also been reported, resulting in higher rates. In a large RCT assessing different screening strategies, Rosendahl and colleagues reported at rates of late detected subluxated, dislocated or dysplastic hips grouped together, with figures of 2.6, 2.1 and 1.4 per 1000 corresponding to clinical screening alone, selective US screening and universal US screening, respectively[281].

The reported prevalence of *acetabular dysplasia in adults* also varies to a great extent. It depends on ethnicity, gender and radiographic definitions of disease. The reported prevalence is estimated at 2-5% in Caucasians[66,144,149,186,304] and at 5-19% for a Japanese population, respectively[144,368]. Higher prevalences are seen for females[194]. The reported prevalences also vary greatly according to which radiographic measurement is being used, and the corresponding pathological threshold value applied. All these factors must be kept in mind when comparing the results of different studies.

4.2.2 Clinical and radiological assessment at birth and during childhood

Newborn clinical examination

A detailed medical history must be supplemented by a routine clinical examination in the undressed and calm child, preferably within the first 24 hours of life[307]. It should be performed by an appropriately trained health professional. The clinical examination aims to detect hip instability, asymmetry of gluteal and thigh folds, leg length discrepancy and limited abduction of the hips. Postural deformities such as foot deformities and torticollis should also be assessed. There are no pathognomonic signs for a dislocated hip. Clinical hip instability is assessed by the Ortolani (fig. 2 A-B) and Barlow (fig. 2 C-D) tests[19,245]. Each hip should be assessed individually, in the supine position with the hip flexed to 90° and in neutral rotation. The examiner places the index and middle fingers along the greater trochanter and the thumb along the inner thigh.

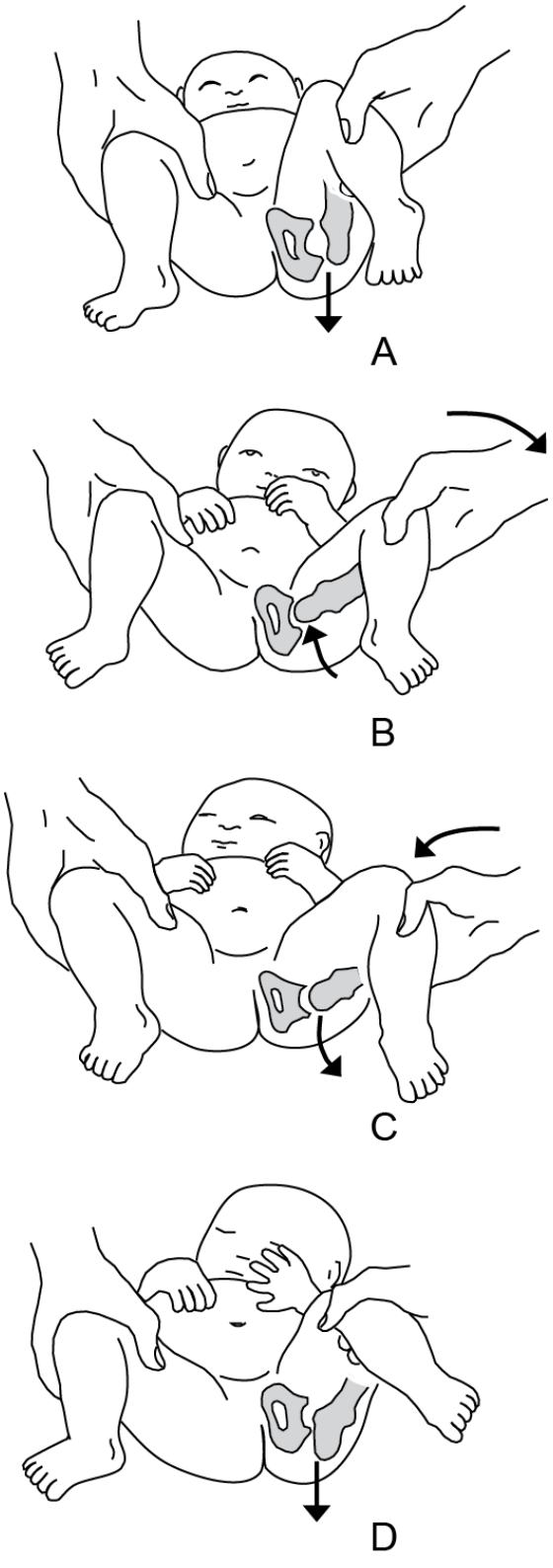


Fig. 2. Ortolani (A-B) and Barlow (C-D) tests

The Ortolani test consists of abduction and forward pressure in an attempt to relocate or reduce a dislocated head back into the acetabulum. A dislocated or subluxated hip is suspected on the basis of a palpable 'clunk' or movement as the femoral head is reduced into the acetabulum. The Barlow test consists of adduction and posteriorly directed pressure in an attempt to dislocate a concentric femoral head out of the acetabulum. A dislocatable or subluxatable hip is suspected if a palpable complete or partial displacement is detected[296]. The Ortolani and Barlow tests in combination have a high specificity (reported at 98-99%) for detecting neonatal hip instability[73]. The sensitivity depends highly on the experience of the examiner, and is reported at 60-97%[20,156,212,264].

In the literature, confusion and poor translation into the English language has led to misunderstanding regarding the sound of a dislocated hip being reduced[352]. This sound is best described as a 'clunk' or a 'jerk', and not as the misleading term 'click'. This latter should preferably be used to describe sounds of soft tissue and ligament movements within the hip joint often elicited during the newborn examination, which are not considered pathologic[352]. A dislocated or decentred hip in the newborn child is detected by the Ortolani test. In rare, severe cases, it is irreducible and cannot manually be repositioned back into the acetabulum. This implies a negative Ortolani test. However, the hip abduction will be limited on the affected side. Bilateral cases of irreducible dislocation might be overseen.

Clinical examination after the newborn period

A limited abduction remains an important clinical sign after the newborn period. It has a high specificity (>95%) but lower sensitivity (70%)[153]. In the supine child with a stabilised pelvis, abduction >75° should be possible[239]. Asymmetric thigh folds and apparent limb length discrepancy are all possible signs of a dislocated hip. The limb shortening is best assessed in the supine position with the hips flexed, as the above-knee shortening becomes apparent by comparing the height of each knee (the

Galeazzi sign)[307,352]. The hip examinations should be performed by appropriately trained staff, and should be repeated periodically at least until walking-age, preferably until the age of two years, in order to detect late presenting cases of DDH[307]. In toddlers with persisting dislocation, asymmetric gait can be observed, often accompanied by a positive Trendelenburg sign. Later in childhood and adolescence, unilateral dislocations can manifest clinically as leg length discrepancy, scoliosis, ipsilateral knee problems and gait disturbances. Activity-related pain might be present. Bilateral dislocations might cause lumbar lordosis and subsequent back pain[317].

Ultrasound (US)

The ability of US to visualise the cartilaginous acetabulum, femoral head position and hip instability in the infant hip has made it a well-established tool in the diagnosis of DDH (fig. 3). The US examination requires detailed knowledge and understanding of the anatomy of the infant hip. While neonatal hip instability can be assessed both clinically and sonographically, the acetabular component, dysplasia, is detectable in newborns by US only. US offers many advantages. It is a safe, non-invasive technique, without exposure to ionising radiation.

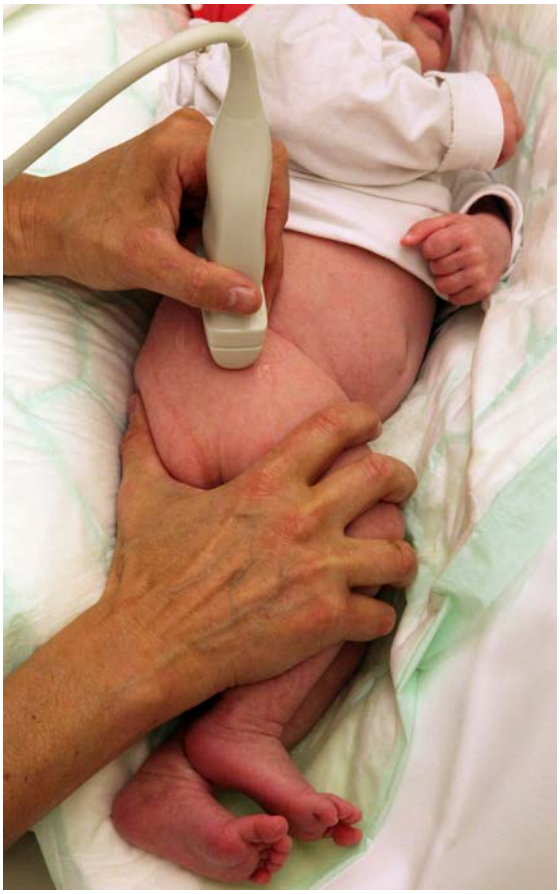


Fig. 3. Ultrasound of the newborn hip

Hip US is observer-dependent, particularly during the first three weeks of life[214,278]. This underscores the importance of a skilled and experienced examiner in order to obtain accurate results. US is the modality of choice from birth until around 4-5 months of age. From this age onwards, the acetabular ossification is sufficient for an AP radiograph to be taken and accurately analysed.

US imaging of the newborn hip was first proposed by Graf in 1980[119].The method was modified and refined the following years, including the use of higher frequency linear transducers (5-7 MHz), real-time US and the use of one single coronal view (fig. 4). The reproducible and standardised coronal section through the mid-acetabulum is paramount for this technique.

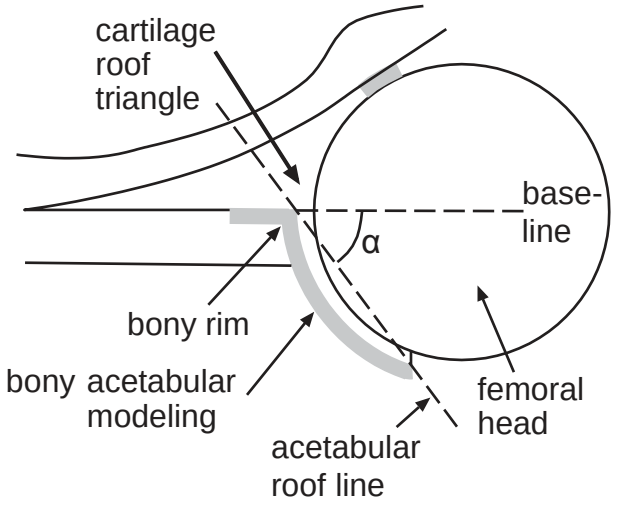


Fig.4. Graf's standard coronal view and the alpha angle (α)

The infant is examined in a cradle in a lateral position. Assessment of acetabular morphology includes a subjective evaluation of the bony rim, the cartilage roof triangle and the bony acetabular remodelling, and measurements of the angle of acetabular inclination (α angle). For the alpha angle, the baseline, or iliac line, has its origin at the apex of the cartilaginous roof triangle. It is tangential to the lateral surface of the iliac wing. The bony acetabular roof line extends from the lower acetabular edge to the promontory. The alpha angle is indicative of the slope of the bony acetabulum, and is the most significant angle in the evaluation of DDH. A wide angle indicates maturity and good femoral head coverage and values ≥60° define a fully developed hip. The acetabular roof angle (β angle) can also be assessed, as the angle formed between the baseline (iliac line) and the cartilage roof line, which connects the fibrocartilaginous labrum to the bony promontory. It indicates the degree of cartilaginous roof coverage, and a small angle indicates either little cartilaginous coverage of the femoral head and thus better bony containment, or a

subluxated/dislocated femoral head. The hip is classified into four main types and nine sub-types[120]. Although Graf's method is a static method assessing the acetabular morphology without assessment of the position of the femoral head, Graf integrated the assessment of hip stability in the dynamic standard minimum sonographic examination, as explained below.

During the 1980s and 1990s, several methods which allow for separate assessment of hip morphology and hip stability were proposed. The most used US techniques can be classified according to their main focus: Acetabular morphology, hip stability, femoral head coverage or a combined assessment of morphology and stability[40]. Whereas in Austria, Graf emphasised the static examination, in the USA Novick and colleagues[240] and Harcke and colleagues[129] both put focus on the dynamic assessment. In 1983, Novick et al proposed transverse views from medial and lateral approaches to assess the position of the femoral head, without any assessment of the acetabular morphology. Harcke and co-workers proposed a method called the 'dynamic four-step method' in 1984, including lateral transverse and lateral views, with the hip both in a flexed and a neutral position, and with and without stress. The acetabular morphology was also assessed subjectively, without any measurements.

As for the methods focusing more on the femoral head coverage, a variation of the Harcke method was proposed by Morin in 1985 in the USA, together with Harcke and MacEwen[224]. The Morin method included the measurement of the femoral head coverage (FHC) on a lateral coronal view with flexed hips. FHC measures the percentage of the femoral head covered by the bony acetabulum, i.e. lying medial to the lateral iliac border (corresponding to Graf's baseline in the standard coronal section). Terjesen and colleagues in Norway proposed a modified Morin method in 1989[325], with the slight difference of using a line drawn parallel to the long axis of the laterally placed US probe rather than using the lateral iliac border (the iliac line). They initially used the term 'bony rim percentage' but later adapted the 'femoral head coverage' term.

In 1992, Rosendahl et al in Norway proposed a combined assessment of morphology and stability (modified Graf method)[280] (table 1). When assessing the acetabular morphology, the hip should be slightly flexed and in a neutral abduction-adduction position, in order to maintain a well-centred femoral head. In hips with a decentring, eccentric or dislocated head (Graf's types 2c, D, 3 and 4a) the femoral head is relocated using mild traction of the thigh prior to morphological assessment. Acetabular morphology is assessed according to a modified Graf's method (without the β angle), based on the α angle: normal (α≥60°), immature (50°≤α<60°), mildly dysplastic (43°≤α<50°) or severely dysplastic (α <43°) (fig. 5 a-d).

Table 1: Rosendahl's classification[280] for combined assessment of morphology and stability by US

Type, α angle,	Morphological description (Corresponding Graf type)
Normal, α≥60°	Well-formed bony acetabular roof with an angular lateral margin and a narrow cartilaginous rim. (Graf Ia/b)
Immature, 50°≤α<60°	Adequately formed bony acetabular roof with a rounded lateral margin and a wide cartilaginous rim, i.e. a physiological retardation of the acetabular rim. (Graf IIa)
Mildly dysplastic, 43°≤α<50°	Deficiently formed bony acetabular roof with a rounded to flattened lateral margin and a wide cartilaginous rim (minor dysplasia), i.e. a maturational deficit. (Graf IIc)
Severly dysplastic, α<43°	Poorly formed bony acetabular roof with a flattened lateral margin and a wide cartilaginous rim (major dysplasia).

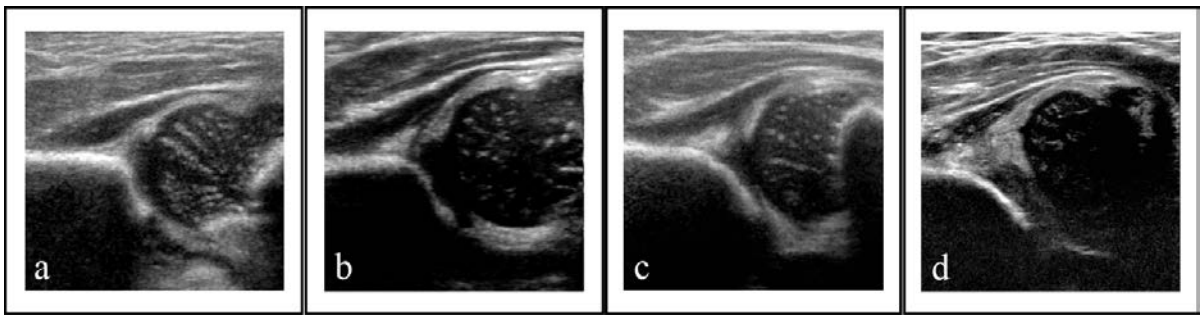


Fig. 5. Sonographic assessment of hip morphology in newborns, using Grafs standard coronal view and the alpha angle. Each hip is morphologically classified as a) normal (α≥60°), b) immature (50°≤ α<60°), c) mildly dysplastic (43°≤ α<50°) or d) severely dysplastic (α<43°) (Rosendahl's classification).

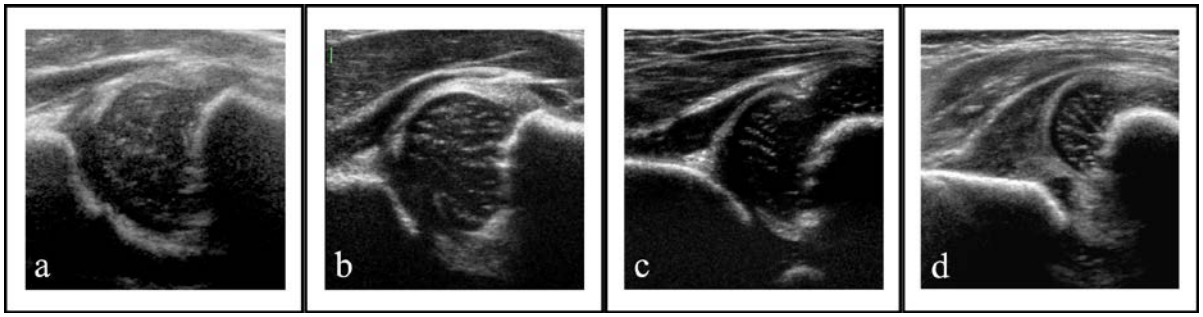


Fig. 6. Sonographic assessment of hip stability in newborns. By using a modified Barlow-manoeuvre, hips are classified as a) stable, b) unstable (significant movement of the femoral head, but not dislocatable), c) dislocatable or d) dislocated.

Thereafter, hip stability is assessed by a stress test (modified Barlow manoeuvre) performed by one hand, with the infant in a lateral decubitus position and a laterally placed US probe in the other hand. Hip stability is classified as stable, unstable, dislocatable or dislocated (fig. 6 a-d). Acetabular morphology and hip stability have been shown to have a high correlation[280]. The combination of dynamic and static assessment allows evaluation of hip stability, position and morphology, and is commonly agreed upon as the preferred method[13].

The year after Rosendahl's method was proposed, a combined morphological and dynamic US technique was proposed by an expert group, including Graf and Harcke. This technique was called the dynamic standard minimum sonographic examination[130]. A lateral coronal view was proposed for static assessment of the morphology, whereas a stress test (analogous to the Barlow manoeuvre) was performed in the flexed hip using a transverse view. A dynamic anterior US approach, Dahlström's method, was introduced in 1986[68], requiring two examiners. Modifications of this method was proposed in 1997, as Finnbogason's method, with only one examiner required[94]. Suzuki and colleagues described a different anterior US method in 1991, aiming to determine the femoral head position[315]. Both hips were examined simultaneously. A refined version also included measurement of the acetabular angle[316]. In Europe, Graf's method or a modified version (Rosendahl's method) is used in Austria, Switzerland and Germany, as well as in Norway, the Netherlands, Italy, France, Hungary and the UK[41,91,122,176,276,281,330,343].

Pelvic radiographs

Plain radiography becomes the method of choice for the assessment of DDH in infants aged 4-5 months and onwards[194]. An anteroposterior (AP) pelvic radiograph provides an overview of the hip joint anatomy, including the bony acetabulum, femoral head and neck. Assessment of the acetabular inclination before closure of the triradiate cartilage includes measurement of the acetabular index (AI) (fig. 7)[174,334]. Age-specific reference values for the AI angle were published by Tönnis and Brunken in 1968[334]. Hips with values ≥2 SD are classified as dysplastic and those between 1 and 2 SD as delayed acetabular ossification. Since the AI angle is influenced by the position of the pelvis, the degree of pelvic tilt and lateral rotation as well as the acetabular depth and the position and the shape of the femoral head should also be assessed[38,334]. Standardised positioning is crucial for accurate diagnosis. The migration percentage (MP) is used by some authors to assess a subluxated and dislocated femoral head[271,324]. A MP<33% and of 33-89% indicate a dislocated or subluxated femoral head, respectively.

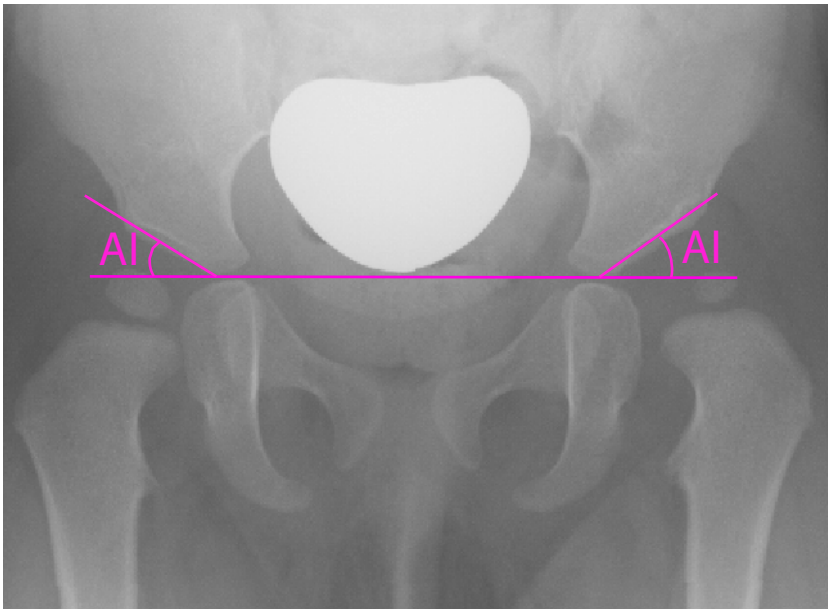


Fig.7. Pelvic AP radiograph at 15 months. The AI is defined as the angle between a line from the inferior margin of the iliac bone through the bony acetabular rim, and the Hilgereiner's line (a horizontal line through the upper margin of the radiolucent triradiate cartilage).

4.2.3 Different screening strategies for DDH in newborns

Organised clinical screening for early detection of DDH was initiated in the 1950s, based on the Barlow-Ortolani manoeuvres[19,245]. The first reports were from Sweden[246,345]. Clinical screening programmes were thereafter reported in different countries, including Norway[348], USA[59,308], UK[19,307], and Israel[353]. As the clinical screening programmes also detected presumably transient neonatal hip instability, some overdiagnosis and overtreatment were seen[27]. Definitions varied from established or persistent DDH, subluxation, dislocation, or neonatal hip instability including dislocatable hips. In addition, some authors also added the late detected cases to the neonatal rates. Overall, studies based on clinical screening alone have reported on prevalences varying from 0.41 to 169 per 1000, with varying rates of late detected cases[27]. In 1972, Mitchell stressed the problem of so-called 'missed' dislocations in early management of DDH, based on his findings in Sweden during 1962-1968, where four late dislocations that required surgery occurred in 31961 live births (0.12 per 1000)[221].

Initial optimism for the clinical screening strategy in newborns did somewhat fade the following decades, as it was not as efficient in reducing the rates of late presenting cases and their need for surgery as first expected[43,139,157,221]. Roberton stated in the Lancet in 1984 that 'CDH screening today is a mess'[275], and emphasised the fact that despite clinical screening, most available studies reported at 0.4-2.0 missed cases of CDH per 1000 livebirths. He further pointed out that given the fact that most late detected cases of CDH and even some cases detected at birth required surgery, the number of children requiring surgery had remained surprisingly constant at around 1 per 1000 live births. This might be explained by poorly organised screening programmes, inexperienced examiners and/or insufficient follow-up[125,178]. Radiographic screening was proposed during the 1970's[92]. Widespread use of hip ultrasound (US) throughout Europe followed, as the new US techniques became available[119,129,224,280], in an attempt to eradicate late detected cases. Universal, or general, US screening was established in 1992 in Austria[122] accompanied by

Germany[123,343], Switzerland (predominantly German-speaking areas)[37], Italy[20,69,274,330] and parts of the UK[73]. Several other regions, such as Norway[142,281], parts of the UK[73,159], France[287], USA (Chicago)[347] and Hong Kong[331] have established routines and protocols for selective US screening in addition to the routine clinical screening, based on risk factors and positive results on the routine newborn clinical examination[285]. This approach is also called targeted or high-risk screening. The risk factors used as inclusion criteria might vary slightly, generally including a positive family history, breech presentation at birth, clinical hip instability and often congenital foot deformities.

An extensive literature related to DDH screening in newborns exists. The topic has been debated for decades and still remains controversial. A major challenge is the methodological shortcomings in the literature. Several extensive reviews have made an attempt to collect, analyse and compare data from the studies available dealing with DDH screening[61,194,250,296,359]. The different rates appear difficult to compare, as the screening programmes differ substantially in the choice of strategy, in the choice of US method if US is performed, in definitions of DDH, in the age of the infant at time of screening, and in definitions of outcome measures for the screening programmes, which mostly include rates of late detected cases or rates of cases in need of surgical treatment.

The rates of treatment, US follow-up, late detected cases and surgery vary, depending on the choice of screening strategy. Treatment rates as high as 7.7% were reported by Altenhofen and colleagues in a study based on universal screening[5]. A systematic review including ten studies on DDH screening confirmed that universal US screening might increase the overall treatment rates as compared to clinical screening alone, although the treatment associated with US screening seems to be shorter and less intrusive[359]. Universal US screening based on Graf's static method initially led to higher treatment and US follow-up rates, compared to the rates reported based on a dynamic method alone detecting neonatal hip instability (dislocatable/dislocated hips): 3-5% vs. 0.4-1.5% for treatment rates and 10-20% vs. 6-7% for follow-up rates,

respectively[35,121,285]. As methods for the morphological assessment technique have improved, these differences seem to have disappeared, as an extensive meta-analysis from 2000 found that the choice of US technique had no influence on the reported treatment rates[194]. The reported rates of late cases also vary substantially. Shipman et al stated in their review that the impact of screening tests on the incidence of late diagnosis of DDH is difficult to quantify[296]. The rate of cases in need of surgery has also been used as an outcome measure in the evaluation of different screening strategies[35,49,112,343]. In clinically screened populations, the rate of those in need of surgery ranges from 0.07 to 1.79 per 1000[191]. Two studies based on similar methods reported at ascertainment-adjusted first operative procedure rates of 0.26 per 1000 live births (95% CI: 0.22-0.32) in a population screened with general US[343] and of 0.78 (0.72-0.84) after clinical screening[112]. Boeree et al reported at 0.40 per 1000 after a selective US screening programme[35].

Screening policies have been influenced by a number of studies, including two randomised controlled trials (RCT)[142,281]. The authors of the two studies concluded independently that both selective and universal US screening tend to reduce the prevalence of late detected cases of subluxation and dislocation as compared to clinical screening alone, although without reaching statistical significance. US screening was also associated with a corresponding increase in treatment rates. Both RCTs advocated a selective US approach in addition to high-quality clinical screening based on their findings, and introduced a selective hip US as part of the newborn DDH screening at their respective centres.

One of the RCTs, performed by Rosendahl and colleagues at our institution[281], evaluated the effect of three different screening strategies for DDH in newborns. In total 11925 babies were assigned to one of the three groups: universal US (n=3613), selective US (n=4388) or no US (n=3924), all of them in addition to routine expert clinical screening. It demonstrated lower rates of late presenting subluxated or dislocated DDH in the universally and selectively screened groups as compared to the group receiving clinical examination alone (0.3 and 0.7 vs. 1.3 per 1000) (p=.11, test

for trend). Treatment rates were, however, higher for the universally screened group as compared to the groups with selective US or no US screening; 3.4% vs. 2.0 and 1.8 ($p<.001$). The other RCT, performed by Holen and colleagues in 2002[142], compared universal US screening (n=7489) to selective US screening (n=7689), both in addition to routine clinical screening.

A systematic review from 2005 that aimed to assess the accuracy and effectiveness of universal US screening concluded that 'clear evidence is lacking either for or against general US screening of newborn infants for DDH'[359]. An extensive literature review performed by Shipman and colleagues in 2006 concluded that 'the net benefits of screening are not clear'[296]. Similarly, a comprehensive review performed by Shorter and colleagues in 2011 that aimed to determine the effect of different screening programmes for DDH on the incidence of late presentation of DDH concluded that 'there is insufficient evidence to give clear recommendations for practice'[297]. In short, the extensive amount of literature within the field of neonatal screening for DDH reflects the debate on the topic and the lack of consensus, and at the same time common efforts and contributions in order to improve the current situation.

4.2.4 Radiographic imaging and common measurements of acetabular dysplasia at skeletal maturity

Careful clinical examination, a detailed medical history and a standardised radiographic protocol in order to ensure high-quality pelvic radiographs are important factors in the initial diagnostic work-up of acetabular dysplasia at skeletal maturity. The clinical examination includes assessment of height, weight, leg length discrepancy and hip range of motion. For conventional radiography, four basic densities exist: fat, gas, all other soft tissues, and calcified structures. X-rays that pass through air are the least absorbed, and therefore give the blackest colour. Calcium absorbs most of the x-rays, causing bone and other calcified structures to appear white on the radiograph. In between, all soft tissues except for fat appear the same shade of grey, while fat appears slightly darker grey because it absorbs slightly less x-rays.

Since the x-rays were discovered over a century ago, the images have been produced by using a silver-based photographic emulsion. The latest decade, digital recording has become commonplace. In this method, the differential absorption of the x-ray beam is measured by a special phosphor screen and thereafter read by a laser. The image is then either written onto film or displayed on a monitor. The projection of a radiograph is described according to the path of the x-ray beam. For the radiographic investigation of dysplasia, the anteroposterior (AP) view remains the preferred view (fig. 8). As the image on an x-ray film is two-dimensional, it is often necessary and preferable to obtain at least two views, at right angles to one another, in order to gain three-dimensional information. An AP view accompanied by a frog-leg view is an often used combination.

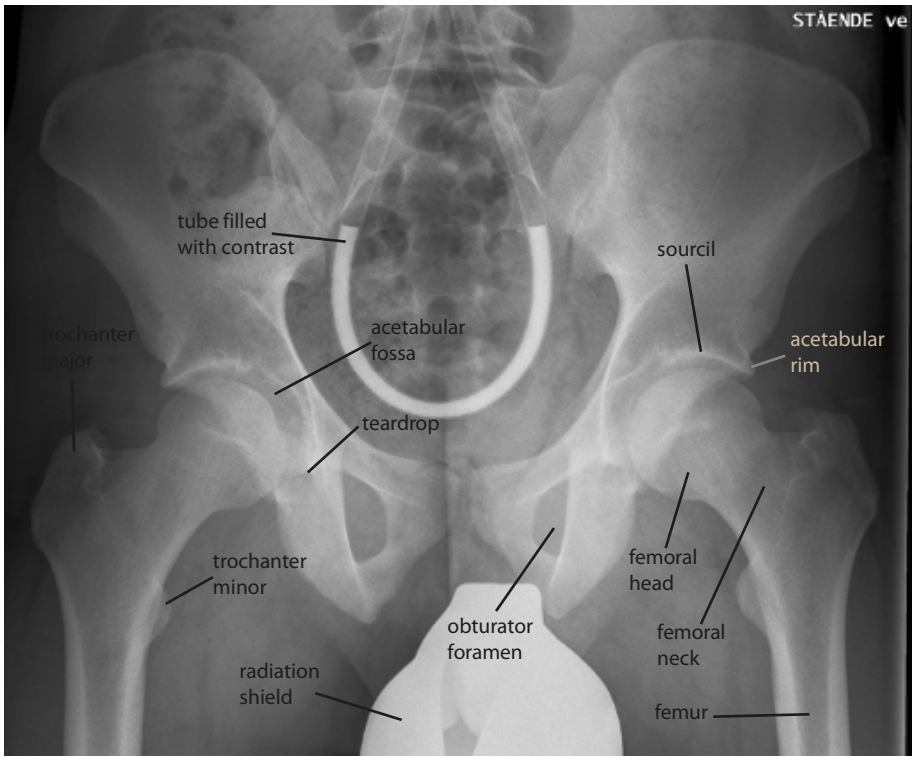


Fig. 8. AP pelvic radiograph, adult anatomy, from the '1989 Hip Project'.

Several radiographic measurements are useful in the assessment of acetabular morphology and relation between the femoral head and the acetabulum (fig. 9).

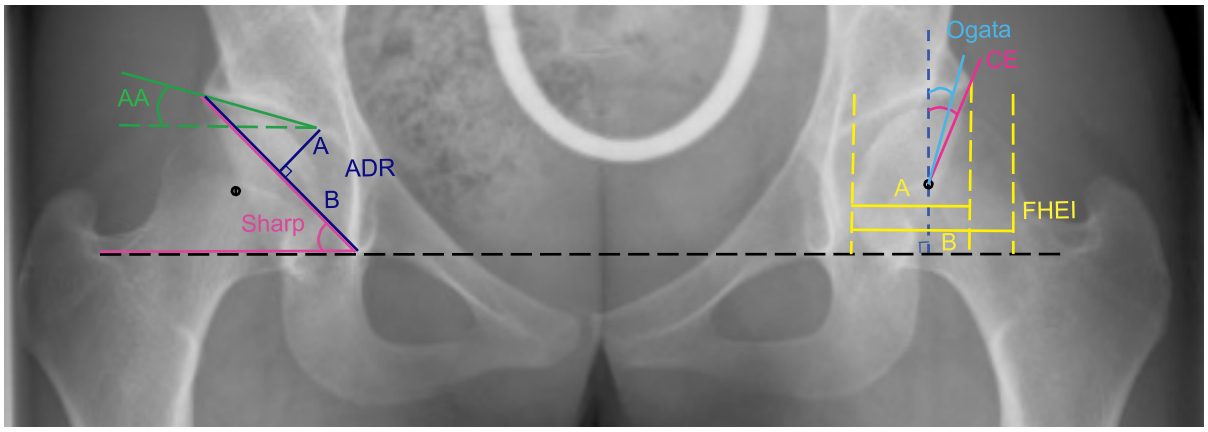


Fig. 9. Common radiographic measurements for acetabular dysplasia at skeletal maturity.

The *acetabular morphology* is commonly described by Sharp's angle[293], the acetabular roof angle of Tönnis (AA)[332,333], and the acetabular depth-width ratio (ADR)[64,313]. The *relation between the femoral head and the acetabulum* is commonly described by the center-edge (CE) angle of Wiberg[356,357], the refined CE angle of Ogata[242], and the femoral head extrusion index (FHEI)[138]. Often, a combination of these radiographic findings is recommended in order to confirm the diagnosis[248,266].

Angle measurements are commonly expressed as the mean value ± 2 standard deviations (SD) from the mean value. The resulting interval corresponds to the estimated range of values that includes 95% of the values among the relevant population[6]. Values outside these percentile-based ranges are not, however, necessarily pathological, but rather values in the top or bottom 2.5% extremities of the normal ranges. Proposed threshold or cut-off values for several of the measurements exist in the literature. Upper threshold values for Sharp's angle have been proposed as >42.3°, ≥43° or ≥45° [229,313,332], and for the AA angle as >10° or >15° [198,229,333]. The lower threshold value used for ADR is usually <250‰[64], <20° for the CE angle of Wiberg[356], and <70% or <75% for the FHEI[64,138].

In addition to the abovementioned measurements, several classification schemes have been proposed for the radiological appearance of dysplastic hips. Hips are classified according to femoral head location and acetabular depth in the Severin score[290],

according to the extent of subluxation in the Crowe classification[67], according to acetabular abnormality in the Hartofilakidis classification[137], and according to joint congruency in the Yasunaga and Okano classifications[243,366].

4.2.5 Treatment, complications and long-term outcome

For hip dysplasia, the main aim of treatment is to obtain and maintain a concentric hip reduction of the femoral head within the acetabulum, as this will increase the chances for correct development and remodelling, and thus a functionally and anatomically good outcome[351]. This aim remains the same regardless of age at diagnosis. The choice of treatment is guided by the age at diagnosis and the severity of DDH. In the neonatal period, simple clinical manipulation accompanied by a splint or harness device that secures the hip in a flexed and abducted position might be sufficient for maintaining the hip reduction. Multiple different splints, orthosis and harness devices are available. There is, however, no consensus on the optimal device and the duration of treatment, and randomised controlled trials that assess the different treatment devices and their clinical effectiveness, safety and optimal duration of treatment are lacking[250,296]. The Frejka's pillow is used in Norway, and has been evaluated as satisfying and efficient[34,323] (fig. 10).

Fig.10. A newborn baby-girl treated with Frejka's pillow

The indications for abduction treatment also differ. A recent randomised controlled trial with six years of follow-up confirmed that active clinical and sonographic surveillance for the first six weeks instead of immediate abduction treatment of newborns with mildly dysplastic but stable or unstable hips is a safe and acceptable strategy[42,279]. Early detection and non-surgical management is also an important aim of treatment. Early detection improves outcome[82]. The success rate of simple, conservative treatment is significantly reduced after seven weeks of age[14,341]. Early detection and treatment cannot, however, entirely prevent the need for subsequent surgery. Patients who are not managed successfully with an abduction splint or harness device typically undergo surgical treatment, and up to 5% of all children who have undergone abduction treatment will eventually be in need of surgery[74,112,191,343]. In addition, severe cases of irreducible dislocations at birth might require closed or open reduction.

Late detected cases (>1 month of age) are often treated with an age-adapted orthosis, worn either all day or only at night. In cases of additional pronounced limited hip abduction, traction treatment in order to facilitate a closed reduction in general anaesthesia followed by cast treatment, might be required. Open reduction in general anaesthesia might become necessary if the hip cannot be reduced during an attempt of closed reduction. Surgical treatments include closed (cast, traction and adductor tenotomy) or open reductions of the hip as well as femoral or acetabular osteotomies. Insufficient acetabular coverage can be corrected by acetabular osteotomies. The two most commonly performed pelvic osteotomies during childhood are the Salter osteotomy and the Pemberton acetabuloplasty[110,286]. The periacetabular osteotomy (PAO) is performed later in childhood and adolescence at some centres, although this method and its indications are debated[102,301]. All children who have undergone surgical treatment should have regular clinical and radiographic follow-ups during infancy.

Normal development and growth of the hip joint remains the main goal of treatment. This can however be disturbed by complications related to surgical or non-surgical

treatment during childhood. This disturbance of growth in the proximal part of the femur is defined radiologically as an avascular necrosis (AVN) of the femoral head, which can be an iatrogenic complication of abduction splints or surgical treatment[162,351]. It can occur in hips both with and without DDH, and might lead to premature osteoarthritis[63,115,250,296]. AVN can be scored radiographically according to Kalamchi and McEwen's often used classification, which assesses the damage to the physis and the ossified nucleus[162]. Reported rates of AVN vary substantially, of around 1-4% of all treated children, and are influenced by type of treatment and age at treatment[179,194,250,296]. Surgery is associated with higher rates of AVN. Other reported adverse consequences after abduction treatment include pressure sores, femoral nerve palsy, epiphysitis, inferior dislocation of the hip, and parental anxiety[74,250,352].

Long-term outcomes of treated DDH depend upon age at diagnosis, severity and treatment and can be assessed in different ways. The long-term outcomes for abduction treatment have not yet been satisfactory assessed in a randomised controlled trial. Radiographic appearance of acetabular dysplasia and AVN in childhood and adulthood, and rates of surgery needed after abduction treatment are outcome variables that are difficult to interpret when no randomised control group exists for comparison. The long-term outcome of DDH can also be assessed by its contribution to the need of total hip replacement (THR), in particular in young adults. A study from the Norwegian Arthroplasty Register showed that around one quarter of all THR were due to hip dysplasia in patients below 40 years of age[87]. In another study from the same register, neonatal hip instability was found to increase the risk for early THR, in particular in female patients[88].

4.3 Femoroacetabular Impingement (FAI) in young adults

4.3.1 General aspects of FAI

Femoroacetabular impingement (FAI) is increasingly recognised as a pathomechanical process within the hip joint that can lead to hip pain and early degenerative change in young adults[10,24,105,145,320]. The diagnosis should be considered in patients with a history of long-standing hip pain, reduced hip motion, particularly internal rotation and flexion, and a positive test for anterior impingement[44,89,104,105,210]. This clinical concept describes an abnormal relationship between the proximal femur on one side, and the acetabulum on the other side[83,105,145,237,273,302]. Although several of the pathomechanical mechanisms associated with FAI were mentioned several decades ago in the literature, FAI is a relatively new concept. Two main subtypes of FAI are recognised, the cam-type and the pincer-type, with the pathoanatomical mechanism located mainly on the femoral and acetabular side, respectively (fig. 11).

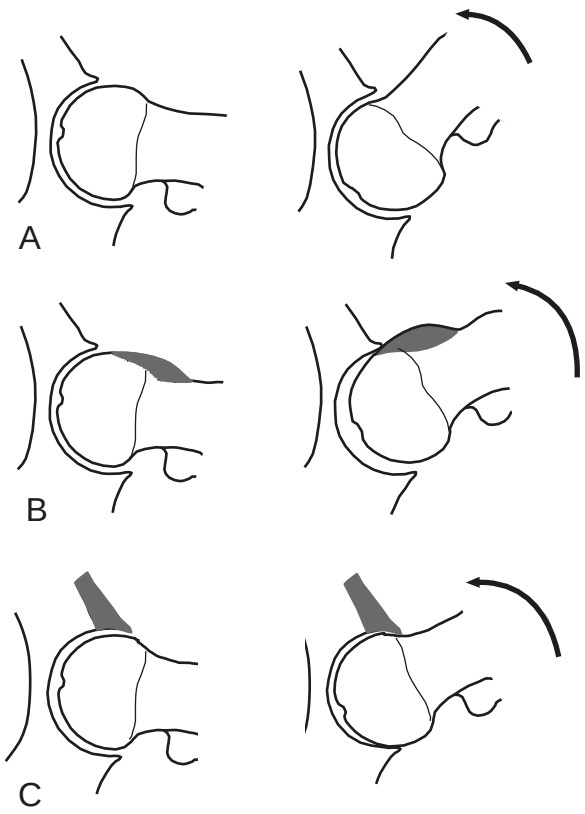


Fig. 11. A: normal anatomy of the hip joint (left) allows sufficient space for the femoral head to rotate properly in the acetabulum during movement (right). In cam-type (B) and pincer-type (C) impingement, abnormal contact between the femoral head-neck junction and the acetabular rim causes reduced clearance of the hip joint and disturbs adequate movement, in particular flexion and internal rotation

Either a prominent femoral head-neck junction (cam-type FAI) or a too prominent lateral acetabular rim (pincer-type FAI) will cause repeated squeezing or impinging of the lateral parts of the labrum, the sensible layer lining the acetabular cup. This pathomechanical process is accentuated during forceful movements, as seen in e.g. sport- or job-related activities. Repetitive microtrauma in an impinging hip will eventually lead to degeneration and tearing of the acetabular labrum and adjacent articular cartilage, which again will lead to early degenerative change and osteoarthritis of the hip joint[105,145]. The patterns of damage in the cam- and pincer-type impingement differ, and need separate pathomechanical explanations. The two sub-types are often reported as co-existing or mixed, although this has been questioned[58].

Pathogenesis and aetiology

The anatomy of the normal hip joint allows for a wide range of hip motion. In cam- or pincer-type FAI, the respective anatomical abnormalities cause reduced clearance of the hip joint[322]. Primary morphological changes of the proximal femur and/or acetabulum are thought to be the most common reason, but several other pathological mechanisms also contribute to FAI, as described below. In cam-type FAI, the femoral abnormalities are characterised by a decreased or absent offset of the femoral head-neck junction (fig. 11B). The main mechanism of pathology is an aspherical head that cannot rotate properly within the acetabulum without causing damage to the labrum. This corresponds to a ‘cam’, i.e. an eccentric part that is added to a rotating service[23]. This asphericity can be seen as a reduced or flattened anterolateral waisting of the femoral head-neck junction, sometimes accentuated as a focal prominence or convex bump of the junction, extending toward the femoral head[302]. During hip flexion and internal rotation, the cam part will slide into the anterosuperior part of the acetabulum and affect the labrum by shear forces and compression. The labrum will be pushed laterally and separated from the acetabular cartilage which will be pushed inwards[23]. Several pathological mechanisms have been proposed as underlying causes to cam-type FAI. Structural abnormalities at the head-neck junction, including the pistol grip

deformity, the tilt deformity, and also femoral anteversion were described several decades ago, and initially proposed by several authors as idiopathic osteoarthritis (OA) of the hip joint[131,172,227,306,311,335]. This idea has been taken much further the last decade[1,17,23,104,105,118,135,150,202,322,346], as described in section 4.4. An anatomical deformity following slipped capital femoral epiphysis (SCFE) has been shown to contribute to cam-type FAI and early degenerative change[95,96,114,202,267], and to be associated with a poorer radiological and clinical long-term outcome[354]. Also Perthes' disease has been shown to cause anterior impingement of the femoral head[305]. An epiphyseal growth abnormality has been stated as an explanation to cam-type FAI[302], causing a flattened aspect of the lateral part of the femoral head. Malunited fractures of the femoral neck are also an established cause of cam-type FAI[83].

In pincer-type FAI, there is generally excessive coverage of the acetabulum (fig. 11C). Linear impact between a global (often referred to as coxa profunda or protrusio) or focal (due to acetabular retroversion) overcoverage is believed to eventually damage the acetabulum and the labrum[105,205,273,302]. Acetabular retroversion implies a posteriorly oriented acetabulum, in which the edge of the anterior acetabular roof lies laterally to the posterior edge[273]. Acetabular retroversion can also occur as an iatrogenic complication after over-correction of initial dysplasia[301]. The cartilage damage is typically located circumferentially, affecting only a narrow strip. The labral damage may be accompanied by ossification of the acetabular rim and ganglion formation, which both will accentuate the pincer-mechanism, and further worsen the overcoverage[23]. A contre-coup lesion associated with pincer-type FAI has also been described, as a chondral injury of the femoral head due to persistent abutment against the posteroinferior acetabulum.

Several risk factors in addition to the anatomical factors mentioned above have been proposed to contribute to the development of FAI. Increased BMI, age, heavy workload and certain type of sport activities have all been suggested[166,257,298]. Also genetic factors have been proposed in the aetiology of FAI in a sibling study[260], and evolutionary aspects of FAI development have been explored[141].

Epidemiology

At the initiation of this thesis, epidemiological aspects of FAI still remained quite unexplored, with a prevalence of FAI as a clinical diagnosis in a healthy young population initially estimated at 10-15% [203]. Cam-type FAI is more frequently seen in young athletic males, while pincer-type FAI is more frequently seen in middle-aged women [24,105]. Gosvig and colleagues reported at prevalences of 17% in males and 4% in females for the cam-deformity, as assessed by the alpha angle and the triangular index on the AP view from a general adult Danish population of 1184 males and 2018 females, aged 22-93 years[117].

4.3.2 Clinical assessment

The diagnosis of FAI should be suspected in patients with a history of hip and/or groin discomfort or pain, and reduced hip motion on clinical examination. In particular, decreased hip flexion and internal rotation are associated with FAI[105,145,364]. The pain in FAI is typically located in the groin (83%), and mean time from symptom onset to definitive diagnosis has been shown to be 3.1 years[55]. The pain is often activity-dependent and related to sports such as soccer, football, ice-hockey and kick-boxing, which all require pronounced hip flexion[55,231,257]. In patients with labral damage or a so-called cartilaginous flap, clicks or blocking of the hip may occur. The pain in FAI-patients can be reproduced by a positive clinical test for anterior impingement[172,210] (fig. 12).

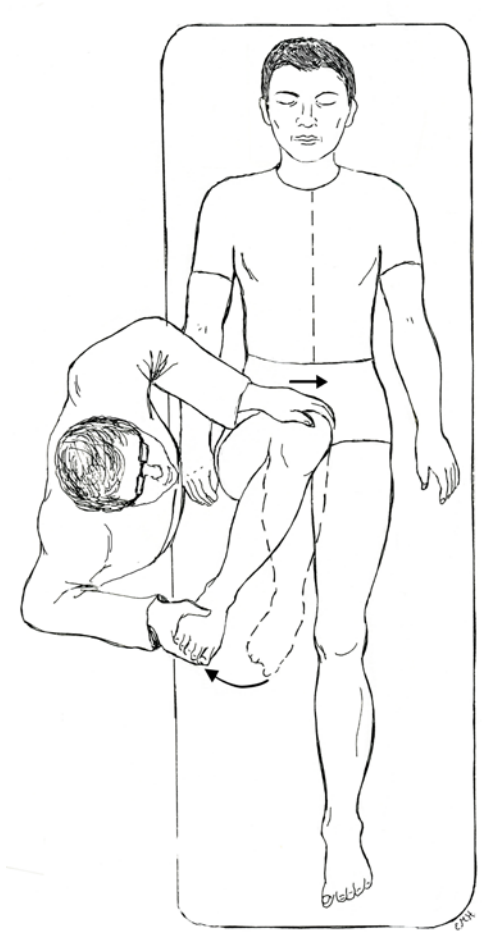


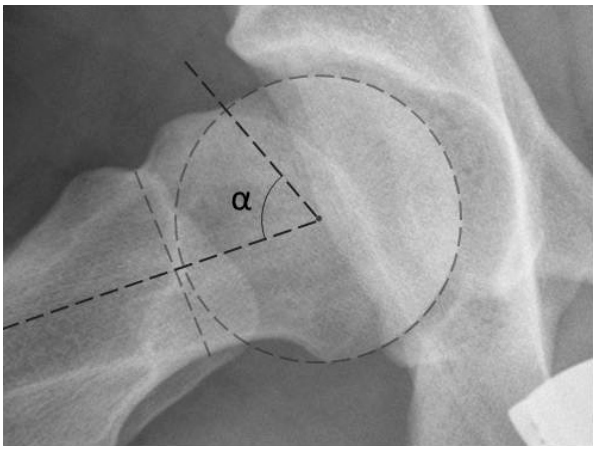
Fig. 12 Test for anterior impingement

This combined manoeuvre consists of 90° passive flexion of the hip, followed by forced adduction and internal rotation. Other clinical tests have also been described, e.g. the FABER test (pain/decreased range of motion with Flexion and ABduction-External Rotation)[216]. The tests alone often have a low diagnostic accuracy[197,215,235,329], and radiographic findings associated with FAI are needed to confirm the diagnosis[320].

4.3.3 Radiological assessment

The role of imaging in FAI is to make a radiological diagnosis or to confirm a clinical diagnosis. All osseous abnormalities of the femoral head-neck junction and the acetabular rim need to be thoroughly localised and described. In addition, signs of hip dysplasia, stress fractures, avascular necrosis, fibrocystic changes and signs of early degenerative change should be documented. The radiological work-up starts with plain radiographs, usually including an AP view and a lateral view. A standardised protocol with particular care in regard to tilting and rotation is paramount in the assessment of FAI[303,320]. The AP view can be obtained in the supine position, but many authors advocate the standing, weight-bearing position as this visualise the hip joint in the physiological position[71,106,146,318,338]. Several lateral views have been proposed[53,220]. The Dunn view, the axial cross-table view and the frog-leg views are commonly used[21,56,105,220]. Radiographic findings associated with cam-type FAI include osseous abnormalities at the head-neck junction, seen as a reduced waisting of the junction, a typical pistol-grip deformity, a focal bump or an aspherical and laterally flattened femoral head[105,145,302,311]. The cam-type deformity can be described qualitatively by the presence of the mentioned findings, or quantitatively by the alpha angle[237] (fig. 13), or alternatively by the triangular index[116] (TI), the femoral head-neck offset[83] or the femoral head-neck offset ratio[255]. The alpha angle has become the most used measurement to depict the cam-deformity. It was initially proposed by Nötzli and colleagues on MRI scans in 2002 with a proposed pathological cut-off value of 50°[237]. The alpha angle was thereafter adapted to radiographs, first lateral and later AP views[56,116].

Fig. 13. Alpha angle in the assessment of the cam-deformity on the frog-leg view



For pincer-type FAI, radiographic findings associated with acetabular retroversion include the posterior wall sign and the cross-over sign (also called 'figure of 8' sign), as first described by Reynolds and co-workers in 1999[105,151,249,273,300]. Some authors also advocate the parallel use of a 'prominence of the ischial spine sign' (PRISS)[163]. The acetabular overcoverage can be described either subjectively by gross visual inspection, or quantified by using the CE angle of Wiberg. These radiographic cam- and pincer type findings are described in detail in section 6.2.5.

So-called impingement pits, also called herniation pits, are *fibrocystic changes (FCC) at the femoral head-neck junction*. They are visible as small areas of cystic radiolucency, surrounded by a narrow margin of sclerotic bone[201]. These pits were first called herniation pits, and they were initially reported as an incidental finding in 5-10% of a healthy population[258]. Leunig and co-workers reported a prevalence of 33% of fibrocystic changes at the anterosuperior femoral neck in patients with underlying FAI, and suggested that they were associated and possibly in a causal relationship with FAI[201]. In contrast, another study on cam-type patients found such cysts in only 5% of the patients[168].

Both Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) are used in the imaging of FAI. MRI and magnetic resonance arthrography (MRA) are the modalities of choice when assessing the labrum and the cartilage of the hip joint, and labral avulsions and chondral injuries can be adequately visualised[145,206].

4.3.4 Treatment, complications and long-term outcome

Surgical treatment of FAI has become more common the last decade. The strength of clinical evidence to support this surgery is somewhat controversial[57]. The main aims of surgery are treatment of pain and increased hip range of motion. In addition, treatment of chondro-labral lesions and delayed onset of early degenerative change and osteoarthritis are important goals. Surgical options include arthroscopic surgery, open surgery with femoral head dislocation, or a combination of these two methods[24,89,101,187,301]. For either method, both the damage to the labrum and the underlying cause must be addressed.

The open approach is considered as the 'gold standard', with full visibility of both the acetabulum and the femoral head, and with few complications[101,188,299]. The patient is placed in the lateral position. A lateral or posterior approach is used. A trochanteric osteotomy is usually performed to improve the exposure of the joint. The main blood supply to the femoral head, the medial femoral circumflex artery, must be protected. The femoral head is then dislocated to provide full visibility. Surgical treatment of a cam-type deformity involves removal of the aspherical parts of the femoral head (excision femoroplasty) in order to recreate the concave contour of the femoral neck. Retroversion, as seen in the pincer-type FAI, can be treated with resection of the excessive anterior acetabular rim, with debridement of the damaged parts of the labrum and the cartilage. Alternatively, a reorientation of the acetabulum can be achieved by performing a periacetabular osteotomy (PAO), as advocated by some centres[301]. If a labral tear exists, it should be treated with repair or partial resection as appropriate[65]. The arthroscopic method is increasingly popular, as it requires less time and resources, and has shorter postoperative recovery periods. It can include examination of both the peripheral and central compartments of the hip joint.

At present, there is a marked paucity of comparative literature regarding outcome after surgical treatment, and there is no prospective long-term data available for surgery vs. conservative treatment. Multi-centre clinical research initiatives are encouraged in order to reach consensus on optimal treatment outcomes[57]. Small

longitudinal studies have reported improved function and quality of life[24,256]. The need for hip replacement might be delayed by using preserving surgical methods, but further studies are awaited. Poorer outcomes are associated with osteoarthritis of the hip joint. Clohisy and co-workers performed a comprehensive review in 2010, where 11 studies with clinical outcome data and minimum two years follow-up were analysed. They found that all studies reported reduced pain and improvement in hip function over short-term follow-up, and that different surgical techniques were associated with improved function and pain relief in 68-96% of patients. Conversion to THA was reported in 0% to 26% of cases, while major complications occurred in up to 18% of the procedures[57].

The most frequent complications are minor ectopic soft tissue ossification and trochanteric non-union, nerve damage, adhesions, fracture, avascular necrosis and long-standing pain. Another important complication is the aspect of iatrogenic dysplasia after over-correction of pincer-type FAI. Non-surgical treatment for FAI includes rest, activity modification, core muscle strengthening, physical therapy and non-steroidal anti-inflammatory medications[188]. In some cases intra-articular anaesthetic injections have been proposed[171]. However, surgical treatment often becomes necessary to allow full return to activity.

4.4 Osteoarthritis

Osteoarthritis (OA) is characterised by loss of joint cartilage that leads to pain and dysfunction. It is the most frequently occurring chronic joint disease, affecting primarily hips and knees, and symptomatic OA is reported to affect almost 10% of men and almost 20% of women aged 60 years or older[360]. Proposed risk factors for OA include age, genetics, high BMI, trauma, physical workload, cellular and biomechanical processes, sporting activities and also abnormal bony morphology[132].

The aetiology of OA was initially considered as either primary, i.e. idiopathic, presumably caused by some underlying abnormality of the articular cartilage, or

secondary, caused by other conditions affecting the hip joint. However, as stated by Harris in 1986, 'either osteoarthritis of the hip does not exist at all as a primary disease entity, or if it does, it is extraordinarily rare'[131]. He linked the development of OA with resultant anatomical abnormalities due to childhood hip disease, including acetabular dysplasia, Perthes' disease and slipped capital femoral epiphysis (SCFE) amongst others. Already in 1965, Murray mentioned 'minimal anatomical variations […] regarded as being within normal limits' as a cause of what was earlier thought to be primary OA, in addition to frank acetabular dysplasia and SCFE[227]. He established that the 'tilt deformity', i.e. a flattened head-neck offset, was found much more commonly in males, and also tended to become symptomatic at an earlier age. He proposed that up to 65% of so-called idiopathic OA was due to a pre-existing asymptomatic anatomical abnormality.

Some years later, Stulberg and colleagues stated that mild acetabular dysplasia and the 'pistol-grip deformity' were important underlying contributors, each of around 40%, to what was earlier thought to be 'idiopathic' OA[311]. The 'pistol-grip deformity' was thought to result from a common degenerating pathway of both SCFE and Perthes' disease. Solomon supported these ideas[306]. This was opposed by Resnick in 1976, who proposed that the 'tilt deformity' was a bone shape pattern caused by a remodelling process in the arthritic hip joint commonly seen in patients with degenerative disease[272]. The last two decades, several contributing factors such as dislocated hips, Perthes' disease and SCFE have become commonly accepted contributors to OA[202,267,352], as well as more subtle bony abnormalities, including femoroacetabular impingement (FAI) and acetabular dysplasia[1,17,64,76,105,118,135,149,234].

Dorrell and Catterall formulated the idea of a 'torn acetabulum' in 1986[78], and Klaue and co-workers described the 'acetabular rim syndrome' in 1991[172]. This concept of labral damage has been central in the explanation of the pathway for both acetabular dysplasia and FAI eventually leading to OA. An abnormally shaped femoral head-neck junction as in cam-type FAI, excessive acetabular coverage as is pincer-type FAI, or insufficient acetabular coverage as in acetabular dysplasia are all proposed as

contributing factors to abnormal stress patterns, associated with pathophysiological mechanisms involving chondral damage and subsequent labral injury of the hip joint[205].

OA can be described by using several classification systems. Tönnis Classification of Osteoarthritis by radiographic changes[335], the Croft classification[66] and the Kellgren-Lawrence scale[169] are all commonly used to grade the severity of the disease (higher scores indicate more severe disease). Measuring the minimum joint space width (JSW) radially is a well-accepted method for quantitative assessment of OA[7,99,113,185], and ≤2 mm indicates disease.

Although OA obviously represents an important economic burden to society and also has a huge impact on the patient's quality of life, there are no methods available that can prevent this disorder or delay the progression of it. If modifiable risk factors for OA can be identified and confirmed, preventative measures might be implemented. Additional research is needed in order to confirm the proposed mechanisms and possible causal relationships for OA development.

The treatment of choice for OA patients depends upon several factors, such as severity and distribution of disease, age, and general health status. Initial treatment should always include adapted information related to physical activity and weight-loss if indicated. Pain killers and/or non-steroidal anti-inflammatory drugs (NSAIDs) might be indicated along with physical therapy. Surgical treatment is often required. A total hip replacement (THR) is offered to a small group and on strict indications. In addition to possible complications seen after many types of surgery, a revision of the prosthesis will most likely become necessary due to limited life expectancy. In Norway, all total hip arthroplasties performed since 1987, including the THR, are reported to the Norwegian Arthroplasty Register.

4.5 Research context for this thesis

This thesis builds upon the works related to a large randomised controlled trial (RCT) in our institution[281] (fig. 14). The RCT evaluated the effect of different screening strategies for DDH in newborns, and included all babies born from January 1988 through June 1990. The '1989 Bergen Birth Cohort' is a population-based sample from the RCT. This cohort, comprising all babies from the RCT born in 1989 with some exclusion criteria described in section 6.2.1, was invited to attend the follow-up study in 2007-2009; the '1989 Hip Project' (fig. 14). Only babies born during 1989 are included in the works of papers II-VI. Informed by the results of the RCT and a few other observational studies, a selective US strategy in addition to routine clinical screening was initiated in our institution in the end of 1990. All babies born at our institution from 1991 through 2006, the '1991-2006 Cohort', were subjected to general clinical screening accompanied by selective US screening for DDH for those at risk (paper I).

The work related to the '1989 Hip Project' has been undertaken at the paediatric sections of Radiology and Orthopaedic surgery, partly in collaboration with the Medical Birth Registry of Norway and the Norwegian Arthroplasty Register. Parts of the work of this thesis have also been performed in close collaboration with the MRC Centre of Epidemiology for Child Health, Institute of Child Health, UK. The work related to the '1991-2006 Cohort' has been undertaken in collaboration with the paediatric and paediatric orthopaedic surgery Departments at the Haukeland University Hospital.

Figure 14 shows the original RCT performed in 1988-90, and the follow-up study '1989 Hip Project', which included the '1989 Bergen Birth Cohort'. The selective US screening programme is also shown.

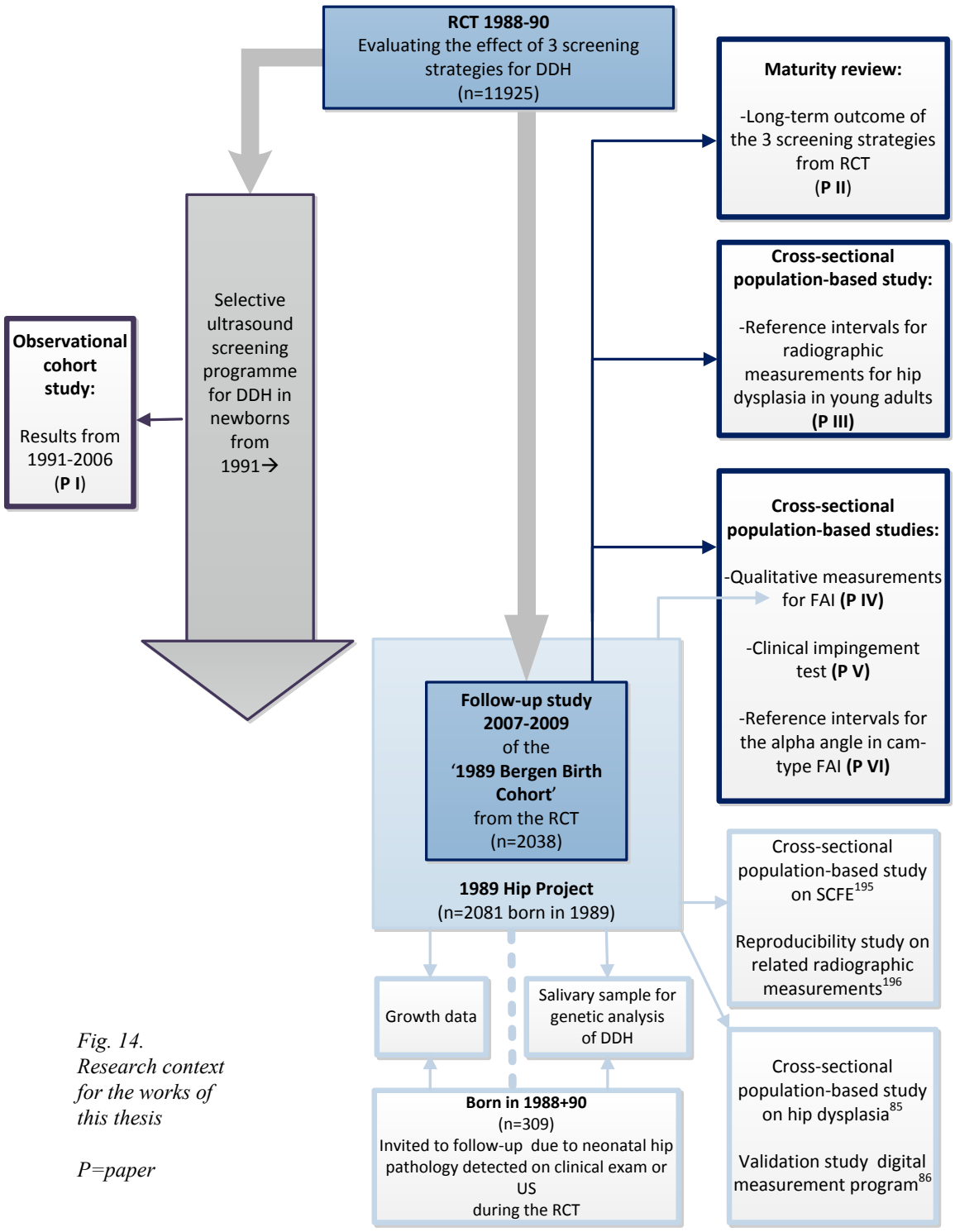


Fig. 14.
Research context for the works of this thesis

P=paper

The papers I-VI of this thesis are shown in dark blue frames. Other works and projects related to the '1989 Hip Project' are shown in light blue frames.

4.5.1 Randomised controlled trial (RCT), 1988-90

The original study base of the RCT included 11925 babies born during January 1988 through June 1990 at the maternity hospital in Bergen, Norway, after exclusion of those with birth weight < 1500 grams, with severe disease/malformations or who died within the first month of life (n=103). The babies studied were randomly assigned to universal US screening (n=3613), selective US screening (n=4388) or clinical screening alone (n=3924)[281].

Randomisation was area-based (cluster randomisation), to keep mothers separate, i.e. to avoid recall bias with respect to risk factors. The maternity unit consisted of three equally sized nursery units, separate from the delivery ward. The three units received patients in a random sequence according to available beds. One of the units (unit two) received somewhat more women recovering from caesarean section deliveries due to the availability of a few single-patient rooms, and thus a slightly higher rate of breech presentation deliveries was expected at this unit. The general screening group represented unit two and half of unit three, and the selective screening group represented the other half of unit three and unit one. Infants born when US was not available comprised the clinical screening only group and represented all three units. Unavailability occurred in periods of one to three weeks spread unsystematically throughout the year. The staff at the delivery unit did not receive any information on the ongoing trial. The mothers of the participants, and the US examiner were aware of group assignment when US was performed.

The aim of the RCT was to determine more appropriate criteria for treatment, and to determine whether the addition of a general or of a selective US screening programme resulted in a reduced prevalence of late DDH compared to clinical examination alone. In order to detect a six-fold reduction in prevalence in a group subjected to screening, the two groups would have to include about 3000 babies each (80% power, 5% significance level). The baseline demographic and clinical characteristics of each group were reported in the original paper[281]. There were no statistically significant differences in gender distribution or in the prevalence of positive Barlow/Ortolani tests between the three study groups or in the total number of infants with risk factors

between the two groups subjected to US screening. The number of infants born in the breech position and with a family history of DDH was significantly higher in the generally screened group than in the selectively screened group. In the original trial, differences in prevalence rates were tested by chi square tests. An exact test for linear trend in the prevalence of late DDH with the groups ordered according to the degree of US screening from the no screening group to the selective group and to the general screening group was used. All reported p-values were two-sided. Intention-to-treat-analysis was applied.

All newborns were assessed by means of known risk factors for DDH (breech presentation at delivery, and/or family history (≥1 first or ≥2 second grade) of DDH) and by means of clinical hip examination. In addition, at-risk infants from the selectively screened group and all infants from the universally screened group were offered a single examiner hip-US (Rosendahl's method)[280] based on Graf's coronal standard section through the mid-acetabulum[119] and separate classification of morphology and stability. The US examination was thoroughly standardised prior to the RCT. All high-risk infants with normal hips at birth had a hip-radiograph at age 4.5 months, regardless of screening group.

Indications for treatment were persistent dislocatable/dislocated hips on a repeated, single-examiner clinical examination or severe, sonographic dysplasia irrespective of clinical or sonographic stability. Hips with a mildly dysplastic morphology ($43^{\circ} \leq \alpha < 50^{\circ}$) were treated if they were also clinically or sonographically dislocatable/dislocated. Sonographically immature ($50^{\circ} \leq \alpha < 60^{\circ}$) or mildly ($43^{\circ} \leq \alpha < 50^{\circ}$) dysplastic but clinically stable hips had sonographic and clinical surveillance every fourth week until normalisation or until treatment was instigated due to lack of improvement. Moreover, all children in Norway have clinical examinations performed regularly during their first two years, as a part of the national healthy child programme, with referral to a specialist if any clinical suspicion of DDH is noted. Routines for abduction treatment included a Frejka's pillow splint from birth until around three months of age. If further treatment was necessary, an age-adapted orthosis was used. Outcome measures in the RCT were rates of 1) late detected DDH

(i.e. number of cases of subluxated/dislocated hips and/or residual dysplasia detected after the first month of age), of 2) US follow-up and of 3) abduction treatment.

In brief, the RCT indicated lower rates of late presenting subluxated or dislocated DDH in the universally and selectively screened groups as compared to the group receiving clinical examination alone (0.3 and 0.7 vs. 1.3 per 1000) (p=.11, test for trend). Treatment rates were, however, higher for the universally screened group as compared to the selectively or 'no US' screened groups; 3.4% vs. 2.0 and 1.8 (p< .001). When compared to the pre-study period, the rates of late cases were significantly lower, e.g. 0.3 and 0.7 per 1000 vs. 2.6 per 1000 live newborns. There were nine girls detected as late cases (six subluxated, three dislocated hips) among the original 11925 participants. All received traction followed by cast and/or orthotic treatment: the three dislocated hips also had an adductor tenotomy or an open reduction. None of the three dislocated cases had had US performed: two came from the 'no US' screening group, and one had been classified low-risk from the selectively screened group. Of the six cases with subluxation, five were low-risk cases from the 'no US' (three) and the selectively screened (two) group, and thus did not have a newborn hip US. The final case was low-risk but in the universally screened group. There were no signs of AVN at the conclusion of the original RCT at a minimum 27 months of age.

4.5.2 The '1989 Hip project' and the '1989 Bergen Birth Cohort'

The '1989 Hip project' was initiated in 2006, as a collaboration project between the sections of paediatric radiology and paediatric orthopaedic surgery. Of 4006 young adults born in 1989 and invited to participate in the follow-up study of the RCT, 2081 attended (51.9%). In addition, 503 young adults born in 1988 and 1990 were invited to follow-up, due to neonatal hip pathology on clinical exam or US detected during the RCT. Of these, 309 young adults attended (fig. 14), but are not included in the works of this thesis. The follow-up consultations were carried out from February 2007 until March 2009. As described in detail in 6.2.1, the establishment of the '1989

Bergen Birth Cohort' based on the original RCT involved slightly different inclusion and exclusion criteria, resulting in 2038 subjects from the '1989 Bergen Birth Cohort' attending the follow-up (all these 2038 are comprised within the 2081 participants in the '1989 Hip project') (fig. 14). The follow-up consultation included questionnaires, two pelvic radiographs and a clinical examination. An optional salivary sample for later DDH-related genetic testing was also collected. From September 2007, all participants were asked to give the salivary sample at the end of the consultation. 2 ml of saliva was collected using Oragene DNA self-collection kits (DNA Genotec Inc., Ontario, Canada). Participants that attended between February and September 2007 were asked to return salivary DNA by post in the appropriate kit. The samples were forwarded to Centre for Integrated Genomic Medical Research (CIGMR), Manchester University, UK (prof. WER Ollier) for extraction, management and storage in a newly established Bio-bank. In parallel with the follow-up, available growth data from the community health care centres in Bergen and suburbs corresponding to the catchment area of the hospital were collected retrospectively for adolescents who initially took part in the RCT.

Data from this follow-up study was used to assess the long-term outcome of different screening strategies (paper II), and to assess radiological, clinical and epidemiological characteristics related to hip dysplasia and FAI in healthy young adults (papers III-VI). Other works which are not part of this thesis also originate from the '1989 Hip Project', focusing on the prevalence of hip dysplasia in young adults and the validation of the digital measurement program used, and the prevalence of slipped capital femoral epiphysis (SCFE) with reproducibility of related measurements (fig. 14)[85,86,195,196].

The literature searches performed in relation to the works of this thesis have been performed mainly in the PubMed database, supplied by searches in the Embase database. Continuous searches have been performed during the whole research period, until May 2013, and articles published after the start of the works of this thesis have been included in the background section when necessary for completeness.

5. Aims of the studies

The overall aim of this thesis was to investigate radiological, clinical and epidemiological aspects related to hip dysplasia and femoroacetabular impingement (FAI), based on two population-based cohorts of newborns and young adults.

The specific aims for papers I-VI:

I: To report on the results in terms of management and late detected cases, from the first 16 years of a selective ultrasound screening programme for developmental dysplasia of the hip (DDH) in newborns.

II: To report on differences in radiological long-term outcome at skeletal maturity for the three newborn screening strategies for DDH evaluated in the original RCT, in terms of radiographic markers of acetabular dysplasia and early degenerative change and avascular necrosis (AVN) secondary to treatment.

III: To establish gender-specific reference intervals for common radiographic measurements for acetabular dysplasia and degenerative change of the hip joint in young adults.

IV: To report on the prevalence of qualitative radiographic findings thought to be associated with cam-type and pincer-type FAI, and the associations among them, and to report on inter-and intraobserver variability of these qualitative interpretations.

V: To determine the prevalence of a positive clinical test for FAI in a healthy young adult population, and to examine possible associations of a positive test with clinical and radiographic findings.

VI: To establish gender-specific reference intervals for the alpha angle on the frog-leg and AP view in young adults, and to examine the associations between this quantitative measurement and other qualitative findings for cam-type FAI.

6. Patients and Methods

6.1 The ‘1991-2006 Cohort’ (Paper I)

6.1.1 Study design, protocol, data and statistical analysis

This population-based observational study reports on prospectively collected data from a selective US screening programme for DDH in newborns. It adheres to the STROBE guidelines for observational studies[342]. It was registered retrospectively at www.clinicaltrials.gov (NCT01866527). All infants born at the maternity unit at Haukeland University Hospital from January 1991 through December 2006 were included in the study cohort (n=81564). Children with DDH due to neuromuscular syndromes were excluded. Minimum observation time was 5.5 years. All newborns had a routine clinical hip examination at birth, including the Barlow/Ortolani tests for hip instability. Risk factors for DDH (breech presentation, a positive family history of ≥1 first grade or ≥2 second grade relatives, or congenital foot deformities) and positive findings on clinical examination were recorded in a specially designed report form which served as a referral to hip US (appendix 1**)**. All babies who were referred to a newborn hip US were included in the ‘at-risk’-group for DDH (n=11539) (fig. 15). For 349 of the filed report forms, the infant could not be identified, and the information reported was also very limited, without any additional forms or reports from further treatment or follow-up. These 349 infants, presumably with hips which did not require treatment as this would have been noted on the initial form, were omitted from further analyses on the at-risk group regarding rates of treatment, follow-up, late cases and surgery, but remained within the main cohort. Thus, 11190 infants were included in the at-risk group for DDH. The paediatric, paediatric orthopaedic and paediatric radiology departments managed the follow-up and treatment of DDH according to a predefined protocol which remained unchanged during the whole period (appendix 2). The protocol, including detailed information

regarding the clinical and US examinations, and the management routines, are described in paper I. Severe sonographic dysplasia and/or dislocatable/dislocated hips were treated with abduction splints from birth. Mild dysplasia and/or pathological instability, i.e. subluxatable but not dislocatable/dislocated hips were followed clinically and sonographically until spontaneous resolution, or until treatment was considered necessary (i.e. watchful waiting). Late detected cases of DDH (after 1 month) were documented as cases with subluxated/dislocated hips. Isolated cases of late residual acetabular dysplasia were also documented. The rate of first surgical treatment (closed or open reduction, or open surgery) included all subjects who received the first surgical treatment between birth and 5 years of age, as 1) initial treatment from birth, 2) after failure of early abduction treatment, or 3) after late detection.

Data collection and analysis

All data on risk factors, on results of clinical, US and radiographic examinations and on treatment were collected prospectively and registered in the DDH-screening report form. Data on late referrals was also collected prospectively. All data was entered in a Microsoft Access 2010 database by one of four persons during 2005-2011. Total numbers and gender distribution for the low-risk babies were obtained from the hospital database. In order to ensure that all babies (including low-risk babies) born at our hospital who had received abduction treatment and/or surgery were included in the dataset, additional searches based on all the DDH-related diagnoses, on surgical procedures for treatment (traction, plaster cast, open and closed reductions, and osteotomies) and on AVN diagnosis were performed retrospectively within the database of the university hospital (including Kysthospitalet in Hagevik) during August-October 2012. Additional information was retrieved from the clinical patient records when needed. Data were summarised as rates per 100 and per 1000 with corresponding 95% confidence intervals (CI) as appropriate[6].

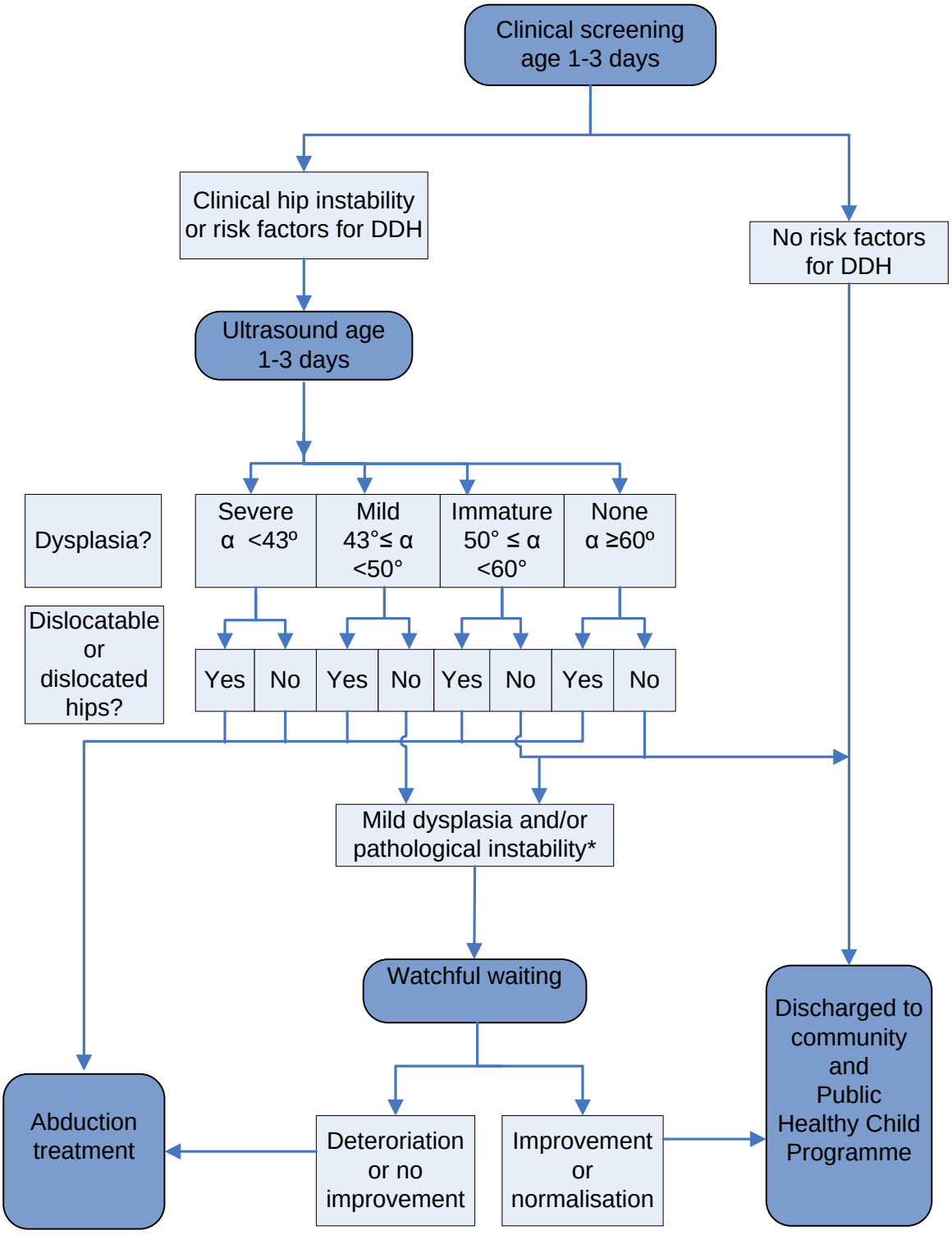


Fig. 15. Selective US screening programme for DDH in newborns

**pathological instability= subluxatable but not dislocatable/dislocated hips*

6.2 The ‘1989 Bergen Birth Cohort’ (Papers II-VI)

6.2.1 Study designs and populations

The ‘1989 Hip project’ was initiated in 2006. According to the database of our hospital, 5068 babies were born during 1989. Of these, 1062 were excluded before invitation to the follow-up study, due to emigration abroad (n=256), death (n=61) or address outside a predefined area including most of the municipalities within the catchment area of the Haukeland University hospital at time of follow-up (n=745). By consequence a total of 4006 subjects were invited, by postal letter (appendix 3). One reminder was sent to all those who did not respond to the initial invitation. Of the 4006 invited, 2081 attended (51.9%) and consented to participate (appendix 4). These numbers do not, however, take into account whether the mother was resident of the hospital’s catchment area and thus expected to give birth at the hospital, or whether she resided outside and had a specific reason for giving birth at the hospital, as this information was not available at the time of invitation to follow-up. After ended data-collection, our files were linked to pre-specified data from the Medical Birth Registry of Norway (MBRN), and thereafter de-identified. The data from MBRN included all babies born at Haukeland Hospital during the RCT period, from January 1988 through June 1990. Of in total 12028 babies born in the given period, 103 were not among the 11925 babies included in the RCT due to low birth weight, severe malformations or death within the first month of life. The dataset from MBRN also included information on the municipalities of the mothers at time of child-birth. This allowed for further adjustments related to the ‘1989 Bergen Birth Cohort’, as it was decided that only babies whose mother were resident in the catchment area at time of child-birth should be included. The study base of the ‘1989 Bergen Birth Cohort’ was thus defined as babies born during 1989 and included in the original RCT, and whose mother resided within the catchment area of the Haukeland University Hospital at time of child-birth (n=4703) (fig. 16). Of the 1062 subjects not initially invited to the ‘1989 Hip project’, 294 also had a mother residing outside the catchment area and had thus already been excluded from the study base of the ‘1989 Bergen Birth Cohort’.

The remaining 768 subjects who had not been invited to the follow-up are shown in the flowchart. This resulted in 3935 subjects from the 1989 BBC eligible for invitation to the follow-up study. Of these, 2038 subjects attended follow-up (51.9%), predominantly ethnic Norwegians. In short, 43 of the 2081 participants who attended the follow-up study did not meet the initial criteria for inclusion in the '1989 Bergen Birth Cohort'. Data from the community health care centres in Bergen and suburbs, corresponding to the catchment area of the hospital, were collected retrospectively. Children are routinely measured (weight, height) at seven years (± three months), and the results are recorded on paper files. Thus, data on sex, age at time of follow-up and height/weight at age seven years were collected for all those born in 1989 within the catchment area, and whose data were available. These data, together with the birth weight obtained from the Medical Birth Registry, were used for comparisons of baseline characteristics between the groups of attendance (n=2038) and non-attendance (n=1897) of the '1989 Bergen Birth Cohort', as shown in paper III (table 1). Of the 2038 participants in the '1989 Bergen Birth Cohort', 27 of these were excluded for further analyses: 19 radiographs were of sub-optimal quality due to an excessive rotation of the pelvis, as assessed by the foramen obturator index (FOI) outside 0.6 -1.8[334]; and 8 radiographs were missing due to uncertain pregnancy status (n=6), one radiograph not taken and one radiograph with severe pathology due to cerebral palsy. Thus 2011 participants were included for analysis; 841 males (42.0%), 1170 females (age range 17.2 -20.1 years, mean 18.6 (SD 0.6), for both males and females).

Paper II is a maturity review of a population-based sample drawn from the initial RCT which is described in detail in 4.5.1. Paper II adheres to the CONSORT guidelines for reporting of RCTs, and was registered at www.clinicaltrials.gov (NCT01818934). The original RCT study included 11925 babies born during January 1988 to June 1990 at the maternity hospital in Bergen, Norway. The babies studied were randomly assigned to universal US screening (n=3613), selective US screening (n=4388) or clinical screening alone (n=3924). Of the 2038 participants at follow-up, 2011 were included after additional exclusion criteria were applied (fig. 16). This

population-based sample of 2011 participants represented equal proportions of the three original RCT screening groups: 551/3613 (15.3%), 665/4388 (15.2%) and 795/3924 (20.3%) subjects originated from the initial universal US, selective US and clinical only screening groups respectively. At the maturity review, radiological outcome measures associated with acetabular dysplasia and early degenerative change were compared for the three groups.

Table 2: Papers II-VI, based on data from the '1989 Bergen Birth Cohort'.

Paper	Study design	Partici-pants	Questionnaires	Clinical data	Radiographic data
II	Follow-up of RCT	2038	Hip discomfort, physical activity	hip ROM, BMI	Measurements for dysplasia and degenerative change
III	Cross-sectional	2038	-	-	Measurements for dysplasia and degenerative change
IV	Cross-sectional	2081	-	-	Qualitative cam- and pincer-type findings
V	Cross-sectional	1170	Hip discomfort, physical activity	FAI test, hip ROM	Qualitative and quantitative cam and pincer findings, JSW
VI	Cross-sectional	2038	-	-	Alpha angle in cam-type FAI, qualitative cam-type findings

The papers III-VI are population-based studies with a cross-sectional design (table 2). Paper IV was finalised before the '1989 Bergen Birth Cohort' was established, and thus included all the 2081 participants that met for follow-up within the '1989 Hip Project'. Of these, 21 were excluded for further analyses due to uncertain pregnancy status, missing radiographs or unacceptable FOI (only 12 FOI were excluded in paper IV as compared to 19 in paper II, III and VI, as also radiographs with FOI=0.6 or FOI=1.8 were accepted in paper IV). In paper V, only about half of the '1989 Bergen Birth Cohort' attended the study on the impingement test (n=1170) (fig. 16). This was because the clinical test for anterior femoroacetabular impingement was not included before in January 2008. In paper VI, a total of 2005 participants are included, because six of the frog-leg lateral radiographs had been destroyed during storage in the digital IMPAX, and therefore could not be measured (fig. 16).

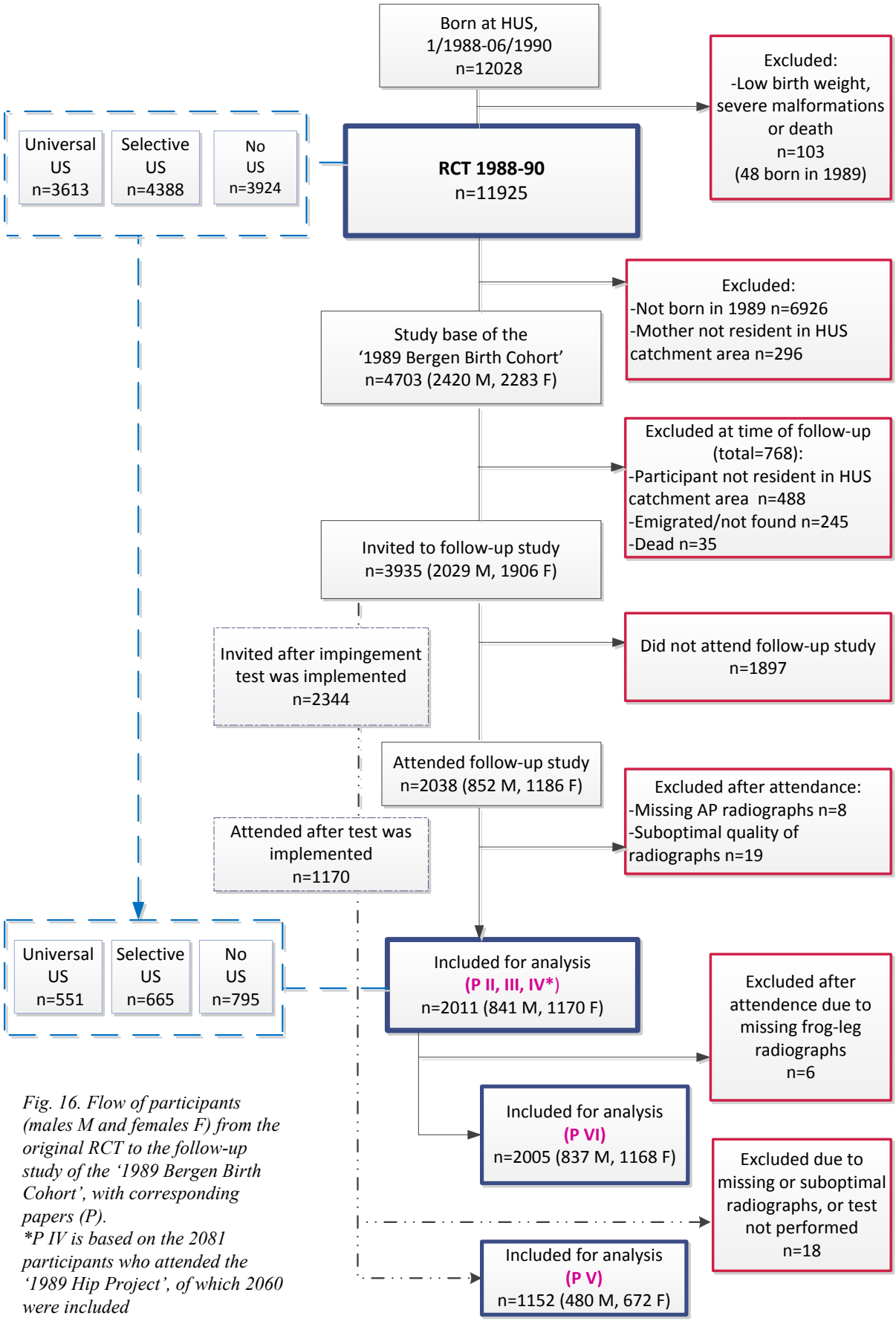


Fig. 16. Flow of participants (males M and females F) from the original RCT to the follow-up study of the '1989 Bergen Birth Cohort', with corresponding papers (P).
**P IV is based on the 2081 participants who attended the '1989 Hip Project', of which 2060 were included*

6.2.2 Questionnaires

The invitation letter sent by post also included a questionnaire with questions on hip-related problems in childhood and hip problems in parents and siblings (appendix 5). Upon arrival at the follow-up consultation, a three-part computer-based questionnaire was completed (appendix 6): 1) Standardised questions on quality of life (EuroQol EQ-5D)[326] and on hip problems (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[25]; 2) Questions addressing physical exercise habits and; 3) Questions regarding pain and discomfort from the hips, back, and neck: specifically including discomfort from either hip during the past 3 months. The EQ-5D score (www.euroqol.org) describes five dimensions of life quality: mobility, self-care/personal hygiene, usual activity, pain/discomfort, and anxiety/depression. Each question has three levels: no problem, some problems and severe problems. The results of each dimension contribute to a common score, or index, where 0= death and 100= "best imaginable health state". Each of the five categories has an individual weighting with pain and mobility being the highest weighted. The WOMAC Index (www.womac.org) comprises 24 questions constructed for patients with hip and knee osteoarthritis. Each question has the same five levels: none, mild, moderate, severe, and extreme, corresponding to a score of 0-4, where 4 indicate the worst situation. The questions are related three subscales: pain (5 questions, max score 20), joint stiffness (2 questions, max score 8), and disability (17 questions, max score 68). The total WOMAC score as used is in this project was created by summing the items for all three subscales, with a max score of 96.

The participants were asked the following questions regarding each hip separately: 'Have you experienced hip discomfort from the hip the past 3 months?', and: 'Outside school hours, how many hours do you usually exercise in your free time —so much that you get out of breath or sweat?' This last question originates from the WHO HBSC (Health Behaviour in School Children) physical activity questionnaire[39] and had six response alternatives: none, about half an hour a week, about one hour a week, about 2 to 3 hours a week, about 4 to 6 hours a week, or 7 hours per week or more.

6.2.3 Clinical examination

One experienced senior orthopaedic surgeon (LBE) standardised the clinical examination and trained the four less-experienced physicians (LBL, IØE, TGL, AMH). They were all blinded to the results of the questionnaires and the radiographs. The standard protocol for clinical examination included assessment of height, weight, hip range of motion (ROM), anterior impingement test, leg length discrepancy and joint hypermobility (appendix 7). Flexion, abduction, and adduction were measured with the patient supine, whereas extension and internal and external rotations were measured with the patient prone and the knee flexed 90°. The joint hypermobility was assessed by the Beighton score[47]. The pain-provocation test for anterior impingement was performed with the patient supine, and a combined manoeuvre, consisting of 90° passive flexion of the hip, followed by forced adduction and internal rotation, was used (shown in fig. 12). The score was 0 (no pain provoked) or 1 (definite pain provoked when asked).

6.2.4 Radiographic protocol

All radiographs were recorded in the paediatric unit of the Radiology department, using a low-dose digital radiography technique (Philips Medical Systems, Digital Diagnost System, version 1.5, Philips Medical Systems, Best, The Netherlands). One weight-bearing, anteroposterior (AP) view and one supine frog-leg lateral view were obtained following a strictly standardised protocol, performed by one specifically trained radiographer (SHT). For the frog-leg view, a pillow was placed under each thigh to ensure a 45° abduction posture. For the AP view, hips were kept in a neutral abduction-adduction position, toes pointing forwards[106,149]. The radiographer ensured correct posture during the exposures. The film/focus distance was 1.2 m and centred at 2 cm proximal to the symphysis for the AP view, and at the pubis symphysis for the frog-leg view. A tube containing a contrast medium was placed in the x-ray field to give the true horizontal level for leg length measurement on the AP view. Males

were offered gonadal shields. In females, however, shields were not offered as they risk obscuring important anatomy. In addition, the effect of shielding on dose reduction in females has been questioned[18]. The total mean radiation dose for the two obtained radiographs together was 0.5 $Gycm^2$. The effective dose can then be calculated using an organ-specific transforming factor, which equals 0.29 mSv/ $Gycm^2$ for the pelvis, yielding an effective dose of 0.5 x 0.29 = 0.15 mSv for both radiographs together. All radiographs were stored in the PACS (Picture Archiving Communication System) of the hospital. A cadaver study including 10 pairs of intact femora of unknown gender was performed to examine the effect of hip rotation on the contour of the femoral head and neck, i.e. whether an excessive inward rotation would produce a false positive cam deformity. Each femur was placed on the x-ray table with the distal femoral condyles abutting the table. AP radiographs were obtained in neutral, internal and external rotation with 10º increments for both hips separately, using a film/focus distance of 1.2 m and the beam centred at 2 cm proximal to an imagined symphysis. We did not detect any visual changes of the femoral head-neck contour which might indicate that excessive internal or external rotation would produce a false positive cam deformity.

6.2.5 Image evaluation and radiographic measurements

The radiographs were assessed manually in the IMPAX (Agfa IMPAX Web1000, v.5.0, Agfa Gaevert, Mortsel, Belgium). The radiographs were also retrieved as DICOM (Digital Imaging and Communications in Medicine) files and measured in a digital program. Except from the reproducibility studies, no measurement or assessment was performed both manually and digitally.

The radiographs from the '1989 Hip Project' were assessed as follows

a. Evaluation of both views within few days on a high-resolution screen by a senior paediatric radiologist (KR). All radiographs were blocked for patient confidentiality. Position of the pelvis on the AP view was noted. Any signs of severe pathology of the pelvis or lower back were documented. Subjective

assessments of findings indicative of acetabular dysplasia, avascular necrosis (AVN) or FAI were performed.

b. Assessment of both views by one of the research fellows (LBL). Measurements for the Foramen Obturator Index (FOI)[334], leg length discrepancy, and several measurements related to the femoral head and neck anatomy were performed manually[195].

c. Assessment of the AP view in a digital measurement program (Adult_DDH) by one of the three research fellows (IØE, TGL, LBL), including all measurements relevant for the present works on acetabular dysplasia in young adults. The program was later extended to include measurements related to FAI on the AP view and the frog-leg view, performed by one observer (LBL).

Measurements on the AP view related to acetabular dysplasia used in this thesis

The ***shape of the lateral acetabulum*** was assessed by gross visual inspection, and classified as normal, immature, mildly or moderately dysplastic[36]. ***Medial flattening of the femoral head*** indicative of avascular necrosis (AVN) as a complication of treatment or secondary to a different aetiology was also documented[162]. ***Leg length discrepancy*** was measured by drawing a true horizontal line through the tube at the two top levels of liquid contrast, and thereafter measuring perpendicularly down to the top of the caput on each side. The digital measurement program 'Adult_DDH' (University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA) has previously been described in detail[86,254]. All measurement results were automatically transferred to an Excel spreadsheet. A detailed common understanding of important pelvic landmarks and of all the measurements was ensured prior to the analyses. The radiographic teardrop is a landmark seen on the AP view (shown on fig.8). Its medial surface consists of the cortical surface of the pelvis, and its lateral border consists of the cortical surface of the middle third of the acetabular fossa[340].

The inter-teardrop-line, connecting the inferior tip of both teardrops was used as the transverse axis of the pelvis. This is consistent with work published by others[53,149]. The most lateral point of the bony acetabulum roof is referred to as the lateral acetabular edge. In normal hips, both the posterior and the anterior acetabular rim will run downwards from the lateral edge point. The 'sourcil cotyloïdien' (sourcil: French for eyebrow) represents the weight-bearing bony area of the hip joint, seen as a hyper-dense arched line along the acetabular roof (shown on fig. 8). In a normal hip joint, this line is horizontal or somewhat curving downward, whereas it has an upward orientation in the dysplastic hip[242]. The lateral edge of the roof can be located more laterally than the lateral point of the sourcil. Measurements of both the acetabular morphology and of the position of the femoral head in relation to the acetabulum were assessed (fig. 17). Figures 17 A and B describes the relation between the femoral head and the acetabulum.

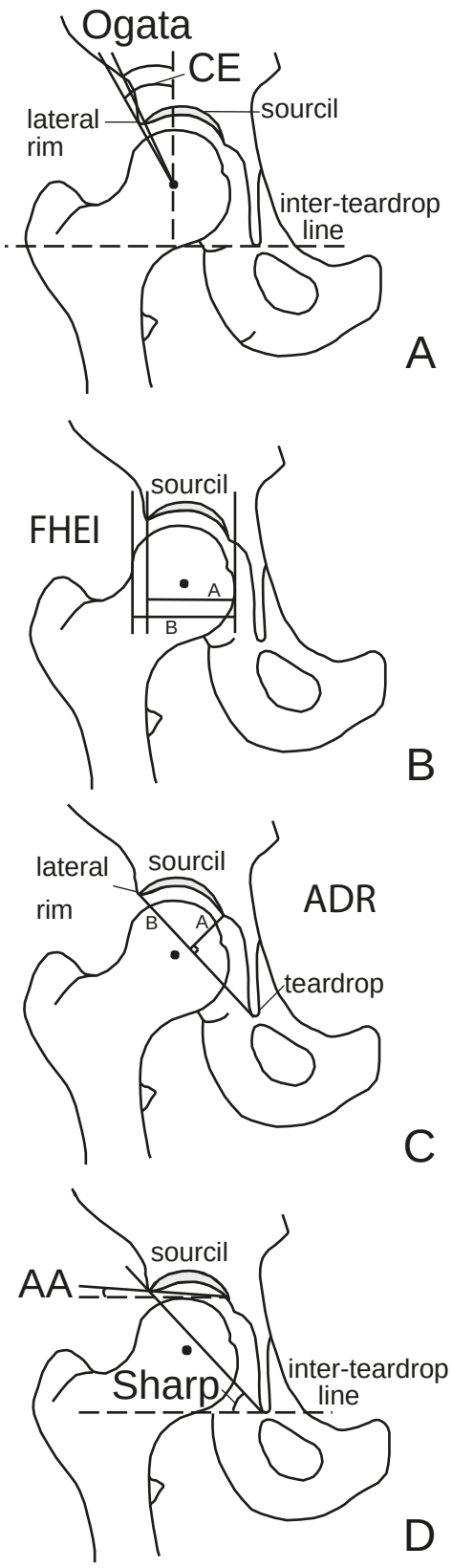


Fig. 17 CE angle and Ogata (A), FHEI (B), ADR (C), Sharp's angle and AA (D)

The ***CE angle of Wiberg***[356] is formed by a vertical line through the centre of the femoral head and perpendicular to the transverse axis of the pelvis (inter-teardrop-line), and a line joining the head centre with the lateral rim of the acetabulum (fig A). The ***refined CE angle of Ogata***[242] uses the lateral end of the sourcil, i.e. the weight-bearing area of the acetabulum, rather than the lateral rim of the acetabulum (fig A). The ***femoral head extrusion index (FHEI)***[138] quantifies how much of the femoral head is covered by the acetabulum, i.e. lies medial to the lateral edge of the acetabulum (A/B)*100 (fig B). Figures 17 C and D describes the morphology of the acetabulum. The ***acetabular depth-width ratio (ADR)***[64,313] is the depth of the acetabulum divided by the width of the acetabulum, multiplied by 1000, presented as a ratio: (A/B)*1000 (fig C). The width is measured from the inferior end of the teardrop to the lateral rim of the acetabulum, and the depth is measured perpendicularly from the midpoint of the width line. ***Sharp's angle***[293] describes the angle formed between the inter-teardrop-line and the line connecting the inferior tip of the teardrop to the lateral acetabular rim (fig D). The ***acetabular roof angle of Tönnis (AA)***[332,333] is the angle between a line intersecting the inferior part of the medial sourcil parallel to the inter-teardrop-line, and a line running from the inferior part of the medial sourcil until the lateral acetabular rim (fig D).

The ***joint space width (JSW)***[147], as a discriminator for early OA, was measured radially at three locations within the joint: namely medially (at the medial margin of the weight-bearing surface), centrally (determined by a vertical line through the centre of the femoral head), and laterally (at the lateral margin of the subchondral sclerotic line) (fig. 18).

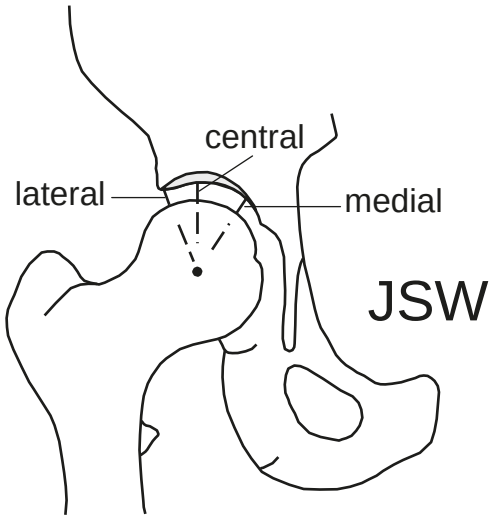


Fig. 18 Joint space width (JSW)

Measurements related to femoroacetabular impingement (FAI) used in this thesis

Qualitative radiographic findings commonly thought to be associated with cam- and pincer- type findings were assessed subjectively by gross vision on both the frog-leg and AP views. *Cam-type findings*[53,145,302,320] (fig. 19 A-C): (A) A ***pistol-grip deformity,*** noted as a flattening of the normal concavity of the femoral head-neck junction; (B) A ***focal prominence***, seen as a bump to the femoral head-neck junction; and (C) A ***Flattening of the lateral aspect of the femoral head,*** where the head was said to be aspherical if the femoral epiphysis extended more than 2 mm outside the reference circle corresponding to a spherical head.

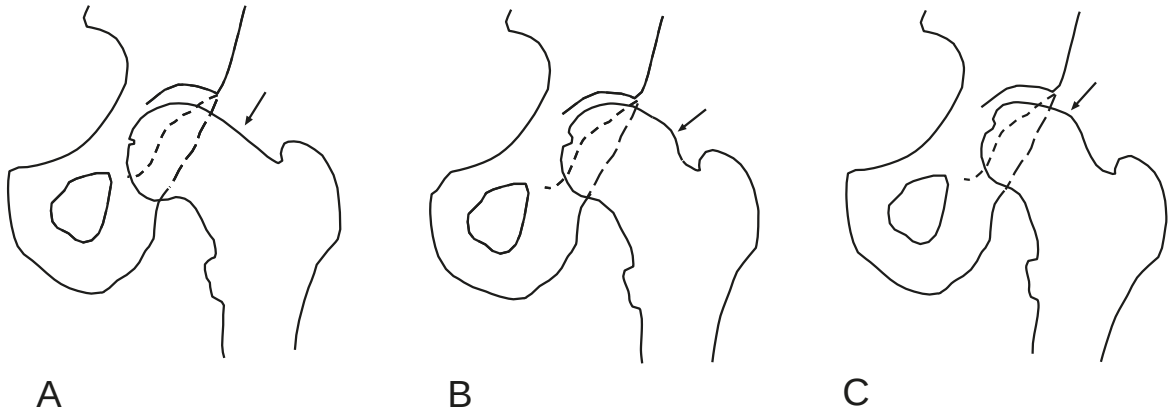


Fig. 19 A: pistol grip deformity, B: focal prominence at the head-neck junction, C: flattening of lateral femoral head

Pincer-type findings[118,151,273,320] (Fig. 20 A-C): (A) The ***posterior wall sign*** was scored positive when the posterior wall lies medial to the center of the femoral head; (B) The ***cross-over sign (COS)*** was scored positive when the upper part of the anterior acetabular wall lies more laterally than the posterior wall and crosses medially. According to Bardakos and Villar, we classified the COS as mild, moderate or severe, corresponding to the level of intersection between the anterior and the posterior rim, namely the superior third, the middle third and the lower third, respectively[17]. All of them were noted as a positive COS when presenting the overall

prevalence of COS, but only those with a moderate or severe COS were included in the number of participants with ≥1 pincer-type feature (paper IV); (C) ***Excessive acetabular coverage*** was seen as a bony extension of the upper acetabular roof. It was also assessed digitally by an increased CE angle. The presence of ***fibrocystic changes (FCC)*** at the femoral head-neck junction in the epiphyseal vicinity was also noted, as small areas of cystic radiolucency surrounded by a thinner sclerotic margin[201]. The pistol grip deformity and the focal prominence as well as the fibrocystic changes were subjectively assessed from both the AP and the frog leg views, and scored as positive if present in one or both views. The other four features were subjectively assessed from the AP view. Definitions were derived from the literature or in consensus.

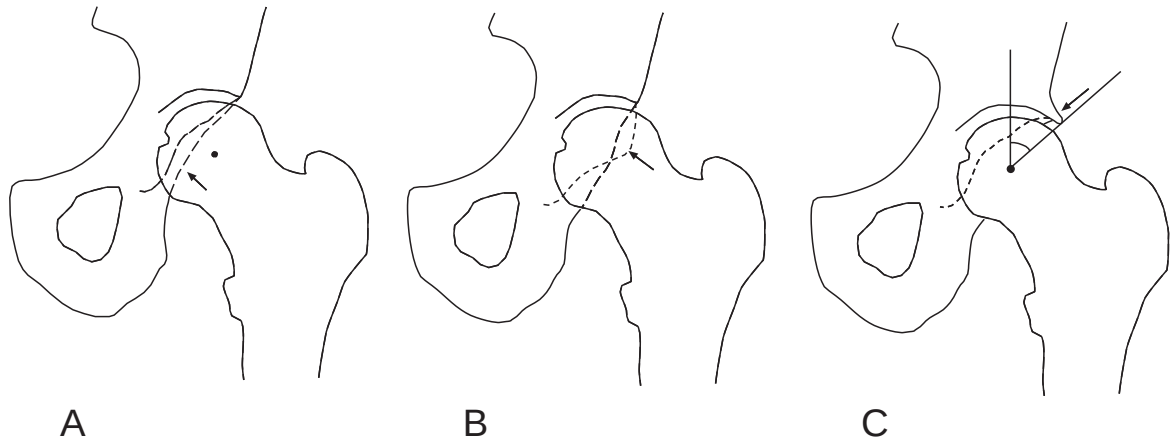


Fig. 20 A: posterior wall sign, B: cross over sign (COS), C: acetabular overcoverage

Quantitative measurements for cam-type FAI, i.e. the ***alpha angle***[237] on both views and the ***triangular index (TI)***[116] on the AP view, were assessed in the digital measurement program. The digital measurement method of the alpha angle was identical for both views. A curser was used to manually place four points corresponding to the circle of the femoral head, avoiding the head-neck junction, allowing the program to determine and draw a circle of best fit. This corresponded to the circle found by using Mose's templates, i.e. a transparent hard plastic sheet with concentric circles[225]. The mid-axis of the femoral neck was found by placing one

point on each side of the neck at its most narrow part, and the program automatically drew the mid-axis passing through the circle centre. The alpha-point was placed where the anatomical bony curvature crossed outside the circle by more than approximately 2 mm. A straight line was drawn from the alpha-point to the head centre, and this line, together with the longitudinal axis of the neck defined the alpha angle (fig. 21). Last, the program automatically draws a line perpendicular to the mid-axis of the collum, at the distance of half the radius from the circle centre. The last point, determining the triangular index, is set where this line intersects with the bony curvature of the head-neck junction (H). The program then calculates the distance from this point until the head center (R). The Triangular Index (TI), expressed as 'R-(r+2 mm)' is measured in mm, where r is the radius of the femoral head, and R is the pathological cam-radius. TI is pathological when R≥(r+2), i.e. when TI≥0 mm (fig. 22).

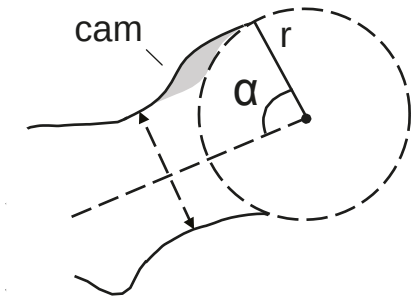


Fig. 21 A. Alpha angle on the frog-leg view

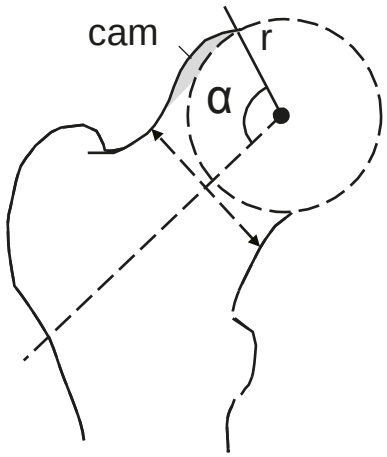


Fig. 21 B. Alpha angle on the AP view

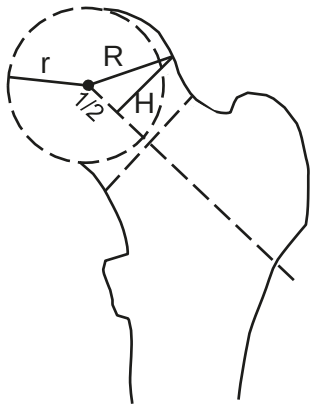


Fig. 22. Triangular index (TI)

6.2.6 Reproducibility of radiographic measurements

Several reproducibility studies of the different measurements and measurement techniques have been performed in relation to the '1989 Hip Project'. All radiographs were blocked for patient confidentiality.

Digital measurement program for hip dysplasia

Details on the reproducibility studies performed in order to validate the digital measurement program and all the included measurements related to hip dysplasia, including joint space width, have been thoroughly presented previously[86]. In short, a balanced set of 95 radiographs was measured manually (five repetitions) and digitally (six repetitions) by three observers (IØE, LBL, TGL) independently. The 95% limits of agreement (LoA)[32,33], the intra-class correlation coefficient (ICC)[219] and the minimum detectable change (MDC)[70,86] were calculated for the reproducibility analyses. Large inter- and intra-observer variations among the different radiographic measurements were noted, independently of measurement technique. The agreements were better for measurements with large absolute values, such as Sharp's angle, FHEI and ADR, compared to measurements with lower absolute values, such as the acetabular roof angle (AA) and JSW. The agreement between digital and manual methods was good.

Subjective assessment of acetabular shape

The inter- and intra-observer agreements for the experienced (KR) and non-experienced (LBL) radiologists were examined in a balanced subset of 145 radiographs. Both inter- and intraobserver analyses yielded good results, with values for Kappa measure of agreement between 0.7-0.9[182].

Subjective assessment of cam- and pincer-type FAI findings

A balanced subset of 350 examinations was re-read by the first observer (KR) after an interval of at least three months, and was also read twice independently and blinded by a second observer (LBL) with one year experience. Cam-type and pincer-type

findings as well as fibrocystic changes were scored. A sample set of 20 images not included in the study cohort was evaluated prior to study initiation. Inter - and intra observer agreements were examined using Kappa measure of agreement (Guidelines slightly adapted from Landis and Koch 1977[183]: <0.2=poor agreement, 0.21-0.40 = fair, 0.41-0.60 = moderate, 0.61-0.80 = good, 0.81-1.00 = very good). Interobserver agreement was good to very good (κ =0.74 to 0.84) in rating cam-type and pincer-type findings. Intraobserver agreement was moderate or good (κ =0.49 to 0.80) for all findings for both observers.

Digital assessment of triangular index and alpha angle

Two of the authors (LBL and KR), measured and remeasured (LBL) a balanced set of 100 AP images (after an interval of at least 8 weeks), and found intraobserver and interobserver agreements of κ = 0.85 and κ = 0.69, respectively for the triangular index as a categorical variable. The balanced set of 100 radiographs was also used to assess intra- and inter-observer and inter-method reproducibility for the alpha angle on both views. Ten frog-leg and AP radiographs were assessed for standardisation prior to and not included in the reproducibility analyses. One observer (LBL) measured all radiographs (both views) in the digital measurement program. The same observer also measured all radiographs (both views) manually in the IMPAX, using Mose's templates to determine the circle of best fit around the femoral head and its circle centre. All digital and manual measurements were remeasured after an interval of two months by the first observer. In addition, one observer (KR) measured all radiographs (both views) once in the digital program. Intra- and inter-observer and inter-method reproducibility were assessed. The 95% limits of agreement (LoA) method was used for examining the mean difference between two sets of readings performed by same observer (intraobserver) between a set of readings performed by two observers (interobserver), and between a set of readings in the digital program and a set of manual readings (inter-method).[32,33] For the inter-method reproducibility, we first calculated the mean for each method and on each subject and used these pairs of means to compare the two methods, as described in a previous paper presenting the

'Adult_DDH' digital program[86]. The 95% LoA were estimated as mean difference between the two measurements ±1.96 standard deviations (SD). The intra-and interobserver reliability were also expressed by the intra-class correlation coefficient (ICC), using a one-way random effect ANOVA table [formula ICC (1)][219]. The inter-method reliability was expressed by ICC calculated using two-way random effect ANOVA table [formula ICC (A,1)]. The intra- and inter-observer and inter-method variability results for the alpha angle showed overall good values as demonstrated by the 95% limits of agreement (fig. 23) and ICC values.

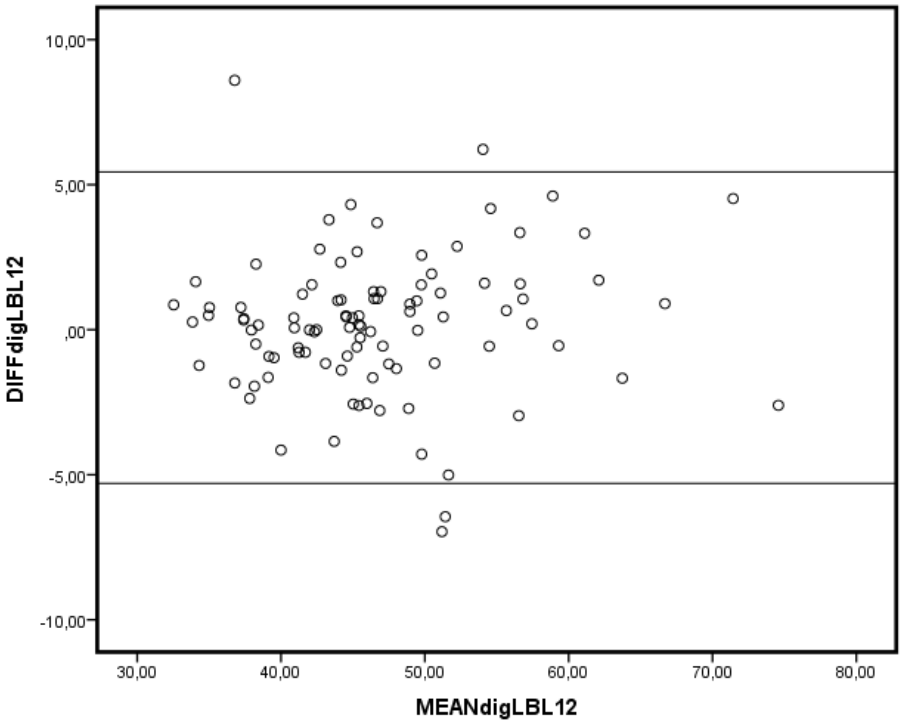


Fig. 23 Bland Altman plot with 95% limits of agreement for intraobserver, digital measurements of alpha angle, frog-leg view

6.2.7 Statistical analysis

For all studies, numeric variables were summarised using mean and standard deviation (SD), or mean and range, as appropriate. Categorical variables were summarised as number and percentage.

Paper II: At skeletal maturity, the outcome variables of the initial RCT were radiographic measurements of acetabular dysplasia (The CE angle, FHEI, ADR, Sharp's angle and subjective evaluation of the sourcil shape) and early degenerative

change (JSW). The radiographic measurements indicating dysplasia that were continuous variables were also categorised, based on gender-specific cut-off values from paper III. An intermediate borderline-group for the CE-angle was also calculated, using a general cut-off of 25°. In addition, we created a categorical variable for acetabular dysplasia, which was positive if one or more markers were present, consisting of the CE angle (dysplastic values only), Sharp's angle, ADR and FHEI, all as categorical variables. JSW was also categorised, defined as 'minimal JSW≤2 mm in at least one position'. In order to compare the three screening groups at skeletal maturity, a general regression model was performed, adjusted by side, sex, family history and breech and taking into account clustering of hips within a subject. Univariate (crude) and multivariate (adjusted) p-values were presented. No correction for multiple comparisons was performed. All p-values were two-tailed. To adjust for non-responders when comparing the three screening groups we calculated inverse probability weights[289] (IPW) based on a logistic regression model including gender, ultrasound performed at birth (yes/no) and DDH treatment received (yes/no) as covariates. Data at skeletal maturity on weekly physical activity, hip discomfort, BMI and hip range of motion were used to compare the functional status between groups.

Paper III: For calculation of reference intervals for hip dysplasia at skeletal maturity, mean values, standard deviation (SD) as well as empirical 2.5 and 97.5 percentiles with their corresponding 95% confidence intervals (CI) were calculated for both sex and sides separately for each radiographic measurement[361]. The CIs were obtained using the binomial method[223]. To take into account possible non-independence of radiographic measurements measured on right and left hip within each subject, repeated measure analysis of variance was used[75]. To evaluate the effects of sex and side on radiographic measurements, subject was considered as random term, side as within subject and sex as between subject factors. A significance level of 0.05 was decided a priori, and all the reported p-values were two-tailed. No correction for multiple comparisons was performed.

Paper IV: The qualitative radiographic findings were treated as categorical variables, and the prevalences were calculated as percentages of the whole cohort, for each

gender separately. Differences in the distribution of the radiographic findings according to gender were investigated using chi-square tests (Fisher's exact test). Associations between the radiographic findings were analysed by calculating the odds ratio (OR) between each of the features separately, and an OR>2 was considered to indicate an association. The probability of false positive findings due to chance is non-negligible due to multiple statistical tests performed on the same data. The relationship between the presence of fibrocystic changes (FCC) and the radiographic findings was investigated by chi-square statistics (Fisher's exact test) and by a model of binary logistic regression for males and females, right and left side, separately. A significance level of 0.05 was decided a priori, and all the reported p-values are two-tailed.

Paper V: The prevalences of a positive impingement test are presented as numbers (percentages) with corresponding 95% CIs. Differences in the prevalence of a positive impingement test according to sex and side were examined using Pearson chi-square test. Descriptive statistics for the variables considered as possible predictors of a positive impingement test were summarised by sex and side and were reported as numbers (percentages) or means (SD) as appropriate. We used generalised estimating equations (GEE) models to study possible associations between the predictor variables and a positive impingement test. P-values and prevalence rate ratios (PRR) with corresponding 95% confidence intervals were estimated with GEE models[128], adjusted by side (left or right), in order to take into account the correlation between bilateral hips[370]. The p-value was used to evaluate the effect of the variables on a positive test. All the reported p-values were two-tailed. A PRR value describes how the presence of a given variable alters the prevalence of a positive test; i.e. a PPR=3.1 means an increase of 210%. For continuous variables (Hip ROM and CE angle) the PRR represents the increase of the prevalence for a unit (5°) change of the continuous variable. Weekly physical activity was treated as a continuous variable with 1 hour increments; i.e. a linear effect was assumed. The hip ROM values were continuous variables with 5° decrements. All the cam-type and pincer-type variables assessed by gross visual inspection were categorical variables. The alpha angle (AP

view) was categorised into normal, borderline, or pathological groups[116]. A CE angle >45° was considered to indicate acetabular overcoverage[118]. The CE angle was also considered as a continuous variable with 5° increments. We created a radiographic composite score of 1, 2 or ≥3 cam-type and of 1 or ≥2 pincer-type findings, respectively. A sensitivity analysis was performed while considering an inverse probability weighted (IPW) approach to take into account a possible no response bias. The results of the observed data were reported, as they gave similar results.

Paper VI: Mean values, standard deviation (SD), range, and empirical 97.5 percentiles with their corresponding 95% confidence intervals (CI) were calculated for both sex and sides separately for the alpha angle on the frog-leg and the AP view, respectively[361]. The binomial method was used to obtain the 95% CIs[223]. Repeated measure analysis of variance was used to account for potential non-independence of radiological findings on right and left hips. In order to evaluate the effects of sex and side on the alpha angle values, subjects were considered as random term, side as within subject and sex as between subject factors. Each of the three qualitative cam-type findings was dichotomised variables (yes/no), and each finding was scored separately on the two views. In order to examine the association of alpha angles with the presence of quantitative cam-type findings, random effect models were fitted with alpha angle as outcome and dichotomised qualitative cam-type finding as exposure variable, for each of the qualitative cam-type findings and for each view. Random effect models take into account a possible non independence of alpha measurements, considered as outcome, for right and left hip measurement within a subject, including a subject effect considered as random variable. The coefficient (°), adjusted by sex and side, resulting from each model indicates how many degrees higher the mean alpha angle is for the group with a positive subjective cam-type finding, compared to the group without the subjective finding.

Statistical analyses were performed in IBM® SPSS® Statistics, versions 17.0 (Release 2008, Chicago, Ill) and 20.0 (Armonk, New York, USA) and in Stata® Statistical Software: Release 11 (StataCorpLP®, College Station, TX, USA).

6.3 Ethical approvals

The research protocol for the ‘1991-2006 cohort’ (paper I) was approved by the Regional Ethical Committee for Medical and Health Research (003.07), and this study was granted exempt status from the parental written informed consent issued by the Norwegian Directory of Health (06/5901). All participants in the ‘1989 Hip Project’ (papers II-VI) gave written informed consent according to the 1964 Declaration of Helsinki (appendix 4). The study research protocol, including analyses of the non-responders, was approved by the Medical Research Ethics Committee of the Western region of Norway (No. 018.06, initially named No. 3.2006.144), and the study was conducted according to the ethical standards set by the Regional Ethical Committee for Medical and Health research. A specific consent form was signed by all subjects who provided a salivary sample for later genetic analysis. The creation of a Research Bio-bank, including export of biological material to the UK, was approved by the Norwegian Directorate of Health (letter of 29.06.2007).

7. Main Results

Paper I:

This observational study based on prospectively collected data from a standardised selective ultrasound (US) screening programme for DDH included all babies born at the maternity unit of our hospital during 1991-2006. In addition to routine clinical screening of all newborns (n=81564), a hip US was performed in those considered to be at increased risk of DDH (14.1%). Of the 81564 infants, 2433 (3.0%) received early treatment; 1882 (2.3%) from birth and 551 (0.7%) after six weeks or more of clinical and US surveillance. Another 2700 (3.3%) normalised spontaneously after watchful waiting from birth. Twenty-six infants (0.32 per 1000, 92% girls, two from the risk group) presented with late subluxated or dislocated hips (after one month of age). Another 126 (1.5 per 1000, 83% girls, one from the risk group) were treated after isolated late residual dysplasia. Thirty-one children (0.38 per 1000) had surgical treatment before age five years. Avascular necrosis was diagnosed in seven of all children treated (0.27%), four after early and three after late treatment.

Paper II:

This follow-up study of the '1989 Bergen Birth Cohort' included 2011 young adults for analyses. It assessed the radiological long-term outcome at skeletal maturity for the three newborn screening strategies for DDH evaluated in the initial randomised controlled trial (RCT): the universal (n=551), selective (n=665) and clinical only (n=795) screening groups. Long-term outcome included radiographic markers for acetabular dysplasia and early degenerative change. Sign of avascular necrosis (AVN) secondary to neonatal treatment was also documented. The rates per screening group of radiographic findings associated with acetabular dysplasia, for left and right side separately, varied depending on the measurement used: The CE angle, FHEI, ADR, Sharp's angle and subjective evaluation of the sourcil shape. Dysplastic rates based on the four quantitative angle measurements ranged from 1.1% (FHEI in the universal group) to 3.4% (CE angle in the no US group). The total rate when including those

with one or more positive dysplastic findings based on the four categorical angle measurements ranged from 5.7% to 7.6% for the left side, and from 5.4% to 7.6% for the right side. Rates based on a borderline CE angle <25° ranged from 9.3% to 13.3% on left and right side separately. No statistically significant differences in acetabular dysplasia, as assessed by the CE angle, FHEI, ADR, Sharp's angle or subjective evaluation of the sourcil shape could be found between the three groups at skeletal maturity. The rates of a positive minimum JSW as an indicator for early degenerative change ranged from 3.1% to 4.7% and from 1.9% to 3.0% for left and right side respectively, without any detectable differences between groups. None of the study participants had a flattening of the medial aspect of the femoral head interpreted as a sign of AVN.

Paper III:

In this population-based cross-sectional study of the '1989 Bergen Birth Cohort', the anteroposterior radiographs of 841 males and 1170 females were assessed for the most common radiographic measurements for acetabular dysplasia (Sharp's angle, acetabular depth-width ratio (ADR), acetabular angle of Tönnis (AA), Wiberg's CE angle, Ogata's refined CE angle and femoral head extrusion index (FHEI)) (table 3). Joint space width (JSW) was also assessed in the lateral, central and medial position.

Table 3 Mean, standard deviation (SD) and range for measurements for acetabular dysplasia

Variable	Males, right hip	Females, right hip
Sharp (°)	38.8 (3.5), 25.0;49.2	40.7 (3.5), 27.4;51.0
AA (°)	5.6 (4.8), -11.1;21.8	5.8 (4.9), -13.9;21.4
ADR (‰)	294.5 (34.9), 193.7;457.7	297.7 (35.8), 165.2;486.7
CE (°)	32.07 (6.1), 12.3;58.5	30.1 (6.1), 11.1;53.1
Ogata (°)	30.4 (6.3), 8.2;58.1	29.1 (6.3), 3.7;51.8
FHEI (%)	85.6 (6.3), 63.9;108.4	85.6 (6.6), 66.8;113.7

Gender-specific reference intervals at skeletal maturity have been presented, with corresponding proposed cut-off values for males/females respectively: Sharp's angle >46°/>47°; AA >15°/>16°; ADR <235‰/<233‰; CE angle <21°/<20°; Ogata

<18°/<17°; FHEI <74%/<73%. The gender difference was statistically significant for Sharp's angle, Wiberg's CE angle, Ogata's refined CE angle (all p<0.0001) and for the ADR (p=0.036), with a tendency towards more dysplastic values in females. The joint space width (JSW) indicating degenerative change of the hip joint was measured on three locations within the joint, with lowest values for the middle position and highest values for the lateral position in both sides and for both genders. Males had statistically significant higher values in all three positions than females.

Paper IV:

In this population-based cross-sectional study, 2060 of the initial 2081 participants of the '1989 Hip Project' had two acceptable radiographs and were included for further analyses. Cam- and pincer-type findings were assessed and the following prevalences based on at least one affected hip were determined in the 868 males and 1192 females, respectively: The pistol grip deformity in 187 (21.5%) and 39 (3.3%); the focal femoral neck prominence in 89 (10.3%) and 31 (2.6%); and flattening of the lateral femoral head in 125 (14.4%) and 74 (6.2%). One or more cam-type findings were seen in 35.0% and 10.2%. The posterior wall sign in 203 (23.4%) and 131 (11.0%) and excessive acetabular coverage in 127 (14.6%) and 58 (4.9%) (all p<.001 according to sex distribution). The cross-over sign (COS) was seen in 446 (51.4%) males and 542 (45.5%) females (p=.004), of which 32 males and 48 females had a positive score for COS in the middle and lower thirds. When including only those with a positive COS in the two lower thirds, one or more pincer-type findings were seen in 34.3% and 16.6%, respectively. There was a high degree of coexistence (Odds Ratio (OR) >2) among most FAI findings, in particular the posterior wall sign and the cross-over sign (OR=13.5).

The prevalence of fibrocystic changes at the femoral head-neck junction was 5.8% and 1.6% in males and females respectively, and an association between these fibrocystic changes and the presence of either a cam- or a pincer-type deformity was seen, in particular for the femoral neck prominence and the acetabular overcoverage.

Paper V:

The test for anterior femoroacetabular impingement was performed in the second half of the '1989 Bergen Birth Cohort' who attended the study as 19-year olds (n=1170). Of the 1152 participants included for analyses, 35 of 480 (7.3%) males and 32 of 672 (4.8%) females had a positive impingement test, based on at least one affected hip. 14 (2.9%) males and 8 (1.2%) females tested positive bilaterally. Self-reported hip discomfort in females ($p<0.001$) and increased physical exercise in males ($p=0.001$) were strongly associated with a positive impingement test. Decreased abduction ($p=0.018$) and internal rotation ($p=0.001$) in males and decreased flexion in males ($p=0.062$) and in females ($p=0.003$), as well as radiographic cam-type findings ($p=0.043$) in males, were associated with a positive test. Radiographic pincer-type findings were not associated with positive tests in either gender (all $p>0.2$).

Paper VI:

In this population-based cross-sectional study, 2005 (837 males and 1168 females) participants from the '1989 Bergen Birth Cohort' were included for analyses of the alpha angle in cam-type impingement. On the frog-leg view, mean alpha angle (right hip) was 47° (range 26°-79°) in males and 42° (range 29°-76°) in females (p (gender) <0.001), with upper 97.5 percentiles corresponding to 68° and 56°, respectively. On the anteroposterior (AP) view, mean alpha angle (right hip) was 62° (range 40°-105°) in males and 52° (range 36°-103°) in females (p (gender) <0.001), with upper 97.5 percentiles corresponding to 93° and 94°, respectively. The random effects models, adjusted by sex and side, demonstrated significantly higher mean alpha values for those with qualitative cam-type findings compared to those without, on both views. The mean alpha angle was 15.3° higher in those with a pistol grip deformity on the frog-leg view, compared to those without.

8. General Discussion

8.1 Methodological considerations

8.1.1 Study designs

Epidemiological research aims to describe and investigate the status and patterns, the causes and the effects of conditions related to health and disease in a defined population. The word *epidemiology* literally means 'the study of what is among/upon the people' derived from ancient Greek. By identifying risk factors for disease and targets for preventive medicine, epidemiology is a pillar of public health, and influences evidence-based medicine and health policy decision-making. The study design, study population and statistical methods should be chosen carefully, according to the research hypothesis. The epidemiological method starts with a research question, or hypothesis. A study must then be designed, and variables intended to be related to the research hypothesis must be defined. At time of implementation of the study, the actual *study population*, departing from a *source population*, will be examined, and actual measurements of the defined study variables will be performed. Once the study results are available, the 'truth' can be inferred for the source population, while taking into account possible random and systematic errors (*internal validity*). The *external validity*, or *generalisability*, is the extent to which the results of a study can be applied to other circumstances and other populations, outside the source population. The evaluation of the external validity of study results is often a matter of judgment, depending on the study setting, the participants, the exposures and the outcomes.

A study can be either *experimental*, including some type of intervention, or *observational*. The *randomised controlled trial (RCT)* is often described as the 'gold standard' in medical research, and provides the highest level of scientific evidence.

An RCT typically provides valuable evidence on treatments and other interventions. A study is defined as 'randomised' when the investigator assigns the treatment at random. An RCT has a longitudinal design, and often requires large resources and is time-consuming. Through randomisation and blinding, possible bias and confounding factors are minimalised, and an RCT study is said to have a high internal validity. The external validity, however, might be lower, as the RCT is performed in a strict setting with many, often narrow inclusion criteria. In contrast, o*bservational studies* have a lower evidence level than an RCT, but can still have a higher external validity, as they are carried out in settings more representative for real life, often over long time periods. They contribute with valuable information related to description of health and disease, and associations between exposures and health outcomes.

There are three main types of observational studies: the *cohort* studies, also called longitudinal or follow-up studies; the *cross-sectional* studies; and the *case-control* studies. All three types represent different approaches of examining the occurrence of health-related events such as disease and the occurrence of risk factors, within a given time period and population. In *cohort* studies, participants are followed over time (papers I and II). Information about the participants and their exposures at baseline is collected, and then, after a given amount of time, the occurrence of outcomes. Closed cohorts, like birth cohorts, include a defined number of participants at study onset, who are followed until an end-date. In *cross-sectional* studies, all individuals in a sample are assessed at a given point in time (papers III-VI). It is the best way to examine the *prevalence* of risk factors, exposure variables or disease. The prevalence corresponds to the proportion of the population having the outcome at the specified time. Cross-sectional studies can usually not evaluate time aspects between exposure and outcome (disease), but can ask the participants about previous events. In *case-control* studies, participants with a defined disease outcome (i.e. cases) are compared with participants without that particular outcome (i.e. controls), in a longitudinal design. When the study goal is to estimate the causal effect of a certain treatment on the outcome variable(s), longitudinal studies are preferred over non-longitudinal (e.g. cross-sectional studies), as the temporal order of treatment and outcome may be

difficult to confirm. In all epidemiological studies, possible *bias* and *confounding factors* need consideration. While bias creates an incorrect association, confounding describes an association which is correct, but potentially misleading. *Bias* can be defined as a systematic, non-random deviation of a study's result from its true value, and should always be addressed. It should not be confounded with random error, which is a deviation, in either direction, from a true value due to statistical variations in the measured data. Bias can arise from incorrect subject selection or incorrect information, leading to incorrect associations. S*election bias* occurs if there is a systematic deviation in the study results due to the way subjects are assembled in the study. In particular, *response bias* occurs if differences in characteristics between those who respond and those who decline to participate in a study affect estimates of prevalence, incidence or sometimes associations. Selection bias will usually affect the *internal validity* of a study. *Information bias* occurs when individuals are misclassified in regard to exposures or outcomes, which can be caused by systematic differences in the accuracy or completeness of the data. Information bias is related to the way information is collected in the study, creating a systematic difference. *Measurement bias* and *recall bias* are considered as information bias. *Confounding* means confusion of effects, due to a *confounding factor* related to both the exposure and the outcome variables. This leads to an incorrect assessment of the potential causal association of an exposure with the outcome.

Paper I is an observational cohort study that describes the effect of a selective US screening programme for DDH in newborns. Data was collected in a prospective manner, by filling in the specific report form at the time of examination. Haukeland University Hospital provides the only delivery unit for a large, defined area with a low annual migration rate. Of the 81564 live-births during the study period, 14.1% (11539 newborns) were defined as at risk for DDH and had a hip US. Of these, 349 babies had incomplete records with insufficient information regarding identity and clinical and US findings at birth and were thus not included in the descriptive analysis of those at risk, but remained within the total '1991-2006 cohort'. They appeared to be mainly newborns without pathological hips, as they had not received further

treatment or follow-up. We also performed detailed searches including all diagnoses and procedures related to late detected DDH and to surgical treatment of DDH in order to reduce the possibility of missing cases to a minimum, and a high completeness of our data was confirmed. It is possible that some infants moved outside the catchment area within the study follow-up period of minimum of 5.5 years, and possibly could have presented with late DDH elsewhere. However, the migration rate is low and children with subluxated or dislocated hips would most likely have been referred back unless the family had moved to another major region of the country since our hospital has a regional service. The long time period, the high number of infants, the unchanged protocols for screening and management and the use of a validated US method all strengthen the external validity of this study. The fact that as few as six, experienced radiologists performed all the US examinations strengthens the internal more than the external validity of the study, but is in line with the often expressed thought that those who perform the hip US examination need high-quality training and sufficient level of experience.

In paper II, we assess the long-term outcome of an RCT, which originally evaluated the effect of three different screening strategies for DDH in newborns. This is a follow-up study of a closed birth cohort, corresponding to about one third of the original RCT. The ‘randomisation’ part of an RCT, purely by chance, aims to avoid selection bias, and the ‘controlled’ part implies a strict, predefined study protocol. In the original RCT, randomisation was area-based (cluster randomisation), to keep mothers separate, i.e. to avoid recall bias with respect to risk factors. This decision was based on experiences from 1987, when all girls and boys at risk were offered US screening. The mothers of the participants, and the US examiner were aware of group assignment when US was performed. The original RCT was adequately designed with sufficient power to detect the desired differences, although the number of late detected cases were lower than expected. However, we have only reviewed a population-based sample of the initial RCT (17%). This weakens the power to detect differences in radiographic measurement values between the three groups at skeletal maturity. Our results should therefore be interpreted carefully as the fact that we

cannot detect any difference at time of follow-up does not exclude that there actually is a difference that would have been detected in a larger study sample (type II error). The fact that each of the three groups had a similar participation rate to follow-up strengthens the study, along with a highly standardised protocol for the RCT and the follow-up study.

The loss to follow-up must be addressed. In the present follow-up study of the '1989 Bergen Birth Cohort', there was a moderate follow-up rate of 51.9%. However, analyses based on growth data at birth, 7 and 19 years of age revealed no differences between the responders and the non-responders except for the gender distribution, as shown in paper III. Possible selection bias needs careful consideration. Those who received a hip US as newborns or experienced hip-related problems including DDH in infancy could possibly be more prone to participate, along with participants with hip-related problems at the time of follow-up. The DDH treatment rates per screening group in infancy were increased for all the three groups at follow-up, indicating that young adults who underwent treatment for DDH were more interested in participation. This could possibly bias the results of paper II. To adjust for non-responders when comparing the three screening groups we calculated inverse probability weights (IPW) based on a logistic regression model including gender, US performed at birth (yes/no) and DDH treatment received (yes/no) as covariates. As hip dysplasia is more common among females, the adjustment according to gender was important, given that more females than males attended the follow-up (58% vs. 42%). In the general regression model performed for comparison of the three screening groups at skeletal maturity, we adjusted for baseline characteristics as possible confounding factors: gender, family history and breech presentation. We also adjusted for left/right side, taking into account clustering of hips within a subject.

The attendance rate at skeletal maturity of 51.9% (50% for paper V) is equally important for the remaining four papers, which all have a cross-sectional population-based design. Because hip dysplasia is more common among females, and because more females than males attended the '1989 Hip project' (58% vs. 42%), the results

are presented for each gender separately in papers III-VI. A selection bias could exist, as the cohort was drawn from a previous population-based hip trial designed to evaluate the effect of US screening in the diagnosis of hip dysplasia in newborns. In paper III, the reference intervals for acetabular dysplasia at skeletal maturity are calculated based on the '1989 Bergen Birth Cohort'. However, none of the results were altered significantly when the same analyses were performed excluding the 102 study subjects who had received DDH treatment as newborns. For paper V, a sensitivity analysis with an inverse probability weighted approach was performed, which did not reveal any no-response bias. An IPW approach would also have been an advantage in paper IV, but this was not done as this paper was written based on the '1989 Hip Project' without available linkage to the newborn data from the RCT regarding breech position, hip US and treatment for DDH. As described, growth data characteristics for attendees and non-attendees revealed no noteworthy differences (papers II-VI).

In paper IV, the reported portion of participants that had been treated for DDH as newborns was lower than what is reported in paper II and III. This demonstrates a recall-type of information bias, as the figure in paper IV is based on self-reported information collected at time of follow-up, while the figures in papers II and III are based on the information obtained through the linkage with the data from the Medical Birth Registry. This is not thought to have influenced the results of paper IV. In order to reduce possible recall bias, the questionnaire related to previous hip disease and hip problems experienced throughout childhood and adolescence was mailed home to the participants together with the invitation, allowing for parents to complete the information. The *generalisability* of the results from the cross-sectional studies (papers III-VI) might be influenced by the fact that the '1989 Bergen Birth Cohort' is quite homogenous in terms of age. This should be kept in mind for the reference intervals (papers III, VI) and prevalences (papers IV, V).

8.1.2 Ultrasound in the diagnosis and management of DDH in newborns

High *reproducibility* and high *diagnostic accuracy* are necessary characteristics of a test with high *diagnostic validity*. The *reproducibility* of a diagnostic test refers to the ability of the same observer (intraobserver) or different observers (interobserver) to reproduce the same findings, often called *repeatability*. In this thesis, *reproducibility* comprises *agreement* and *reliability*[70], although these terms are sometimes used interchangeably in the literature. In diagnostic imaging reproducibility of both the *recording (i.e. the image acquisition)* and the *reading (i.e. image interpretation)* need to be addressed, although assessment of the recording process more accurately defines the reproducibility. For US in the diagnosis of DDH, both hip morphology and hip stability should be assessed separately, and thus the corresponding reproducibility measurements should be performed separately too. In summary, various methods of US as a diagnostic test used in the screening for DDH in newborns have been reported sufficiently reproducible for screening purposes[40,278,285]. Moreover, the interobserver reproducibility related to the morphological classification of infant hips does not seem to adversely affect the management of patients with DDH, especially in the more severe cases[40].

The ability of a diagnostic test to correctly classify individuals into two categories (positive and negative) is assessed by two parameters: *sensitivity* and *specificity*. The sensitivity corresponds to the proportion of true positives correctly identified as such, and the specificity to the proportion of true negatives correctly identified as such. When interpreting the results of a diagnostic test, it is also of interest to know the probability that a patient is truly positive if the test is positive. The proportion of test positives that are truly positive is called the *positive predictive value (PPV)*. The *negative predictive value (NPV)* similarly represents the proportion of test negatives that are truly negative. The *diagnostic accuracy* of US is highly dependent on the *sensibility* and *specificity* of US, i.e. the ability of US to detect DDH if present and thus avoid false negative cases, and at the same time detect as few as possible false

positive cases. For the purpose of screening the rate of false negative cases should be as low as possible, as this could otherwise have serious implications for the missed cases, whereas a slightly higher rate of false positive cases might be accepted[358]. Possible overtreatment should be avoided, as avascular necrosis of the femoral head is a rare but severe adverse effect of abduction treatment[162]. Short-term results from the original RCT showed low positive predictive values (PPV) for all three screening groups, corresponding to possible overtreatment.

The *construct validity* describes how well US actually measures what it is intended to measure. In the case of US screening for DDH, it can be evaluated by assessment of radiographic occurrence of DDH later in infancy. The *clinical validity* of US screening for DDH can be assessed by measuring the effect of US on late detected cases of DDH, or also the ability of US to predict isolated acetabular dysplasia at skeletal maturity. According to the pyramidal model for clinical efficacy of diagnostic imaging presented by Thornbury[327] in 1993, all of the abovementioned aspects related to US as a diagnostic tool in the screening for DDH should be assessed as part of the clinical efficacy, after assessment of technical efficacy. Furthermore, patient-outcome efficacy related to individual risks and benefits, as well as societal efficacy including cost-effectiveness, need consideration in the evaluation of US as a tool for DDH screening.

8.1.3 Validity of questionnaires and clinical examinations

In paper II and V, patient-reported information from the different questionnaires is used. Validation of questions and questionnaires is performed in order to make sure that what is asked measures what it is intended to measure, independently of the setting or population it is asked within. Both the EQ-5D and the WOMAC questionnaires used in the ‘1989 Hip project’ are validated. The EQ-5D questionnaire is validated for a Swedish population[45], but has not been validated in a Norwegian population. The version used in our project allows three levels for the response (none-moderate-severe). However, this three-level approach lowers the sensitivity of the

questionnaire since very few will qualify for the ‘severe’ alternative in a healthy population. Therefore a modified form of the EQ-5D questionnaire was proposed in 2005, with five rather than three levels of response. The WOMAC score was validated by Bellamy et al, for patients with OA[26]. The question regarding hip discomfort during the past 3 months for each of the hips was not properly validated, but appeared to be appropriate and without risk for confusion.

As for the clinical examination, data on hip range of motion and the femoroacetabular impingement test is included in the works of this thesis (papers II and V). A total of five physicians performed the clinical examinations, increasing the risk of introducing bias. The clinical examination was thoroughly standardised prior to study start. While hip ROM was examined in all participants, the impingement test was not included before mid-duration of the study. Paper V therefore reports on fewer patients (n=1170 vs. n=2038). Interobserver reliabilities for flexion, extension, abduction, adduction, and external and internal rotations presented as intraclass correlation coefficients (ICC), have been reported as 0.87, 0.44, 0.34, 0.54, 0.18, and 0.79, respectively[265].

As for the impingement test, the kappa (κ) value for interobserver variability has been reported at 0.58 (95% CI, 0.29-0.87)[216], and the interobserver agreement for the impingement test at 96%[265]. The small interobserver study (30 right hips, 30 left hips) performed in our project showed an interrater agreement for the impingement test of 95%. In addition to this varying reproducibility of the impingement test, its *diagnostic validity* is affected by the possibility of a false positive or false negative test. According to the literature, the sensitivity and specificity of the test for anterior impingement are 70% and 44%, when the test represents the most painful provocative movement[235]. In addition, patients with acetabular dysplasia could test positive[199]. A high positive predictive value (PPV) of the anterior impingement test was recently reported[127].

8.1.4 Radiographic protocol: pelvic views, tilting and rotation

The radiographic protocol of the '1989 Hip Project' included a pelvic *AP view* and a *frog-leg lateral view*. The AP view is the preferred view for assessing hip dysplasia at skeletal maturity. In order to assess radiographic aspects of FAI, both AP and lateral views are useful. The acetabular aspects of pincer-type FAI are assessed on the AP view. The cam-type deformity, usually located on the anterosuperior aspect of the femoral head, can be assessed both on the AP and the lateral view. A lateral view, including the frog-leg, cross-lateral or Dunn views, is usually preferred[21,56,220,233]. In particular, the frog-leg lateral view visualises the head-neck junction adequately, although there is a risk of the great trochanter obscuring the anatomy[53]. For paper V, our digital software program allowed measurements of the alpha angle in cam-type FAI on the AP view only. We therefore included the scoring of the subjective cam-type findings from the frog-leg view into a composite cam score, as discussed more in detail under 8.2.4/5.

In the assessment of the dysplastic hip, the use of a true pelvic AP radiograph is important[71,103,230]. Several other retrospective studies are based on urograms or abdominal radiographs[192]. A weight-bearing AP view was used in the present study, as this is the most physiological position for assessment of the acetabulum and related structures[146,338]. Some authors advocate the use of computer tomography (CT) rather than conventional radiographs[310]. We believe that a conventional AP view with a minimal radiation dose following a strictly standardised protocol allows images of very high quality, and in particular allows weight-bearing images, which are recommended in the assessment of acetabular dysplasia. CT imaging can only be performed in the supine position. However, we recognise the need of CT and 3D reformatting tools when planning surgical interventions in dysplastic hips[152,173].

A correct posture was ensured by one particularly trained radiographer and a highly standardised radiographic protocol in order to avoid *pelvic tilting and rotation*[303]. The pelvic tilt was not assessed in a standardised manner, but all radiographs were subjectively evaluated by a senior musculoskeletal radiologist (KR). Obviously pelvic

positioning, i.e. the pelvic tilting, influences the 2D projection of the acetabulum, and hence the assessment of hip dysplasia and of pincer-type FAI, in particular the cross-over and posterior wall signs. Several techniques have been suggested to control for pelvic tilting on an AP pelvic view[300,319,321]. In paper IV, we considered using the distance between the coccyx and the symphysis[319], but found it difficult to assess in a high proportion of images due to overlying bowel-content. Kalberer and colleagues found a high correlation between the projection of the ischial spine into the pelvis and the acetabular retroversion as assessed by the cross-over-sign[163]. Although others have found this prominence of the ischial spine sign (PRISS or ISS) a valid marker for acetabular retroversion regardless of pelvic tilting and rotation[161], we were not able to reproduce their findings in a subset of 146 cases, and as such did not include ISS in our analysis.

All radiographs were evaluated in regard to *rotation*, by assessment of the Foramen Obturator Index (FOI). The two obturator foramina should be symmetric in appearance (as seen on figs. 8 and 9). Also, as reported in paper IV, we performed a small cadaver study that did not detect any visual changes of the femoral head-neck contour which might have indicated that excessive internal or external rotation on the AP view would produce a false positive cam deformity. Monazzam and colleagues, on the other hand, found that femoral rotation on AP radiographs did affect morphological features of the proximal femur related to FAI[222].

8.1.5 Definitions of radiographic measurements for hip dysplasia, FAI and early degenerative change at skeletal maturity

The centre-edge (CE) angle of Wiberg has become one of the most used parameters in the diagnosis of acetabular dysplasia. Wiberg initially proposed that the transverse axis be formed by an inter-centre line between the two femoral heads, although the inter-teardrop line is often used for this purpose[149], including in this paper for both the CE angle and the refined CE angle of Ogata. It is important to be aware of an ongoing discussion in the literature regarding the use of the lateral edge of the bony acetabular

rim vs. the lateral point of the weight bearing sourcil. Many authors advocate the use of the superolateral point of the sourcil rather than the lateral edge of the bony acetabular roof when performing measurements such as Sharp's angle, acetabular angle of Tönnis, and also the CE angle of Wiberg which then corresponds to the refined CE angle of Ogata[2,146,242,244]. The present study population is young and without the formation of lateral osteophytes, but this should be kept in mind when analysing radiographs in older age groups[192]. The radiologist should clearly state which of the two lateral points are used in order to avoid confusion.

The femoral head extrusion index (FHEI)[71,138] is also called 'femoral head coverage' or 'acetabular head index'[189]. Some authors use the FHEI to describe the opposite, i.e. how much of the femoral head lies laterally to the acetabular edge[218], also termed 'migration index'[149]. Sharp's angle was originally described as 'angle of inclination of the acetabulum'-'the acetabular angle' by Sharp[293]. It has occasionally been referred to as 'AA' in the literature. However, 'AA' is more commonly used to designate the acetabular roof angle of Tönnis (AA)[332,333]. This angle also has various synonyms, including 'horizontal toit externe' (HTE)[198,226], 'acetabular roof obliquity' (ARO)[208,217], and also 'acetabular index' (AI), a term originally proposed as a measurement in children with open triradiate cartilage, where the inter-triradiate-line (Hilgereiners line) is used instead of the inter-teardrop line[334].

In the acetabular depth-width ratio (ADR) the depth was originally measured along a line running perpendicularly from the width line to the deepest point of the medial sourcil arc[64,313]. The depth of this present study was measured slightly different to the original, corresponding to the perpendicular depth at the midpoint of the width, rather than the depth given by the deepest medial sourcil point, although they often coincidence. Another depth-width ratio is also proposed in the literature, that of Heyman and Herndon from 1950, using the inferiolateral point of the acetabulum rather than the teardrop tip, and the ratio is multiplied by 100 instead of by 1000[138].

The acetabular sourcil shape as a marker for acetabular dysplasia in paper II and the cam- and pincer-type findings presented in paper IV were subjectively assessed,

according to existing literature. In particular, the need to estimate the femoral head centre in order to score the posterior wall sign might prove challenging on gross visual inspection. It might be discussed whether the lateral flattening of the femoral head per se is a valid marker for cam-type impingement, as it describes the shape of the head more than the femoral head-neck junction[53]. According to recommendations by Clohisy and co-workers, it should be assessed on both AP and lateral views.

For the alpha angle in paper VI, three factors might influence the result of the alpha value: The diameter and position of the reference circle relative to the femoral head, the evaluation of the exact alpha-point where the cam deformity is said to extend outside the reference circle, and also the evaluation of the narrowest part of the neck in order to establish its longitudinal axis. As for the CE-angle, we chose >45° as an indicator for pincer-type overcoverage, in accordance with Gosvig and colleagues[118]. Values >40° are also often used to indicate acetabular overcoverage[320].

The joint space width (JSW) was measured at three positions, namely medially, centrally and laterally[147]. In paper III, all three values are reported, rather than just the smallest value for each subject, in order to establish all three reference intervals. In paper II, the minimum JSW as a discriminator for early degenerative change was assessed, both as three continuous variables and as one variable categorised as normal or pathologic, defined as minimum JSW≤2 mm in at least one position.

8.1.6 Validity and reproducibility of radiographic measurements

Knowledge of the intra and intervariability of measurements and measurement methods is important when interpreting results. The terminology is often confusing. The *reproducibility* of a measurement concerns de degree to which repeated measurements yield similar results[70]. This term can be seen as an umbrella term for the concepts of *agreement* and *reliability*. For continuous variables, measurement *agreement* within or between observers and methods can be expressed by the 95% limits of agreement (LoA) proposed by Bland and Altman[32,33], and easily visualised through so-called ‘Bland-Altman plots’. The *reliability* can be expressed by the

calculation of intraclass correlation coefficients (ICC)[219], in numerous ways. The *agreement* parameter reflects how good the agreement between repeated measurements is, taking into account the measurement error. This allows for a pure characteristic of the measurement instrument. The *reliability* parameters assess how well study subjects can be distinguished from each other, despite measurement errors. The measurement errors are related to the variability between the study subjects, which makes the reliability parameters highly dependent on the heterogeneity of the study sample and therefore only generalisable to samples with a similar variation. Agreement parameters will be more stable across different population samples than the reliability parameters, and thus have a higher validity. Another advantage of the agreement compared to the reliability parameters for the clinical interpretation is that agreement parameters are expressed on the actual scale of measurement, and not as a value between 0 and 1, which is the case for the reliability. The choice of reproducibility parameter is debated. Despite the criticisms mentioned above, ICC values are often the only reported parameter in measurement studies. We chose to include the ICC together with 95% limits of agreement for the assessment of reproducibility for the continuous measurements of hip dysplasia in the digital measurement program, as discussed in a previous paper not part of this thesis[86], and also for the alpha angle on the frog-leg lateral view (paper VI). The ICC values found for the alpha angle in paper VI compared well with other studies[56,116,218,261].

The digital measurements for hip dysplasia were performed by one of three investigators; however, efforts were made to standardise the measurements prior to study start. Intra- and inter-observer variation for the measurements have been shown earlier to differ to some extent, with poorer results for the measurements with lower absolute values, namely the AA and the JSW[86]. Intra- and inter-observer variation and subsequent measurement errors related to a measurement performed in a study is likely to increase further during everyday clinical practice, due to more observers, varying experience of the observers, less standardisation of both radiographs and measurements, and a tighter time schedule. Subjective assessment is likely to require more experienced readers, and it might be more difficult to compare the results

between studies. Recently, several papers have assessed the reliability and agreement of common measures used in radiographic evaluation of the adult dysplastic hip, as described by Mast and colleagues[218]. Taken together, the results from several papers indicate clinical utility of the radiographic hip measures, based on their reliability and agreement. Some studies have also reported on limited reliabilities for some of the most common measures[46,54]. One paper found that the reproducibility improved when angles were drawn as compared to subjective assessment of the same measurement[339]. Similar findings have been shown for the alpha angle in FAI[238].

For categorical variables, kappa (κ) values for agreement are used[183]. The intra- and interobserver agreement for the quantitatively assessed markers for cam- and pincer-type FAI and fibrocystic change as described in 6.2.6 compared well with other studies[151,165,218]. Clohisy and co-workers found lower values for both the head sphericity and the head-neck offset as assessed subjectively[54]. In the present studies, the experience of the observers varied, although detailed standardisations were performed. This also introduces the possibility of an induced correlation between the observers' readings affecting the inter-rater variability, due to the standardisation of 10-20 images prior to interobserver readings. The use of a digital measurement program proved efficient and accurate for measurements related to both hip dysplasia and FAI, as discussed previously. In particular, the automatic appearance of a circle of best fit based on the four curser-placed points when measuring the alpha angle appeared to be a more precise and efficient method than using the hard plastic sheet with embedded concentric circles ad modum Mose.

8.1.7 Ethical considerations

Taking radiographs of healthy young adults needs consideration. By using fully digital equipment, the *total mean radiation dose* for both the AP and the frog-leg view together was 0.5 $Gycm^2$, corresponding to an effective dose of 0.15 mSv for both radiographs together. The effective dose in the present study without gonadal shields equaled 2 weeks of daily background radiation in Norway, given that the daily background radiation in Norway is about 0.01 mSv[236]. In addition, gonadal shields

reduced the effective dose further, up to 50-80%. The ethical aspect of incidental findings in healthy individuals should also be addressed. During the study period 2007-09, 15 subjects presenting with uncertain or severe incidental clinical and/or radiographic findings related to hip, back or pelvic pathology were immediately scheduled for an appointment with a senior radiologist (KR) or a senior paediatric orthopaedic surgeon (LBE), as appropriate. Last, salivary samples for later genetic analyses were provided on a voluntary basis, and carried out after detailed oral and written information and the signing of a special consent form. The specimen will be used only for the intended purpose related to hip dysplasia.

8.2 Discussion of results

8.2.1 Selective ultrasound screening for DDH – a reasonable approach (Paper I)

Paper I suggests that the selective US screening programme applied is a reasonable approach. In the study, 11539/81564 (14.1%) newborns were defined as ‘at-risk’ and had a hip US performed. Other studies that describe selective US programmes based on risk factors including clinical hip instability, report on varying rates of selectively screened babies (table 4). Comparisons with other studies that report experiences of selective US screening programmes in addition to routine clinical screening can be challenging. The observed variations are likely to reflect different protocols, US techniques, definitions of disease and indications for treatment as well as true differences in the prevalence of DDH in the different populations. Large variations in treatment rates are seen between different screening strategies, as some centres advocating universal US screening have reported at treatment rates as high as 77 per 1000[5]. In our study, 3.0% received early treatment; 2.3% from birth and 0.7% after six weeks or more of initial watchful waiting, i.e. clinical and US follow-up. Another 3.3% normalised spontaneously after watchful waiting and were thus not in need of treatment. The observed decrease in annual, early treatment rates was partly due to

watchful waiting rather than treatment of mild DDH, reflecting better adherence to the implemented screening programme. This gradual change was encouraged by an ongoing RCT that showed that there were no differences in radiographic outcome at six years of age between children who did or did not receive abduction splinting for mild DDH from birth[42,279]. The delayed acetabular ossification or persistent dysplasia seen in a third of infants from both groups at one year of age had resolved spontaneously in all but one of the females from the treatment group.

Table 4: Studies reporting on programmes of selective ultrasound screening

Author, year	Country, Study years	Number screened with US per total live births (%)	US method	Rate of treatment, per 1000	Rate of late cases, per 1000	Rate of first surgical treatment, per 1000
Clarke[51] et al '89	UK, 1986	448/4617 (9.7)	Dyn	3.7	0.6	-
Boeree[35] et al '94	UK, 1988-92	1894/26952 (7)	Stat/ Dyn	4.4	0.22	0.4
Rosendahl[281] et al '94	Norway, 1988-90	518/4388 (11.8)	Stat/ Dyn	20	0.7	0.23 [a]
Lewis[207] et al, '99	Wales, 1988-92	2683/17792 (15)	Stat	NR	0.34	NR
Paton[252] et al '02	UK, 1992-2000	1806/28676 (6.3) [c]	Stat/ Dyn	NR	0.39 [b]	1.5 [d]
Holen[142] et al '02	Norway, 1988-92	872/7689 (11.3)	Stat/ Dyn	8.6	0.65	0.13 [e]
Clarke[52] et al '12	UK, 1988-2008	20344/107440 (18.9) [c]	Stat/ Dyn	7.2	0.34	79
Laborie et al '13	Norway, 1991-2006	11539/81564 (14.1)	Stat/ Dyn	30	0.32	0.25

Stat=static US method, Dyn=dynamic US method, NR=not reported. [a] calculated as 1/4388 based on one reported patient, [b] Reported in 1999, when 20452 newborns were included[253], [c] US at 2 weeks if clinical instability detected at birth, US at 6-8 weeks if anamnestic risk factors present, [d] calculated as 0.87/1000 for dysplasia + 0.63/1000 for dislocations =1.5/1000, [e] calculated as 1/7689 based on one reported patient.

Several observational studies have shown that 97% of sonographically immature (Graf type IIa) hips will normalise spontaneously within the first three months of life[72,184,281,336]. Lower rates of spontaneous normalisation have also been reported, followed by a recommendation that these hips should be followed by US[121]. The present study supports the view that stable, immature newborn hips can safely be discarded without further sonographic follow-up or treatment. On the other hand, there is some disagreement regarding the significance of isolated hip instability (pathologically unstable/dislocatable/dislocated hips). Some authors have reported results indicating that a co-existing instability seems to have no importance in morphologically normal newborn hips[270,274]. According to our protocol, newborns with pathological hip instability (i.e. subluxatable but not dislocatable/dislocated hips) as detected clinically and/or sonographically are subject to watchful waiting for six weeks before clinical and sonographical re-examination. This is in line with the idea that concentric reduction of the hip is important for normal acetabular development. As for the indication of treatment, there is no consensus regarding what degree of sonographic abnormality warrants treatment[74,359]. It is reasonable to believe that many children are treated unnecessarily[27]. Universal US screening has been associated with higher treatment rates than selective US screening[281], although a review found the treatment associated with universal US screening to be usually shorter and less intrusive[359]. The authors reporting at the results from the UK Hip Trail further stated that the use of selective US for babies with positive findings at the neonatal clinical screening, reduces the treatment rates as compared to clinical screening alone[84].

In our study, family history of DDH was the most frequent risk factor, in agreement with a recent review[294]. However, there is no consensus on the best way to measure the different risk components, and calibration of risk scoring methods in different populations is frequently poor. Future identification of susceptibility genes for DDH may help improve the validity of methods and their effectiveness in guiding management decisions[93].

The major objective of the selective US screening programme was in fact met, in that the rate of late subluxated or dislocated hips was significantly lower than those based

on a previous RCT, and on historical data (0.32 vs. 1.3 and 2.6 per 1000 births, respectively)[281]. The rate compare well to other studies that report on selective US (0.2-0.7 per 1000) (table 4) or universal US screening (0.13-0.3 per 1000)[142,281]. The rates of late detected cases of subluxated/dislocated hips in the setting of a selective US screening programme vary in the literature, and rates are not always comparable due to different definition of 'late', as some studies define it as after 4 weeks[142,281], whereas others use 12 weeks[35,52], 6 months[252] or even later. The rate of late detected cases of subluxated/ dislocated hips is often used as an outcome in the evaluation of screening programmes, and the goal of an ideal programme can be expressed as the eradication of late detected cases. This emphasises the importance of a high-quality newborn clinical screening in order to try to find all unstable hips detectable at birth[125,178,212].

Interestingly, no screening programme has succeeded in eradicating all late cases. However, the natural history of 'late' cases of DDH is not entirely understood. Some authors explain this by the fact that some late detected cases are likely to have featured undetected acetabular dysplasia at birth, which may evolve into established irreducible dislocation if left untreated[158]. The development of a clinically and sonographically normal newborn hip into later dislocation appears less likely based on our data, since all but three of the late presenting cases in our survey were low-risk babies. In our study, 26 (0.32 per 1000) cases of subluxated/dislocated hips were detected late (after one month of age). 24 of these had not had a hip US performed. In retrospect, no additional risk factors but female gender could be identified for these children. This compares well with other studies[35,52,142] that reported that all their late detected cases were among the low-risk babies who had not received US. Only two of the 26 babies were boys, confirming the pronounced gender-difference of late cases[31,80]. Also, 125 of the 126 cases with late residual dysplastic but stable hips (not included in the rates of late detected cases with subluxation/dislocation) were judged to have clinically stable hips at birth and did not have any other risk factors, and thus had not been screened with US at birth. These 126 children were mainly referred for asymmetry on hip abduction, which in absence of subluxation is positional due to e.g.

preferred sleeping position, secondary to torticollis. The natural course of acetabular dysplasia remains unknown, but radiographic residual dysplasia has been shown to occur in 2-3% of healthy five months old children without any risk factors[43]. This suggests that at least the majority of these infants would have recovered the following months, without treatment. It is not unlikely that many of these late detected cases of residual acetabular dysplasia, as well as the cases of dislocated hips, would have been detected as dysplastic hips at birth if examined by US. On the other hand, the relatively low rate of late detected subluxations and dislocations in our study suggests that a universal US screening programme may not be cost-effective, since it would require considerable resources both for initial screening and follow-up[284]. We therefore support an approach based on selective US, at least in areas with low prevalences of late detected cases. This is in keeping with the newly published guidelines from the European Society of Paediatric Radiology (ESPR) task force group[13].

The rates of surgery or the need of a first surgical intervention or operation procedures, have also been used as a surrogate outcome for screening programmes. Previous studies have reported at rates of one child per 1000 live births that will eventually require surgical treatment for established subluxation/dislocation, in an unscreened population[211,291]. In a report from 1998, the Medical Research Council (MRC) Report on Congenital Dislocation of the Hip found that the scientific basis for conducting a neonatal clinical screening programme was weak, and concluded that the routine clinical examination in newborns had not reduced the rate of late detected cases that required surgical treatment[112]. We found the rate of children in need of a first surgical treatment before five years of age to be 0.38 per 1000, similar to a rate of 0.4 per 1000 reported in another selectively screened population[35]. A significantly decreased rate of ‘first surgical intervention’ from 0.78 to 0.26 per 1000 children aged from ten weeks to five years was also shown after a universal US screening programme was established in Germany[343]. The same German group recently performed a case-control study that also confirmed that universal US screening reduced the rate of first operative procedure for DDH, although they acknowledged

the need for further studies addressing potential overtreatment and adverse effects of treatment[344].

We found as few as seven cases of avascular necrosis of the femoral head (AVN) as a complication to treatment in our study (2.7 per 1000 treated infants). All of the seven affected infants had initial pathology in the equilateral hip. Four of the cases occurred in high-risk infants, of whom three had received abduction treatment from birth while the last had had an open reduction at birth. Only one of these four high-risk cases, a pre-term baby girl presenting with a dislocated and severely dysplastic hip at birth, did not have surgical treatment performed. The three cases of AVN detected in the low-risk group, i.e. those who did not fulfil the criteria for a hip US at birth, were all late detected cases of subluxated/dislocated hips requiring surgical treatment. These results indicate a very low risk of AVN following routine abduction treatment with a Frejka's pillow. This is further supported by findings from paper II, showing that increased treatment rates were not associated with increased rates of AVN. The overall low rate of AVN associated with the selective US screening programme carried out in our institution is also likely to reflect low rates of first surgical treatment procedures. A thorough review based of in total 17 articles defined AVN as the primary complication of DDH therapy, and studied the incidence of AVN depending on the age of the patient at time of referral, and on the type of treatment received[194]. They found that after early referral (within the first two months of life) the rates varied substantially, from 0 to 123 per 1000 infants referred. Rates as high as 216 cases of AVN per 1000 children referred, were seen in the late referred group. These numbers show increased risk of AVN following late rather than early referral and treatment.

The concept of watchful waiting for at least six weeks for those presenting with clinically stable but mildly dysplastic hips at birth proved helpful as hips in four out of five infants normalised spontaneously within the first six months. At some centres, the selective US screening and thus the start of treatment is delayed until 2-6 weeks of age[52,253], presumably causing lower treatment rates as cases of transient neonatal instability will have the time to recover spontaneously. We have suggested four

arguments against delayed US screening. Firstly, treatment may be unduly delayed in newborns with clinically undetected but severe pathology on US. This was true for one in ten of those treated from birth in this study. This figure is conservative as some of the dislocatable or dislocated hips were first acknowledged at the clinical re-examination after first being identified on US. Secondly, knowledge of the baseline appearance of the newborn hip will help interpretation of clinical and sonographic development during the first six weeks, and thus allow for personalised management decisions. Thirdly, postponing hip US to six weeks or later will increase costs as all babies would have to be scheduled for out-patient radiology and paediatrics visits. Finally, some babies may not show up at six weeks due to lack of parental compliance.

Most authors agree that US should play an important role in detecting cases in need of early abduction treatment and in monitoring the treatment. In a recent review from 2011, Shorter and colleagues for the Cochrane Neonatal group assessed the effect of different screening programmes for DDH on the incidence of late presentation of dislocations[297]. They concluded that there is 'insufficient evidence to give clear recommendations for practice'. In contrast, a thorough decision analysis performed by Dezateux and co-workers in 2003 concluded that US-based screening strategies appear to be most effective and sensitive, although also associated with higher risks of potential adverse iatrogenic effects in unaffected children[73]. A review from 2007 recommended a selective US screening approach in areas with high prevalence of late detected cases, given a well-organised screening programme of high quality is available[285].

Several cost-effectiveness analyses of different screening strategies have been undertaken. A robust analysis associated with the UK Hip Trial found that the use of US in the diagnosis and management for DDH could reduce costs to families and health services[84]. A decision analysis of the utility of screening for DDH performed by Mahan and colleagues in 2009 indicated that selective US screening in addition to routine clinical screening was associated with the highest probability of having a hip free of osteoarthritis at age 60 years and appeared to be the best strategy[213]. Following

the meeting of the ESPR task force group in 2011, recommendations including a selective US approach, a combined static and dynamic US examination and a standardised report form were agreed upon[13]. It was also stated that if selective US screening proves inefficient in decreasing the prevalence of late cases, a universal US screening approach should be considered. In their recommendations, emphasis was put on the importance of a high-quality US screening, as well as on the training of the staff performing the US examinations.

The importance of highly qualified examiners both for the clinical and the sonographic examinations has been emphasised on several occasions throughout the literature[212,278,307]. It seems clear that no screening programme will succeed in abolishing late cases unless great efforts are made to standardise the screening routines and optimise the clinical and US examinations. Well-organised surveillance programmes in child health centres or similar structures are necessary, with regular visits preferably during the first two years of life, in order to clinically detect late cases[12,307].

The early detection of DDH does not entirely fulfil the criteria required for a technique of screening or for a disease to be screened[97,358]. This is related to the incomplete understanding of the natural course of disease, the lack of universal agreement on early treatment and the varying reports of the accuracies of both clinical and sonographic tests, amongst others, although the condition is recognised as an important problem. In fact, the change of terminology as proposed by Jones in 1998[157] from ‘screening’ to ‘surveillance’ when discussing diagnosis and management seems appropriate, supported by the need of continuous vigilance during infancy.

In the light of the ongoing debate of different screening strategies and the difficulties met for most of all the extensive review articles dealing with this topic when trying to create guidelines and recommendations, we support a well-organised screening programme based on general routine clinical screening with a selective US of those with risk factors including clinical hip instability as the strategy of choice, at least in areas with a low prevalence of late detected cases.

8.2.2 Long-term outcome of different screening strategies in newborns (Paper II)

Our study confirms that rates of radiographic findings indicating acetabular dysplasia and degenerative change of the hip joint in young adulthood were similar across the three screening groups. Offering universal hip US, and treating those testing positive, had no additional impact on acetabular shape at a group level, or on the numbers of immature or mildly dysplastic hips identified at skeletal maturity. Assessment of acetabular dysplasia at skeletal maturity is important as it is associated with early onset hip osteoarthritis[131,149]. We have previously shown that the prevalence of acetabular dysplasia varies between 1.7% and 20% in this cohort, depending on which measurements and which cut-off values are being used[85]. This highlights an important challenge in the diagnosis of acetabular dysplasia at skeletal maturity. Despite the large variation in prevalences according to the different measurements, no clear differences were seen between the three groups for any of the measurements. The results from the present study must be interpreted with care as the original trial was not designed with sufficient power to detect such differences between the three groups at time of follow-up in young adulthood.

Increased treatment rates following US screening were not associated with avascular necrosis (AVN). An important aspect of AVN is the fact that it can be an iatrogenic complication of treatment in children who are treated based on a false positive diagnosis of DDH. AVN might lead to premature osteoarthritis[63,115,250].

The wide variety of management strategies used for DDH reflects our poor understanding of its natural course and the short- and long-term effects of different treatment and follow-up programmes. Based on a follow-up study of 468 adults, Hartofilakidis and colleagues suggested that dysplasia, low dislocation, and high dislocation in adults are the results of untreated dysplasia, subluxation, and complete dislocation in infancy, respectively[136]. Several comprehensive and well-performed reviews have proven unable to provide clear guidelines as to screening strategy and the role of US in neonatal DDH screening the last decade[194,250,296,297,359]. As pointed

out by Bracken, 'the main controversy regarding US screening is the lack of good quality evidence linking screening to improved functional outcome for patients'[40]. US is able to identify newborns with dysplastic and unstable hips in need of early treatment, thus reducing the number of late, subluxed or dislocated cases in early childhood. It remains unconfirmed whether those at risk for isolated acetabular dysplasia at skeletal maturity can be identified as newborns, and whether early abduction treatment has the ability to prevent that dysplastic acetabulae persist or develop[74,158]. While detection of neonatal instability or dysplasia remains the aim of the screening test, prevention of pain, limitation of function and disability due to dislocated and subluxated hips and prevention of osteoarthritis associated with isolated acetabular dysplasia in childhood remain the aims of screening.

8.2.3 Reference intervals for acetabular dysplasia in young adults (Paper III)

Updated gender-specific reference intervals for common radiographic measurements used in the diagnosis of acetabular dysplasia at skeletal maturity were presented in paper III. Overall, similar or slightly wider reference intervals based on the appropriate 2.5/97.5 percentiles were found, as compared to cut-off values often used in the literature. The gender difference was statistically significant for all measurements except the FHEI and the AA, emphasising the need for gender-specific intervals.

For Sharp's angle, the mean values of 38.8° in males and 40.7° in females are slightly higher than several of the other studies performed on AP radiographs (table 5), and reference intervals for both males and females are slightly wider than earlier presented in the literature. Cut-off values of >42.3°, ≥43° and ≥45° have been proposed[229,313,332]. Sharp initially proposed a normal range of 33°-38°, with 39°-42° as an upper normal limit[293].

Table 5. Mean and SD values for radiographic measurements for acetabular dysplasia at skeletal maturity, compared to other studies

Radiographic measurement, Author, year	Country, sex (M,F), age, side (R/ L/ R+L [b])	Mean (SD), Males	Mean (SD), Females
Sharp's angle (°)			
Jacobsen '05[149]	Denmark, 1429M, 2430F, 22-93 yrs, R	37.0 [a] (3.5)	39.1 [a] (3.7)
Jeremic '11[155]	Serbia, 170M, 150F, 21-65 yrs, R+L	37.5 (3.6)	38.5 (3.9)
Laborie '13	Norway, 841 M, 1170 F, 19 yrs, R	38.8 (3.49)	40.7 (3.52)
AA of Tönnis (°)			
Jeremic '11[155]	Serbia, 170M, 150 F, 21-65 yrs, R+L	6.2 (4.9)	9.0 (6.0)
Laborie '13	Norway, 841 M, 1170 F, 19 yrs, R	5.64 (4.8)	5.84 (4.9)
ADR (‰)			
Jacobsen '05[149]	Denmark, 1429 M , 2430 F, 22-93 yrs, R	293 [a] (38)	304 [a] (41)
Laborie '13	Norway, 841 M, 1170 F, 19 yrs, R	294.5 (34.9)	297.7 (35.8)
CE Wiberg (°)			
Shi '10[295]	China, 45 M, 55 F, 19-30 yrs, R+L	31.7 (6.1)	30.0 (5.2)
Jeremic '11[155]	Serbia, 170M, 150 F, 21-65 yrs, R+L	33.6 (5.8)	31.3 (6.9)
Laborie '13	Norway, 841 M, 1170 F, 19 yrs, R	32.1 (6.1)	31.0 (6.1)
Ogata (°)			
Jacobsen '05[149]	Denmark, 1429 M , 2430 F, 22-93 yrs, R	35 [a] (7.3)	35 [a] (7.4)
Laborie '13	Norway, 841 M, 1170 F, 19 yrs, R	30.4 (6.3)	29.1 (6.3)
FHEI (%)			
Jacobsen '05[149]	Denmark, 1429 M , 2430 F, 22-93 yrs, R	12.0 [a] (8.7) [c]	8.0 [a] (7.8) [c]
Aly '11[8]	Egypt, 134 M, 110 F, 18-60 yrs, R+L	86.6 (4.7)	84.0 (4.0)
Laborie '13	Norway, 841 M, 1170 F, 19 yrs, R	86.0 (6.3)	85.6 (6.6)

[a] median values; [b] values based on both right and left hips together; [c] percentage of uncovered portion (lateral migration index), equals the inverse FHEI value. M=males, F=females, yrs=years.

For the AA angle of Tönnis, mean values of 5.6° and 5.8° for males and females separately are presented, with corresponding 97.5% cut-off values of 14.8° and 15.6°. Other studies report varying results with mean values ranging from around 3° to 10°[126,155]. Tönnis supported findings by Lequesne, and proposed 10° as an approximate upper normal limit, based on extensive work on AA in children and corresponding measurements in adult hips[198,333]. Interestingly, the results of the present study compare better with a cut-off value of >15° suggested by Nakamura[229], although ethnic differences in DDH risk and pelvic configuration must be kept in mind when comparing an ethnic Norwegian with a Japanese population. Previously published data have shown a non-negligible intra- and inter-observer variation in relation to the AA measurement[86]. As for the ADR, mean values of 294.5‰ and

297.7‰ for males and females respectively were found, giving 2.5% cut-off values of 235 and 233‰. The most used cut-off value in the literature has been <250‰[64]. The CE of Wiberg had mean values of 32.1° and 31.0°, with corresponding cut-off values of 20.8° and 19.6° for males and females, respectively. The CE angle was originally described in 100 (50 males/50 females) healthy Swedish subjects, and reported to have a physiological range of 20-40°, with cut-off values of <20° indicating dysplasia, 20°-25° indicating borderline cases, and >25° indicating normal hips[356]. These cut-off values have been confirmed by others[11,98,154,313]. The mean values of the present study compare well with other studies[3,155,229,295]. The Danish study used the lateral margin of the subcondral sclerotic 'sourcil' as the lateral point when measuring the CE angle, identical to the modified CE angle of Ogata, favoured by Ömeroglu et al[244]. The Danish study reported median values of 35° for both males and females, respectively. In the present study, the Ogata angle had mean values of 30.4° and 29.1°, with corresponding cut-off values of 18° and 17° for males and females, respectively. These figures are lower than figures found in the Danish study. However, Park and colleagues have shown that the CE angle increases with age, and it is possible that age-related alterations in the sourcil-shaped weight bearing zone could partly explain this difference, as the Danish study group ranges from 22 to 93 years[248].

The femoral head extrusion index (FHEI) was originally presented with a normal range of 70-100%, with an average of 90%[138], with reference to the amount of femoral head covered by the acetabular roof. A cut-off value of <75% was later proposed[64]. This has been supported by findings by the Danish group, presented as an inverse index, called the *lateral migration index*, with values above 25% being indicative of dysplasia[149]. The results of the present study compare well with previous findings[8], with cut-off values of 74% and 73% for males and females, respectively. Overall, the findings of the present study compare well with previously published data, also in terms of gender and age.

The joint space width (JSW) is well accepted as a radiographic discriminator of hip osteoarthritis (OA)[99,113,148,185]. Fredensborg originally measured JSW both vertically

and horizontally radiating from the head centre, and he also obtained an integral JSW, based on the average from nine measurements in the superior part of the joint. He concluded that the vertical JSW was a good measurement used alone, and that the normal value varied between 3 and 5 mm, on average slightly above 4 mm[99]. Lanyon and colleagues measured the JSW at the site of maximum narrowing and reported a mean minimum JSW of 4.1 mm in 433 males and of 3.8 mm in 598 females (both mean age 64 years)[185]. In a Turkish study by Goker and colleagues, 17 males and 14 females (age 20-29 years) demonstrated a mean value (SD) of 3.67 (0.65) mm for the right hip, measured in the narrowest of three locations. They found that values were significantly lower in females compared to males, but no longer after adjusting for height[113]. However, the studies by Lanyon and colleagues and Goker colleagues were performed with supine urograms and abdominal radiographs, respectively, whereas the weight-bearing AP position has been shown to be favourable for assessment of hip dysplasia[149,338]. Lequesne and colleagues measured minimum JSW in the three locations on pelvic supine radiographs of 96 males and 127 females (mean age 51.3 years) without any hip-related problems, and found lower values in females, and overall higher values in the lateral position[200]. Jacobsen and colleagues measured the JSW radially in three locations of the hip joint; at the lateral end of the sourcil, in the central position corresponding to the vertical axis through the head centre, and at the medial end of the sourcil[148]. They found right-sided minimum JSW values of 3.88 mm in males, and 3.91mm in females.

The minimum JSW represents the lowest value regardless of the three positions in the joint, and a value of ≤2mm indicates OA. The study in paper III reports on values from three locations, since the aim of the study was to highlight reference values based on the two 2.5% extremities, rather than prevalence of disease. A statistically significant difference for gender in each of the three locations was found, and for side in the central and lateral location. Again, attention should be drawn to the clinical significance of these results, as a quite large intra- and inter-observer variation for the JSW has previously been shown[86].

Knowledge of the reference intervals is important when interpreting radiographic measurements. Values outside these percentile-based ranges are not, however, necessarily pathological, but rather values in the top or bottom 2.5% extremities of the normal ranges. None of the results were altered significantly when similar analyses were performed excluding the 102 subjects who were treated for DDH as newborns. Measurement values obtained in clinical practice should also be interpreted in the light of the varying intra- and inter-observer variations for each of the measurements[86].

8.2.4 Qualitative and quantitative radiographic findings related to FAI in young adults (Papers IV+VI)

Femoroacetabular impingement (FAI) has become a well-recognised clinical concept. Knowledge of the prevalences and reference intervals of radiographic findings thought to be associated with FAI in healthy young adults might prove helpful in establishing accurate diagnostic criteria and management strategies for this condition. Radiographic cam-type features include a pistol grip deformity, a focal prominence or bump to the anterolateral or anterosuperior aspect of the femoral neck, or a lateral asphericity of the femoral head. We have shown that radiographic features suggestive of cam- and pincer type FAI are quite common in a population of healthy young adults, especially in males, with a high degree of coexistence between most findings (paper IV). With respect to the findings suggestive of a cam-deformity, our results are similar to those of others (table 6). In a study of 244 unselected, asymptomatic young males, cam-type deformities as assessed by a scoring system on magnetic resonance imaging (MRI), were seen in nearly one fourth of all subjects[268]. A smaller MRI study of 200 healthy adults, assessing the cam deformity by measuring the alpha angle, also reported at similar results, with a pronounced gender-difference[124]. In a cross-sectional population-based study of 3620 subjects (mean age 60 years) a pistol grip deformity was found in one fifth of males and in 5% of females[118].

Table 6. Prevalences of FAI in males (M) and females (F) based on radiographic cam-type findings, compared to other studies

Study, year, country	Study population	Prevalence of FAI, based on radiographic cam findings	Radiographic modality and cam-type FAI findings
Gosvig et al. 2008,[117] Denmark	3202 (1184 M, 2018 F)	M: 17%, F: 4%, age range, 22-93 years	Standardised AP pelvic radiographs, gender-specific alpha angle values, and triangular index
Hack et al. 2010,[124] Canada	200 (89 M, 111F); mean age, 29 years (range, 21-51 years)	14% (M+F) (10.5% unilateral, 3.5% bilateral) M: 25%, F: 5%	MRI, alpha angle (>50.5°)
Reichenbach et al. 2010,[268] Switzerland	244 M; mean age, 20 years	M = 24%	MRI, scoring system for grading the maximum offset of the head-neck junction
Kang et al, 2010,[164] New Zealand	50 M (100 hip joints) Age range 15-40 years	At least one hip (M): alpha (>55°): 12% (6/50), (8% bilateral); decreased head-neck offset: 12% (6/50), all bilateral cases.	Abdominal CT scans, Alpha angle (>55°), decreased head-neck offset (<8mm)
Jung et al. 2011,[160] USA	380 (108 M, 272 F); M: mean age, 63 years (range, 27-93 years), F: 60 years (range, 26-91 years)	Pathological: 14% M; 6% F; Borderline 15% M; 6% F	AP pelvic CT scout, alpha angle. Pathological (≥ 83° M, (≥ 57° F); Borderline (69-82° M, 51-56° F)
Laborie et al. 2011, Norway	2060 (868 M, 1192 F); mean age, 19 years (range, 17-20 years)	At least one hip, M: 35% , F: 10%; Bilateral, M: 25%, F: 6%.	Standardised AP and frog-leg pelvic radiographs, subjective evaluation of cam type deformity (pistol grip, hump, laterally flattened head)
Chakraverty et al, 2013,[48] Wales	50 healthy adults (100 hip joints) (30 M, 20 F); mean age 31 (20-40) years	M: 60% (36/60 hips) F: 35% (14/40 hips)	Abdominal and pelvic CT scans.Alpha angle>55°; decreased head-neck offset (<8mm); pistol grip deformity

A smaller study of 380 healthy adults assessed the alpha angle on AP pelvic CT scouts, and confirmed the gender difference[160]. These last studies included assessment of only one AP view, with the possibility of missing anterolateral deformities. A small study of 50 healthy adults[164] assessed the cam-deformity by the alpha angle and the head-neck offset, and found positive findings in 12%, with high degree of bilateral findings.

A recent study on 80 asymptomatic females (mean age 19.3 years) found that 15 subjects had evidence of cam-type deformities although none were judged as definite. They concluded that definite cam-type deformities in females are rare compared to males[204]. Chakraverty and colleagues recently reported high frequencies of FAI-like findings on CT scans, and also proposed that the cut-off values for defining morphological abnormalities associated with FAI might have been set too low in the current literature[48]. They reported findings based on hips, not subjects, without any adjustments for a possible dependency between right and left hips within same subjects. They also reported high rates of two or more cam-type findings within the same hip, which is supported by our findings in paper IV.

Consensus on the best way to define cam-type FAI is lacking. Obviously, standardised radiographic protocols in particular with respect to tilting and rotation, and adequate radiographic views are important for accurate assessment, as discussed in 8.1.4. The clinical validity for each of the qualitative and quantitative markers needs a more detailed investigation. The alpha angle is often used as a quantitative measurement of the cam-deformity, although its accuracy and diagnostic value have been questioned[209,259,314]. Subjective assessment of the alpha angle was judged suboptimal in one study unless the observer was confident of a bone abnormality[238]. The alpha angle was first proposed on MRI scans, together with a pathological threshold value of 50° for both genders[237]. This measurement has been transferred to CT[22], and different lateral radiographs[53]. In the literature, threshold values for lateral views of all three modalities are commonly defined as 50° or 55°[4,237]. Recent studies of the alpha angle based on healthy populations indicate that these threshold values are set too low (table 7).

Table 7. Mean, standard deviation (SD) and/or range for the alpha angle on different radiographic views, as published in the literature

Author, year	Population	View	Mean (±SD)	Range	P-value*
Pollard et al,[261] 2010	83 healthy adults with normal hips (43 M, 44 F, mean age 46 (22-69) years)	Cross-table lateral, 15° internal rotation	M: 48° (±8°) F: 47° (±8°)		-
Toogood et al,[337] 2009	375 normal femora of adult skeletons (188 M, 187 F, mean age 44 (18-89) years)	Pelvic AP and a lateral view	AP: 53.5° (±12.7°), Lateral: 45.6° (±10.5°) M lateral: 47.5° (±10.7°) F lateral: 43.7° (±9.9°)	AP: 31.2°-111.5° Lateral: 16.9°-78.6°	<0.01 (lateral view)
Clohisy et al,[56] 2007	24 normal subjects (24 hips, mean age 35 (18-49) years), 46% F	Frog-leg lateral, cross-table lateral, and AP	Frog-leg: 43.7° (±12.1°), Cross-table lateral: 47.2° (±15.4°) AP: 51.2° (±15.7°),		-
Gosvig et al,[116] 2007	2803 healthy adults (1055 M, mean age 62 (23-93) years, 1748 F, mean age 65 (22-92) years)	Pelvic weight-bearing AP radiographs (left hips)	M AP: 53.1° (±13.9°) F AP: 45.5° (±5.1°)	M AP: 30.0°-94.0° F AP: 32.0°-108.0°	<0.0001
Laborie et al, 2013	2005 healthy young adults (837 M, 1168 F, mean age 18.6 (17.2-20.1) years	Pelvic frog-leg lateral and weight-bearing AP (right hips)	M, frog-leg: 46.9° (±8.4°) F, frog-leg: 42.3° (±5.7°) M, AP: 61.6° (±14.2°) F, AP: 51.9° (±14.1°)	M frog-leg: 26.2°-78.9° F frog-leg: 29.3°-75.6° M AP: 39.7°-105.2° F AP: 36.4°-103.4°	<0.0001 (frog-leg) <0.0001 (AP)

*gender difference, AP anteroposterior, M males, F females.

Higher threshold values of 62° for both males and females have been proposed based on the 97.5 percentile estimated from 83 individuals with normal hips[261]. Also, an increased cut-off value of 60° rather than 55° was recently proposed, in order to reduce false-positive results and still maintain an acceptable sensitivity[314]. The results from paper VI support the thought that threshold values often used in the literature seem to have been set too low for the lateral view. The alpha angle is also reported on the AP view in the literature[116,160], although the validity on this view is debated. A Danish study suggested gender-specific threshold values of ≥83° and ≥57° for males and females, respectively[116]. The reference intervals for the AP view in the study presented in paper VI are wide, and suggest that the existing threshold values are set too low, especially in females.

As reported in paper VI, higher alpha angles were associated with the presence of qualitative cam-type findings on both views. The random effects models, adjusted by sex and side, demonstrated significantly higher mean alpha values for those with qualitative cam-type findings compared to those without, on both views (all p values <0.0001). The mean alpha angle was 15.3° and 11.4° higher in those with a pistol grip deformity on the frog-leg view and the AP view respectively, compared to those without. For the frog-leg view, the largest differences in mean values for the alpha angles were seen for those with and without a pistol-grip deformity (15.3°), and thereafter for those with a focal hump (6.5°). For the AP view, the mean values for the alpha angles were equally larger (around 10-11°) for all three cam-type findings compared to those without.

The intra- and inter-reproducibility statistics for observers and for measurement technique were overall satisfying for the alpha angle. Others have also reported on good reproducibility results, presented as ICC values.[56,116,261]. However, the 95% limits-of-agreement method according to Bland Altman is preferable when assessing reproducibility of continuous measurements. Similarly, both intra-and interobserver reproducibility results were satisfying for the qualitatively assessed radiographic cam- and pincer-type markers, in accordance with other studies[151,165].

Taken together, radiographic cam-type findings are frequent among healthy adolescents, with males being three- to fourfold more likely to have findings suggestive of a cam-deformity than females. This gender difference is also reflected in the alpha angle measurement. The fact that so many healthy, asymptomatic young males have radiographic findings associated with cam-type FAI is intriguing.

Siebenrock and co-workers compared the prevalence and occurrence of a cam-type deformity on MRI in athletes during childhood and adolescence, with an age-matched control group who had not participated in sporting activities at a high level[298]. They demonstrated that the athletes had a tenfold increased likelihood of having an alpha angle greater than 55° in at least one measurement position, and suggested that high intensity sporting activity during adolescence is associated with a pronounced risk for developing cam-type FAI and possibly also subsequent early degenerative change. This hypothesis was first formulated by Murray and Duncan in 1971[228]. This is further supported by findings by Kapron and co-workers, who quantified the prevalence of FAI in 67 asymptomatic collegiate football players (age 21 ±2 years)[166]. They assessed the alpha angle (>50°) and the femoral head-neck offset (<8 mm) on frog-leg radiographs, and the CE angle, acetabular index (corresponding to AA in paper IV), the cross-over sign, and the alpha angle on AP radiographs. They found that the prevalence of both cam- and pincer-type associated findings were substantially higher than previously reported in the general population. 72% had an alpha angle >50°, 64% had a decreased femoral head-neck offset. 57% had both signs. 95% of the 134 hips had at least one sign of cam or pincer FAI; 77% had more than one sign. In accordance with these hypotheses, early preventive measures during childhood and adolescence by adapting type of activity and activity levels receive increasing attention.

For the pincer-type, radiographic features suggestive of pincer-type impingement include the cross-over sign (COS) and the posterior wall sign (focal overcoverage) and excessive coverage of the femoral head (global overcoverage) by the lateral acetabulum. In paper IV, we report on higher rates for all of the pincer-associated

findings in males than in females. The clinical pincer-type FAI is commonly seen in middle-aged women[105]. It might be that a higher rate of clinically silent radiographic pincer-type FAI exists in males, or alternatively several of the females with normal hips in our cohort will go on to develop clinically manifest pincer-type FAI over the next decades. Chakraverty and co-workers recently reported at high rates of pincer-abnormalities in a healthy young population, with as many as 36.7% male hips and 42.5% female hips having at least one pincer-characteristic[48].

We report on as many as 51.4% males and 45.5% females with a positive COS. These high numbers include all three levels of intersection, as described in 6.2.5[17]. It might be that only intersections on the lower level(s) are clinically relevant. 31 of the 446 male and 48 of the female participants had a positive score for COS in the middle third, and one additional male in the lower third. Based on a positive posterior wall sign, acetabular overcoverage and a positive COS in the middle or lower third, we found that 34.3% of males and 16.6% of females had one or more positive pincer-type findings. This gender difference was also shown in a prevalence study on elite soccer players (75 males and 20 females), where pincer morphology was seen in 26.7% of males and 10.0% of females, respectively[108].

The coxa profunda, i.e. a deep acetabular socket, is present radiographically when the floor of the acetabular fossa touches or lies medial to the ilioischial line. Although commonly viewed as an indicator for pincer-type FAI, recent reports advocate that this radiographic parameter should not be used, as it seems to be unrelated to acetabular coverage[9,232].

The high degree of coexistence (OR>2) was true in particular for the coexistence between the COS and the posterior wall sign. This multi-colinearity has already been described in the literature[17,273]. Around half of the subjects, both males and females, had a positive COS, with the majority crossing in the upper third. A positive COS indicates acetabular retroversion in the weightbearing position, as the upper part of the anterior acetabular wall lies more laterally than usual, and crosses over the posterior wall. A positive posterior wall sign indicates a deficient posterior wall.

According to Clohisy, the combination of these two signs indicates a true acetabular retroversion, while a positive COS alone indicates anterior overcoverage[53]. Our figures for both the COS and the posterior wall sign are high as compared to others[111], in part reflecting differences in pelvic positioning and definitions used for a positive COS. Obviously pelvic positioning, i.e. the pelvic tilting, influences the 2D projection of the acetabulum, and hence the prevalence of both the cross-over and posterior wall signs. However, a recent paper by Zaltz and co-workers showed that the COS is frequently present on well-positioned AP views without acetabular retroversion, i.e. the COS overestimates acetabular retroversion[369]. Tilting and rotation are discussed more in detail in 8.1.4. Werner and co-workers assessed the COS on the AP view of 1325 trauma-patients with presumably normal hips, and found that the presence of the COS was more common than first thought[355]. 48% had at least a mild overlap, i.e. intersection of the two acetabular walls in the upper third, and 40% had bilateral positive COS. Kang and co-workers assessed the diagnostic accuracy of the COS in the abdominal CT scans of 50 asymptomatic subjects, and found the sensitivity and specificity to be 71% and 88% respectively[164].

As for the acetabular overcoverage, a subjective assessment was performed in paper IV. A total of 14.6% males and 4.9% females had a positive finding. This overcoverage can also be quantified by the CE angle of Wiberg. Values greater than 40° or 45° are indicative of a deep acetabular socket with relative overcoverage of the femoral head. Kutty and co-workers recently assessed the reliability and predictability of the CE angle in the assessment of pincer-type FAI[181], and found that a CE angle ≥40° was a reasonably good predictor of FAI, with specificity and sensitivity of 100% and 84% respectively. Taken together, the pincer mechanism can manifest as either focal or global overcoverage, and there are several methods and markers to describe the condition. The presence of pincer-type findings are dependent upon the tilting and positioning of the pelvis.

In paper IV, we also assessed the prevalence of fibrocystic changes (FCC) at the femoral head-neck junction, seen in 5.8% of males and in 1.6% of females. We detected an association between FCC and the presence of either a cam-type or a

pincer-type deformity, especially the focal prominence. This confirms the thought that FCC may be a radiographic indicator of FAI, as described by Leunig and colleagues in 2005[201]. They reported a 33% prevalence of FCC in patients with underlying FAI, and suggested that these FFC located at the anterosuperior femoral neck were associated and possibly in a causal relationship with FAI. In contrast, another study on cam-type patients found such cystic changes in only 5% of the patients[168], and others have showed that such cysts, also called herniation pits, were not necessarily correlated with FAI findings[165,170]. Panzer and co-workers emphasised that in order to avoid overestimation of the incidence of FCC related to FAI, they have to be differentiated from other cystic-like appearances at the anterior femoral head-neck junction[247].

8.2.5 A positive clinical test for femoroacetabular impingement in young adults (Paper V)

The prevalence of clinically assessed FAI has been estimated at 10%-15% in a general adult population[203], as compared with our figures of 7.3% in males and 4.8% in females at age 19 years. The difference may in part be age-related, as the impingement test turns positive after labral damage has occurred; i.e. with time. The prevalences presented in paper V therefore are likely to be age-dependent, as there might be at-risk patients who have not fully developed the anterior acetabular labral disorder that will make the impingement test positive, even though they have typical radiographic cam-type findings. A study presenting the prevalence of cam type FAI morphology in 200 asymptomatic volunteers (89 men, 111 women; mean age 29.4 years) reported three of 200 patients (1.5%) had tested positive for anterior impingement[124]. Patients with ongoing hip or groin problems and/or earlier childhood hip problems were not included, which may explain the lower prevalence of positive tests compared with our results. As shown in table 6, numerous studies have reported the prevalence of radiographic cam type FAI. Overall, the radiographic prevalence in young males was higher than the prevalence of the positive impingement test. Follow-up studies are needed to understand if these radiographic cam-type findings actually

represent a potentially large amount of at-risk patients in a presumed presymptomatic FAI stage, or if they will remain clinically silent. The role of a positive impingement test in the diagnosis of FAI is not entirely defined. The reproducibility of the impingement test is discussed in 8.1.3: According to the literature, the sensitivity and specificity of the test for anterior impingement are 70% and 44%, when the test represents the most painful provocative movement[235]. In addition, patients with acetabular dysplasia could test positive. The specificity and the sensitivity parameters are not affected by the prevalence of a positive impingement test. However, they don't assess the accuracy of the impingement test in a clinically useful way. In contrast, the predictive values depend strongly on the prevalence, but are clinically useful, because they indicate the probability of a test giving the right diagnosis. A high positive predictive value of the anterior impingement test, i.e. the proportion of patients with positive test results who are correctly diagnosed was recently reported[127]. It is important to acknowledge that the specificity and sensitivity are calculated in relation to the diagnosis (i.e. a positive impingement test) although we cannot be certain that the diagnosis is always correct. In other words, specificity and sensitivity evaluate the ability of the impingement test to predict the diagnosis, not the true state of disease, as there is no definite gold standard for diagnosing FAI. A recent comprehensive review of the accuracy and validity of physical tests in the diagnostics of FAI and labral pathology found that none of the studies that have investigated these physical tests are of sufficient quality to provide a conclusive recommendation for clinical practice[197]. They therefore concluded that no physical tests are available to the clinician that can reliably discard or confirm the diagnoses of FAI and/or labral pathology of the hip.

It must be kept in mind that population-based studies with a cross-sectional design can assess prevalences and associations of disease and of related parameters, but cannot assess causal relationships. We found that radiographic cam-type findings were associated with a positive impingement test in males, for a composite score value of one or two findings. No such association was seen in females. Interestingly, we found no association between the alpha angle measurement and a positive

impingement test, in accordance with earlier findings[124]. The study in paper V used gender-specific cut-off values for the alpha angle on the AP view according to existing values from a Danish study: ≥83° in males, ≥57° in females[116]. In paper VI, we suggest that these cut-off values are set too low for the AP view. Similarly, Hack and colleagues use a cut-off value of <50.5° for the alpha angle assessed on MRI, which also appears to be a too low value according to the findings in paper VI and by other authors.

Ochoa and co-workers investigated the prevalence of radiographic FAI-related findings in a population of young, active patients with hip complaints, recruited from primary care and orthopaedic clinics[241]. They found that 94% of the 98 patients investigated had at least one radiographic FAI finding (cam-findings: alpha angle >50° on frog-leg view, pistol grip deformity; pincer-findings: CE angle ≥40° indicative of coxa profunda, CE angle ≥45° indicative of coxa protrusion, and cross-over sign). A total of 65% had signs of combined cam-and pincer features, while 17% had signs of pure cam-type FAI. Tibor and co-workers also recently assessed the presence of anatomic factors related to FAI, in patients with hip pain[328]. They concluded that several radiographic findings, including elevated alpha angles and CE angles and acetabular anteversion, were present in patients with hip pain but without associations between them. They therefore recommended individual assessment of each of the findings in painful hips.

The radiographic cam-type findings might be associated with lower-limb dominance in sporting activities, particularly those involving hip flexion, for instance, soccer. We found that a higher level of weekly physical activity was associated with positive tests in males. Others have found that 70% of patients with FAI participated in sporting activities, 30% of them on a high-level basis[235], supported by our results. As described earlier, increasing focus is put on the activity level and type of activity during childhood and adolescence, in relation to the development of cam-type FAI. It would have been interesting to know more details about the physical activity for the analyses in paper V.

Paper V also confirmed that a positive test is associated with decreased hip range of motion (ROM) in both genders for flexion, and for internal rotation and abduction in males. In a prospective study of 51 patients with FAI (29 males, 22 females; mean age, 35 years), 88% had positive tests for anterior impingement, and internal rotation and flexion were confirmed to be reduced in symptomatic patients with FAI[17]. Kapron and colleagues and Audenaert and colleagues have also shown that internal rotation is correlated to radiographic cam-type findings[15,167]. It might be that combinations of an increased activity level, perhaps accompanied by an increased arc of movement, on one side and the durability of the labrum on the other side act together and contribute to trigger if, and when, a normal hip should develop clinically symptomatic FAI.

8.2.6 Challenges related to the diagnoses of hip dysplasia and FAI

Both hip dysplasia, including DDH in infants and acetabular dysplasia in young adults, and FAI, including the cam- and pincer-types in young adults, are diagnostically challenging entities. Several factors come into play and need consideration. There is no clear consensus on the definitions of disease or diagnostic criteria for hip dysplasia and FAI, and the notions of ‘normal’ vs. that of ‘abnormal’ or ‘pathological’ are not straightforward in these conditions. Also, the accuracy and clinical validity of the tests and measurements used in the diagnoses of hip dysplasia and FAI are variable or remain unconfirmed.

Definition of a condition or disease: normal variants vs. pathology

The diagnosis of DDH in newborns depends on several factors. The diagnosis can be based on clinical instability (Barlow/Ortolani tests), sonographically abnormal morphology, or a combination of both. The choice of US method, the level of experience of those performing the clinical and US exams, the age of the baby at time of US assessment and the choice of screening strategy all are of importance. At skeletal maturity, both acetabular dysplasia and FAI can be assessed by several radiographic markers and measurements. In addition to various accuracies of the different measurements, there is no strong consensus as to which of the measurements

should be preferred. Last, the threshold or cut-off values describing at what point hips presumably become pathological vary, affecting the prevalence of the conditions. Cut-off values for various measurements in the literature are based on different methods. Values based on measurement values in healthy subjects vs. patients with actual pathology have been used. Another method is to assess the 95% reference intervals of a given measurement in a large, healthy population, and use the appropriate upper or lower 2.5 percentiles to estimate the cut-off value. Values outside these percentile-based intervals are not, however, necessarily pathological, but rather values in the top or bottom 2.5% extremities of the normal intervals[6].

The anatomy of the acetabulum, the relationship of the femoral head to the acetabular fossa and the anatomy of the femoral head and head-neck junction range from normal variants through borderline cases to pronounced pathology. All of these three features need to be evaluated when making a diagnosis of hip dysplasia or FAI. Subjects with radiological signs of pathology related to either condition might be asymptomatic, i.e. clinically silent findings. It is important to emphasise that a diagnosis of hip dysplasia or FAI should be made not solely based on one measurement or cut-off value, but rather based on a radiological evaluation combined with the whole clinical picture. The creation of composite scores based on both qualitative and quantitative markers might prove helpful for both conditions at skeletal maturity, possibly in addition to clinical parameters such as hip pain and range of motion, and also the impingement test for FAI.

Validity of radiographic measurements

In short, clinical validity is strongly related to how useful the different measurements for both hip dysplasia and FAI are in a clinical setting for predicting disease, including early degenerative change. The use of several measurements in combination or as integrated composite scores needs more attention. Also, assessment of the construct validity of the measurements, i.e. if the measurements really measure what we want to measure, needs to be taken into consideration when deciding on optimal diagnostic criteria for both FAI and hip dysplasia.

9. Main conclusions, clinical implications and future perspectives

Main conclusions related to hip dysplasia

I: Selective ultrasound screening of those at increased risk in addition to routine clinical examination appears to be a good screening strategy for DDH in newborns, with acceptable rates of early treatment and ultrasound follow-up and low rates of late detected subluxations and dislocations.

II: Assessment of long-term outcome at skeletal maturity for different neonatal screening strategies for DDH did not demonstrate any additional reduction in the rates of radiographic findings associated with acetabular dysplasia and early degenerative change in young adults, although both selective and universal ultrasound screening tended to reduce the rates of late detected cases in infancy when compared to expert clinical screening alone as shown in the initial trial during 1988-90. Increased treatment rates were not associated with increased rates of avascular necrosis.

III: Gender-specific reference intervals for radiographic measurements for acetabular dysplasia at skeletal maturity were similar or wider to those already existing in the literature. Statistically significant gender differences were confirmed for most of the measurements, with a tendency towards more dysplastic values in females.

Clinical implications and future perspectives related to hip dysplasia

A standardised and well-established screening programme for DDH appears to be beneficial for newborns, parents and health workers. We believe that sufficient evidence exists to encourage the establishment of common national guidelines in Norway, in accordance with the recently published guidelines by the ESPR task force group[13]. The screening programme should be organised with highly qualified examiners both for the clinical and ultrasound examinations, and followed by a well-organised clinical surveillance programme in a child health centre or similar structure

with regular visits during the first years of life. Further studies in order to determine and confirm the role and importance of risk factors for DDH are needed.

Updated reference intervals for common measurements for hip dysplasia might prove helpful when evaluating the acetabular and femoral morphology in adult hips. The establishment of a composite score containing both clinical and radiographic characteristics would help to better understand symptomatic acetabular dysplasia at skeletal maturity. A more detailed understanding of different neonatal phenotypes and their natural course until skeletal maturity is awaited. During the '1989 Hip Project', salivary samples were collected from nearly all participants for future analysis related to hip dysplasia, contributing to a unique pheno- and genotype bank for DDH. Within few decades, genetic aspects of hip stability and acetabular development will probably be better understood. Identification of susceptibility genes for DDH may help improve the validity of risk scoring methods for DDH and their effectiveness in guiding management decisions, with important clinical implications for adult hip health.

Main conclusions related to femoroacetabular impingement (FAI)

IV: Overall, radiographic findings thought to be associated with cam- and pincer-type FAI are quite common in a population of healthy young adults, especially in males, with a high degree of coexistence among most findings. The appearance of fibrocystic changes at the femoral head-neck junction was associated with both cam- and pincer type findings.

V: A positive clinical test for anterior FAI was not uncommon in healthy young adults, especially not in young males, and associated with increased physical exercise and radiographic cam-type FAI in males, hip discomfort in females, and decreased hip range of motion in both genders. We believe it should always be performed along with pelvic radiographs in young, active patients presenting with hip pain as part of the initial work-up for diagnosing FAI.

VI: This cross-sectional study presents wide reference intervals with significantly higher mean alpha values in males than females on both frog-leg and AP views. The

reference intervals are wider for the AP view. Higher alpha angles are associated with the presence of qualitative cam-type findings on both views.

Clinical implications and future directions related to femoroacetabular impingement

Knowledge of the prevalences and reference intervals of different radiographic and clinical findings related to FAI in healthy young adults might prove helpful in establishing accurate diagnostic criteria for this condition. The diagnostic accuracy and clinical validity need to be improved and confirmed for several of the radiographic markers. Accurate classification of morphological abnormalities and staging of patients are needed in order to improve management strategies for FAI. A composite scoring system for FAI patients that takes into accounts both radiographic and clinical information might be very helpful. Further studies with long-term follow-ups are needed to understand who among those with radiographic FAI findings will become symptomatic, and also who of those affected with FAI both clinically and radiographically will continue onto early degenerative change and osteoarthritis of the hip joint. Increased knowledge of genetic aspects related to the FAI entity will probably become available the next decades.

10. References

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11. Appendices

App. 1	Report form for babies at risk for DDH referred to hip ultrasound at birth, ’1991-2006 cohort’
App. 2	Protocol for management of DDH at Haukeland University Hospital, ’1991-2006 cohort’
App. 3	Invitation letter ‘1989 Hip Project’
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App. 6	Questionnaire 2, ‘1989 Hip Project’
App. 7	Clinical examination, ‘1989 Hip Project’

Appendix 1: Report form for babies at risk for DDH referred to hip ultrasound at birth

Report form Referral Hip Ultrasound Referring clinician: _____

_____ _____ ☐ Girl ☐ Boy
Surname Birth date

_____ _____
Birth date mother Date of examination

Reason for referral (please indicate all reason(s)):

- ☐ Positive clinical findings
- ☐ Equivocal clinical findings
- ☐ Breech position at birth ☐ extended legs ☐ not extended legs
- ☐ Family history of DDH (siblings/parents): who _____
- ☐ Family history of DDH in at least two second grade relatives (grandparents, aunts, uncles): who: _____
- ☐ Foot deformities (pes equinovarus) or other particular reason, as indicated: _____

Tonicity:

- ☐ Hypo-tonicity- both legs fall easily until 90° of abduction
- ☐ Normal tonicity-both legs can easily be brought until 80-90° of abduction
- ☐ Hyper-tonicity- Abnormally high tonicity; 75° or less of abduction

Other clinical findings:

	Right		Left	
	yes	no	yes	no
Stable clicking (1)	☐	☐	☐	☐
Stable hips (2)	☐	☐	☐	☐
Slightly unstable, but within normal (3)	☐	☐	☐	☐
Pathological instability, not dislocatable (4)	☐	☐	☐	☐
Positive Barlow test (dislocatable) (5)	☐	☐	☐	☐
Positive Ortolani test (dislocated, reducible) (6)	☐	☐	☐	☐

Ultrasound findings: Date: _____

	Right	Left
Graf type (morphology) (Normal; Immature; Mild; Severe)	_____	____
Stability (1-stable, 2-unstable not dislocatable, 3-dislocatable. 4-dislocated)	_____	____

Re-evaluation: Date: _____ Clinician: _____

	Right	Left
Clinical findings (numeration as above):	_____	_____
Ultrasound:	_____	_____

Appendix 2: Protocol for management of DDH at Haukeland University Hospital

Routines for management of developmental dysplasia of the hip (DDH).
Departments of Paediatric Radiology, Paediatrics and Paediatric Orthopedic Surgery, Haukeland University Hospital

1. Screening of newborns:
   Premature babies (gestational age < 33 weeks) are not referred to hip ultrasound after breech presentation at birth, but on all other indications as for full-term born babies. Ultrasound is performed before departure from the hospital, unless the clinical circumstances require earlier examination.

2. Indication for treatment and further follow-up at 6 weeks in children that are not already under treatment:
   a. Persisting mild dysplasia (<50º): Initiate treatment with Frejka's splint. Clinical re-exam within 2-3 weeks, clinical and sonographic re-exam at 12-14 weeks.
   b. 50-55º: No treatment. New clinical re-exam at 12 weeks.
   c. ≥55º: No re-exam, unless siblings with late presenting DDH. If it is the case, a re-exam should be performed at 12 weeks, unless the alpha angle is ≥60º at 6 weeks.

3. Indication for treatment and further follow-up at 3 months in children that are not already under treatment:
   a. No improvement from 6 weeks of age (50-55º): Orthosis
   b. 55-58º: Radiograph at 5 months
   c. ≥58º: No re-exam.

4. Indication for continuation of treatment at 3 months in children with abduction treatment:
   a. <55º: Continuation of treatment for 1-2 months, followed by radiograph
   b. 55-58º: Continuation of Frejkas splint treatment for 1 month. Parents stop treatment alone at home. New re-exam and radiographs at 6 months.
   c. ≥58º: Stop treatment. Re-exam with radiograph at 6 months of age.

5. Indication for later follow-up and treatment (after 3 months of age):
   a. Dysplasia: Acetabular index (AI)* > 2 standard deviations (SD) above mean: Orthosis
   b. Delayed acetabular ossification (1 SD≤AI≤2 SD): new radiograph within 2-4 months
   c. Normal (AI <1 SD above mean)
   d. Children who are followed until 10-11 months of age due to unsatisfactory AI: Last radiograph at 18-24 months of age.

6. Late presenting DDH in need of treatment:
   a. All cases where traction is considered: referral to orthopaedic surgeon
   b. Older than 6 months of age and newly detected: referral to a paediatric orthopaedic surgeon.
   c. Younger than 6 months of age, and in some cases older than 6 months but already followed some time at the paediatric radiology department: continuation of treatment managed by the paediatric radiology department.

*Age-adapted mean values of the acetabular index (AI) with one and two standard deviations (SD) according to Tönnis et Brunken 1968.[19]

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Haukeland Universitetssykehus

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Navn
Adresse

Invitasjon til å delta i

Hofteundersøkelsen, Haukeland Universitetssykehus

Du kontaktes nå fordi du ble født på Kvinneklinikken, Haukeland Universitetssykehus i 1988, 1989 eller første halvdel av 1990. Alle som ble født i denne perioden inngikk i en studie som tok sikte på å avdekke medfødt hoftefeil (hofteleddsdysplasi). I tillegg til vanlig klinisk undersøkelse, fikk en tredjedel av dere undersøkt hoftene med ultralyd. De fleste hadde helt normale hofter, 15% hadde litt grunne hofteskåler og ble kontrollert videre, mens en liten gruppe hadde hofteleddsdysplasi (=veldig grunne hofteskåler og løse leddhoder) som trengte behandling fra fødselen av.

Vi tror i dag at grunne hofteskåler i nyfødtperioden er en viktig årsak til slitasjegikt i hofteleddet senere i livet. Studien som du nå inviteres med i, vil for første gang i historien vise utviklingen av hoftene fra fødsel og frem til avsluttet vekst. En tilsvarende studie har aldri blitt gjort tidligere i verden. Resultatene fra denne studien kan få stor betydning for fremtidig behandling og oppfølging av nyfødte med medfødt hoftefeil, og forhåpentligvis redusere forekomsten av slitasjegikt hos voksne.

Å være med innebærer utfylling av et spørreskjema, to røntgenbilder av hoftene og undersøkelse av bevegeligheten i hoftene. Det medfører ikke noe ubehag og resultatet får du med en gang. Det hele vil ta ca. 20 minutter.

Undersøkelsen vil foregå på Barnerøntgen (i Barneklinikkens 2. etasje), Haukeland Universitetssykehus.

Det er selvsagt frivillig å delta, men for kvaliteten på studien er det avgjørende at flest mulig deltar. **Som belønning vil du få en MP3-spiller eller 150 kroner!**
Dokumenterte bussutgifter innen Stor-Bergen vil også bli refundert.

Du har fått time …. : ….-2008 kl:…….

Mange av dine jevnaldrende vil også bli bedt om å delta i denne studien. Hvis det er et sterkt ønske fra deg, kan vi prøve å ordne det slik at flere venner kan komme sammen. For å endre den timen du har fått, tar du kontakt med oss på telefon 55 97 64 66 eller 911 02 568 eller trude.gundersen.lehmann@helse-bergen.no

UTFYLLENDE INFORMASJON OM HOFTESTUDIEN

Medfødt hoftefeil (=hofteleddsdysplasi) forekommer hos ca 2-3 % av alle nyfødte. Tilstanden oppdages vanligvis ved nyfødtundersøkelsen, og de fleste blir bra etter 3-4 måneders behandling med "hoftepute". Hos enkelte blir imidlertid tilstanden oppdaget senere, og behandlingen er da mer omfattende med gips og/eller operasjon. Hos andre ser vi at hofteskålen utvikles ufullstendig; at den blir "grunnere" enn normalt. Det er grunn til å tro at dette kan disponere for hofteslitasje senere i livet. I tillegg tror vi at enkelte har hofteledd som er normale ved fødselen, men utvikler hoftefeil i de første leveår. Hoftestudien som du inviteres til å være med på, vil kunne klarlegge dette.

I perioden 1988 - 1990 gjennomførte vi en stor studie ved Haukeland Universitetssykehus der vi viste at ultralydundersøkelse av hofteleddene hos nyfødte kunne bedre diagnostikken av hofteleddsdysplasi. Siden 1990 har derfor alle nyfødte med økt risiko for medfødt hoftefeil blitt undersøkt med ultralyd. Dette har resultert i at forekomsten av alvorlig, senoppdaget hoftefeil har sunket fra 18 til 2 per år hos barn født i Bergen. Hos enkelte barn oppdaget vi at hofteskålen var litt grunnere enn normalt (umodne). Disse barna ble fulgt opp ved Barneklinikkens poliklinikk til hofteleddene var normalisert.
Målet med denne studien er å finne ut om der er en sammenheng mellom "grunne" hofteskåler i nyfødtperioden og utvikling av røntgenologisk hofteslitasje ved 17-19 års alder. Med andre ord, om de som hadde normale hofteledd ved fødselen fortsatt har normale hofteledd og om de som hadde grunne hofteskåler fortsatt har grunnere hofteskåler enn de andre. Funnet vil få stor betydning for nyfødtundersøkelse av alle barn, samt oppfølging av dem som får påvist grunne eller dysplastiske hofteskåler.
Det vil bli tatt to røntgenbilder der vi benytter en moderne teknikk med lav stråledose. Utover denne lille stråledosen er det ingen bivirkninger med å delta i studien og det gir ingen ubehag for deg. Undersøkelsen tar 20 minutter. Resultatet av røntgenundersøkelsen får du selvsagt vite. Dersom det avdekkes sykdom, vil du få tilbud om rask oppfølging av lege. Informasjonen vil bli lagret på røntgenavdelingen på Haukeland Universitetssykehus og vil være tilgjengelig som nyttig informasjon senere i livet. Innsamlete data for øvrig vil bli lagret til 2016.
Spørsmål om undersøkelsen eller praktiske forhold kan rettes til Trude Lehmann på telefon 55 97 64 66 / 911 02 568. Alle opplysninger vi mottar vil bli behandlet konfidensielt, alle ansatte i studien har taushetsplikt og prosjektet vil følge retningslinjer fra Regional komité for medisinsk forskningsetikk. Studien er også godkjent av Datatilsynet. Du kan når som helst trekke deg fra prosjektet uten at du trenger å begrunne det nærmere. Dersom du trekker deg vil alle opplysningene som er samlet inn, både fra du var nyfødt og i dette prosjektet, bli anonymisert.

Vennlig hilsen

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Navn/personnummer……..

Samtykke til deltagelse i Hoftestudien, Haukeland Universitetssykehus

Jeg har mottatt muntlig og skriftlig informasjon om prosjektet, og sier meg villig til å delta. Jeg er klar over at dataene som fremkommer vil bli lagret på Haukeland Universitetssykehus. Jeg kan når som helst trekke meg fra deltagelse, uten å oppgi grunn og uten at det får konsekvenser for meg.
Jenter som mistenker at de er gravide, må selv utelukke dette før oppmøte til røntgen.

Bergen,……..2009 Signatur: …….

Dersom du er under 18 år må en av dine foreldre/foresatte godkjenne at du deltar i studien.

Bergen,……2009 Forelder/foresattes signatur:……..

TA MED DENNE SAMTYKKE ERKLÆRINGEN NÅR DU MØTER TIL UNDERSØKELSE.

NAVN

Tidligere hofteplager eller andre leddplager

Før du møter til undersøkelse er det fint om du spør foreldrene dine om du noen gang har hatt noe galt med hoftene dine eller en annen leddlidelse.Kryss av i rubrikkene under på det som er aktuelt. Leveres med samtykkeerklæringen.

☐ Ingen problemer
☐ Medfødt hofteleddsdysplasi
☐ Serøs coxitt (ikke-bakteriell betennelse i hofteleddet)
☐ Septisk artritt i hofteledd (bakteriell betennelse i hofteleddet)
☐ Calvé Legg Perthes` sykdom
☐ Epifysiolyse
☐ Brudd
☐ Leddgikt (Reumatoid artritt)
☐ Annet (Spesifiser:…….)
☐ Vet ikke
☐ Har oppsøkt lege / Legevakt pga. problemer med hofte. Spesifiser:…….
☐ Har du noen sykdom som har vart over 3 måneder? Hvilken:…….

Hofteplager i nærmeste familie

Har du søsken som har medfødt hoftelidelse og har vært behandlet med pute?

☐ Ja ☐ Nei ☐ Vet ikke Hvis ”ja”, antall: (eks. 1 bror 2 søstre)

.....bror/brødre …...søster/søstre ……halvbror/halvbrødre …..halvsøster/halvsøstre

Har du foreldre som har hatt medfødt hoftelidelse? ☐ Ja ☐ Nei ☐ Vet ikke

Hvis ”ja”, hvem: ☐ mor ☐ far

Har foreldrene dine plager med hoftene i dag? ☐ Ja ☐ Nei ☐ Vet ikke

Hvis ”ja”, hvem: ☐ mor ☐ far

Mors høyde……cm Fars høyde……cm

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Mange takk for at du tar deg tid til å være med på Hoftestudien. Skjema brukes også for undersøkelse av helsetilstanden til eldre og alvorlig syke personer. Noen av spørsmålene kan derfor virke lite relevante for deg om du er helt frisk. Likevel ber vi deg lese gjennom hele skjema, og svare på alle spørsmålene. Der er totalt 43 spørsmål.

1. Deltakernummer:…….

2. Navn: ……

3. Fødselsnummer: |__|__| |__|__| |__|__| |__|__|__|__|__|

4. Yrke ☐ skoleelev ☐ annet (Spesifiser:…….)

5. Har du noen gang hatt plager fra høyre hofte (varighet over 1 måner)? ☐ Ja ☐ Nei

   Hvis ”JA”, spesifiser…….

6. Har du hatt plager fra høyre hofte siste 3 måneder? ☐ Ja ☐ Nei

   Hvis ”JA”, spesifiser…….

7. Har du noen gang hatt plager fra venstre hofte (varighet over 1 måner)? ☐ Ja ☐ Nei

   Hvis ”JA”, spesifiser…….

8. Har du hatt plager fra venstre hofte siste 3 måneder? ☐ Ja ☐ Nei

   Hvis ”JA”, spesifiser…….

9. Hvor ofte har du vondt i nakken?

   ☐ omtrent hver dag
   ☐ mer enn 1 gang pr uke
   ☐ omtrent hver uke
   ☐ omtrent hver måned
   ☐ sjelden eller aldri

10. Hvor ofte har du vondt i ryggen?

- ☐ omtrent hver dag
- ☐ mer enn 1 gang pr uke
- ☐ omtrent hver uke
- ☐ omtrent hver måned
- ☐ sjelden eller aldri

11. Har du problemer som du relaterer til hoften, som gjør at du har vansker med å gå?

☐ Ja ☐ Nei Hvis "JA", spesifiser…….

12. Er det andre årsaker enn hofteplager som gjør at du har vansker med å gå?
(For eksempel smerter fra andre ledd, ryggsmerter, hjerte-karsykdom eller andre sykdommer som påvirker gangevnen din)

☐ Ja ☐ Nei Hvis "JA", spesifiser……

13. Utenom skoletid: Hvor mange GANGER i uken driver du med idrett/mosjon slik at du blir andpusten og/eller svett?

- ☐ hver dag
- ☐ 4-6 ganger i uken
- ☐ 2-3 ganger i uken
- ☐ 1 gang i uken
- ☐ 1 gang i måneden
- ☐ mindre enn 1 gang i måneden
- ☐ aldri

14. Utenom skoletid: Hvor mange TIMER i uken driver du med idrett/mosjon slik at du blir andpusten og/eller svett?

- ☐ ingen
- ☐ ½ time
- ☐ 1 time
- ☐ 2-3 timer
- ☐ 4-6 timer
- ☐ 7 timer eller mer

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deltakernr:……..

Navnelapp

Klinisk undersøkelse

Us dato……..

Høyde:……..cm

Vekt:……kg

Status:	Høyre	Venstre
Fleksjon:	☐☐☐	☐☐☐
Ekstensjon:	☐☐☐	☐☐☐
Abduksjon:	☐☐☐	☐☐☐
Adduksjon:	☐☐☐	☐☐☐
Innadrotasjon:	☐☐☐	☐☐☐
Utadrotasjon:	☐☐☐	☐☐☐
Forkortning	☐☐☐mm	☐☐☐mm
Impingement	☐	☐

Mobilitet	**Høyre**	**Venstre**
Hyberekstensjon i albu > 10º?	☐	☐
Hyperekstensjon i kne > 10º?	☐	☐
Legger tommel ned på underarm?	☐	☐
>90º dorsalfleksjon i 5. fingers grunnledd?	☐	☐
Ta i gulvet med håndflate med strake knær	☐	

12. Errata

Paper IV:

Table 2:

‘**’ and corresponding footnote missing after ‘pincer type (one or more findings)’ on the second-last line -> Table: ‘pincer type (one or more findings)**’, Footnote: **‘COS was included if scored positive in the middle or lower third**’.

13. Papers I-VI

Selective ultrasound screening for developmental hip dysplasia: Effect on management and late detected cases

A prospective survey during 1991-2006

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Mr. Henrik Davidsen, MSc, Department of Clinical Medicine, University of Bergen.

Dr. Kari Røine Brurås, MD. Department of Radiology, Section for Paediatrics, Haukeland University Hospital, Bergen.

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Abstract:

Background Early treatment is considered essential for developmental dysplasia of the hip (DDH), but the choice of screening strategy is debated. We evaluated the effect of a selective ultrasound (US) screening programme.

Methods All infants born in a defined region during 1991-2006 with increased risk of DDH, i.e. clinical hip instability, breech presentation, congenital foot deformities or a family history of DDH, were subjected to US screening at age one to three days. Severe sonographic dysplasia and/or dislocatable/dislocated hips were treated with abduction splints. Mild dysplasia and/or pathological instability, i.e. not dislocatable/dislocated hips were followed clinically and sonographically until spontaneous resolution, or until treatment became necessary. The minimum observation period was 5·5 years.

Findings Of 81564 newborns, 11539 (14·1%) were identified as at risk, of which 11190 (58% girls) were included for further analyses. Of the 81564 infants, 2433 (3·0%) received early treatment; 1882 (2·3%) from birth and 551 (0·7%) after six weeks or more of clinical and sonographic surveillance. Another 2700 (3·3%) normalised spontaneously after watchful waiting from birth. Twenty-six infants (0·32 per 1000, 92% girls, two from the risk group) presented with late subluxated/dislocated hips (after one month of age). Another 126 (1·5 per 1000, 83% girls, one from the risk group) were treated after isolated late residual dysplasia. Thirty-one children (0·38 per 1000) had surgical treatment before age five years. Avascular necrosis was diagnosed in seven of all children treated (0.27%), four after early and three after late treatment.

Interpretation The first 16 years of a standardised selective US screening programme for DDH resulted in acceptable rates of early treatment and US follow-ups, and low rates of late subluxated/dislocated hips compared to similar studies.

Funding Western Norway Regional Health Authority. University of Bergen, Norway. Arthritis Research Campaign UK.

Key words

Developmental dysplasia of the hip, hip dysplasia, hip ultrasound, paediatric, neonatal screening

Introduction

Developmental dysplasia of the hip (DDH) is the most common musculoskeletal disorder in infants, and early detection and treatment of at least severe DDH is considered essential in order to avoid later complicated treatment and possible disability.[1] DDH as a pathological entity encompasses features related to both morphology and instability. Acetabular dysplasia has been reported in around 0·5-4% of newborns, and neonatal hip instability in 1-2%.[2-5] While hip instability can be assessed both clinically and sonographically, the acetabular component (dysplasia) is only detectable by ultrasound (US) in newborns. Although a close association between hip stability and morphology has been demonstrated, a normal acetabulum can coexist with a dislocatable femoral head and vice-versa.[2] Late cases with subluxated or dislocated hips have been reported in 0·1-3 per 1000 after clinical screening alone,[5-7] and in 0·2-0·7 per 1000 when selective US is added to the clinical screening.[7-12] Different US methods for diagnosing DDH have been advocated, i.e. a static method (Graf's method),[13] followed by dynamic methods, and later by a combination of the two (Rosendahl's method).[14] Treatment rates based on the different screening strategies vary, from around 1% to 7·7% of all newborns.[6,15] Avascular necrosis of the femoral head (AVN) is a severe, albeit rare iatrogenic complication, reported in 1-4% of all treated infants.[3,16,17] Based on the experience of a large randomised controlled trial (RCT),[7] selective US screening was established in our institution during 1990, in addition to the existing clinical screening. We here report on rates and management of DDH, and rates of late detected cases and surgical treatment, during the first 16 years of this screening programme.

Materials and methods

Population

All infants born at the maternity unit at Haukeland University Hospital from January 1991 through December 2006 were included. The hospital provides the only delivery unit for the city and suburbs of Bergen and a large rural area within Hordaland County. It serves a population of approximately 400 000 inhabitants, predominantly ethnic Norwegians. The annual birth rates varied from 4723 to 6010. The annual migration rate of this area is low (1·6%).[18] Minimum observation time was 5·5 years. Children with DDH due to neuromuscular syndromes were excluded.

DDH screening programme

All newborns had a routine clinical hip examination within the first three days, before being discharged from the maternity unit. During the study-period, around 40 different paediatricians with at least two years of experience were involved in the clinical assessment of the hips, including stability using the Barlow/Ortolani tests (figure 1). Limited hip abduction was also noted. Risk factors for DDH from the medical history or clinical examination (Table 1) were recorded in a report-form which also served as a referral to hip US (Appendix 1).The paediatric, orthopaedic and paediatric radiology departments managed the follow-up and treatment of DDH according to a predefined protocol which remained unchanged during the whole period (Appendix 2). Mild acetabular dysplasia was, however, often treated from birth rather than followed with US during the first years of the protocol.

Hip ultrasound

The US examination was performed within one-two days after the clinical examination while still in the maternity unit. During the whole period, the US was performed by one of five consultant paediatric radiologists with two to 20 years of experience in hip-US (AA, OE, SMA, KB, KR), using a GE RT200 machine until 1996 and thereafter a GE RT3600, both equipped with 5-MHz linear transducers (General Electric, Munich, Germany). A modified Graf technique (Rosendahl's method) was used to assess hip morphology (figure 2) and stability (figure 3).[14] Morphologically immature hips were considered within normal. In cases of US findings suggestive of DDH, or if clinical instability had been demonstrated prior to the US, the child had a clinical re-examination by one of the paediatricians the following day. The results were recorded in the report form (Appendix 1) which also served as a referral to early abduction treatment or follow-up at the paediatric out-patient clinic.

Treatment and follow-up

Newborns with a persistent dislocated or dislocatable hip as assessed clinically or sonographically, and/or with severe sonographic dysplasia, received immediate abduction treatment with a Frejka's splint (Appendix 2). Newborns with clinical or sonographic unstable but not dislocatable hips (i.e. pathological instability), and/or with mild sonographic dysplasia were subject to watchful waiting and were reviewed clinically and sonographically at six

weeks of age. Treatment was then initiated if the clinical or sonographic examination showed deterioration or no improvement (figure 5). The rest were discharged at six weeks, or had a repeat US exam at 12 weeks, and/or a pelvic radiograph at four and a half months as appropriate (Appendix 2). Newborns with stable (clinically and sonographically) and morphologically normal or immature hips at birth were discharged to the routine follow-up within the public healthy child programme, except that infants with a significant family history of late DDH were referred for a pelvic radiograph at 4.5 months of age. Abduction treatment initiated at birth was typically continued for three months with clinical and US assessment at six weeks and at the end of treatment, but extended if necessary. In severe cases detected at birth, or in cases where initial treatment was followed by deterioration or no improvement, the paediatric orthopaedic surgeons were involved. The Frejka's pillow was either replaced with an age-adapted abduction orthosis, or sometimes traction and closed or open reduction followed by cast abduction treatment was initiated. All US examinations after the initial newborn examination were performed at the paediatric radiology department, by one of six consultant paediatric radiologists (AA, OE, SMA, JAB, KB, KR) using a high-resolution US machine (Acuson 128 XP Siemens until 1996, and later a ATL HDI 5000, both with a linear 5-10/12 MHz transducer), and the same modified Graf's technique. The results were archived manually until 2001 and thereafter in the RIS/PACS system (Agfa IMPAX Web1000, v.5.0, Agfa Gaevert, Mortsel, Belgium). Pelvic radiographs replaced US examinations from 4·5 months of age, and were performed by one of six paediatric radiographers according to a standardised protocol and read by one of the six paediatric radiologists. On radiographs, hips were classified morphologically based on the acetabular index (AI) according to Tönnis and Brunken[19] (Appendix 2) with or without a subluxated or dislocated femoral head (figure 4).[20] A flattened femoral head or a thinned femoral neck suggestive of an undergone AVN were also noted.[16] Children with pathology on radiographs or who had been treated surgically were regularly seen by a paediatric orthopaedic surgeon until skeletal maturity or normalisation. Surgical treatment included closed reduction (including traction, cast treatment and adductor tenotomy), open reduction and osteotomies.

The Healthy Child Programme and recognition of late DDH

In this national programme, hips are examined at six weeks, six months and one year in order to detect late presenting DDH (i.e. after one month of age). If clinical suspicion of late DDH,

usually limited abduction of flexed hips, the child is referred for hip imaging and/or a clinical expert hip-assessment at the paediatric out-patient clinic until three months of age, and thereafter to the paediatric orthopaedic clinic. During the study period, an associate orthopaedic hospital, Kysthospitalet in Hagevik, received some referrals querying late DDH. The corresponding radiographs were re-analysed in consensus (KR, KI) in order to standardise the diagnosis of late DDH.

Data collection and analysis

All data on risk factors, on results of clinical, US and radiographic examinations and on treatment were collected prospectively and registered in the DDH-screening report form (Appendix 1). Data on late referrals were also collected prospectively. All data were entered in a Microsoft Access 2010 database by one of four persons during 2005-2011. In order to ensure that all babies (including low-risk babies) born at our hospital who had received abduction treatment and/or surgery were included in the dataset, additional searches based on all the DDH-related diagnoses and procedures (abduction treatment, traction, plaster cast, open and closed reductions, and osteotomies) and on AVN diagnosis were performed retrospectively within the database of the university hospital (including Kysthospitalet in Hagevik) during August-October 2012. Additional information was retrieved from the clinical patient records when needed. The Access database was exported into IBM® SPSS® Statistics, version 20.0, (Armonk, New York, USA). Data were summarised as rates per 100 and per 1000 with corresponding 95% confidence intervals (CI) as appropriate.[21]

Ethical Approval

The research protocol was approved by the Regional Ethical Committee for Medical and Health Research (003.07). This study was granted exempt status from the parental written informed consent issued by the Norwegian Directory of Health (06/5901).

Role of the funding source

The founding sources had no role in study design, data collection, data analysis, data interpretation, or in the writing of the report.

Results

Of 81564 live-births (49·1% girls), 11539 (14·1%, 95% CI 13·9-14·3) were identified as at risk for DDH, and had a hip US. Of these, 349 newborns with incomplete report forms from the newborn examination (unidentifiable subjects with substantial lack of clinical or sonographic information) and without further treatment or follow-up were excluded from further analyses related to early treatment and follow-up. For the 11190 infants (57.6 % girls) with adequate information, indications for hip US are presented in table 1. Of these, 67.9% had normal acetabular morphology, but 5.2 % of those with normal morphology had dislocated or dislocatable hips (Table 2). The remaining 70025 (85·9%) newborns were classified as low-risk (figure 5).

Treatment and follow-up of early detected cases

In all, 2433 infants received abduction treatment after early detected DDH (3·0% of the whole cohort, 21.7% of those at risk); 1882 (2·3%) were treated from birth and 551 (0·7%) were treated after clinical and sonographic surveillance (414 after a mean of six (range 4-9) weeks, 105 after a mean of 12 (range 10-18) weeks and 32 after 20 weeks). Of the 1882 infants treated from birth, 315 (0·4% of whole cohort) received early treatment without a valid indication according to the protocol (Table 3 A), of whom 231 (73·3%) were treated based on mild dysplasia alone. Another 2700 (3·3% of the whole cohort, 24.1% of those at risk) were followed clinically and sonographically from birth until significant improvement or normalisation (Table 3 B), with a mean follow-up time of 11 weeks (range 4-64 weeks). The yearly rates of both abduction treatment and of US follow-up declined slightly throughout the study period (figure 6). Of the 1882 infants who were treated from birth, 1351 (1·7% of the total cohort, 71·8% of those treated from birth) had clinically and/or sonographically dislocatable or dislocated hips; 695 of them also had severe sonographic dysplasia (table 3 A).

Late detected cases

Of the 81564 infants, 26 (0.32 per 1000, 92% girls) were treated for severe late DDH with a subluxated or dislocated hip (Table 4). Of these 26 children, two were from the risk group. These two girls were reported to have normal hip US at birth, but evaluated in retrospect one of them had a mildly dysplastic hip. Another 126 infants (1.54 per 1000, 83% girls) were treated after a late diagnosis of isolated residual dysplasia (table 4); one girl was from the risk

group. Median age at diagnosis was 16 weeks (range 6-156 weeks) for the 26 late cases with subluxation/dislocation, and 11 weeks (range 5-208 weeks) for the 126 late cases with residual dysplasia. An additional five cases presented with residual dysplasia later than five years of age; two girls at ages 16 and 18 years were from the risk group and had received routine abduction treatment from birth, and three at ages eight, 17 and 19 years (one girl) were from the low-risk group. Additional details are summarized in Appendix 3.

Surgical treatment

Thirty-one children underwent a first surgical treatment until five years of age (0·38 per 1000) (Table 5). From the at-risk group, nine cases had initial surgical treatment (two open and seven closed reductions), and seven cases underwent surgical treatment after failure of initial abduction treatment. Fifteen low-risk infants underwent surgical treatment due to late detected DDH. Further details are provided in Appendix 3.

Avascular necrosis (AVN)

AVN was diagnosed in seven of the 2585 treated children (0·27%, 95% CI 0·07-0·47%). Four cases occurred after treatment from birth, and three after treatment of late detected DDH (Appendix 3).

Discussion

In this population-based prospective study, 14·1% of all newborns were identified as being at risk for DDH and had a hip US at birth. Of the whole cohort, 3% received treatment based on early screening and 0.32 per 1000 were treated for late detected subluxation or dislocation, all but two from the group who did not have early US. The proportion identified as at risk of DDH compared well to 7-18% reported in similar surveys.[7,8,10-12] Identification of groups at risk for DDH has been addressed in several studies.[3] In our study, family history of DDH was the most frequent risk factor, in agreement with a recent review.[22] However, there is no consensus on the best way to measure the different risk components, and calibration of risk scoring methods in different populations is frequently poor. Future identification of susceptibility genes for DDH may help improve the validity of methods and their effectiveness in guiding management decisions. The rates of immediate treatment (2·3%),

treatment after watchful waiting (0·7%), and monitoring until spontaneous improvement (3·3%) compares well with the results of a previous RCT performed in our institution.[7] In some regions, selective US screening has resulted in treatment rates of 1-4%,[23,24] while universal US screening have resulted in treatment rates of up to 7·7%.[15,24,25] The observed decrease in annual, early treatment rates was partly due to watchful waiting rather than treatment of mild DDH, reflecting better adherence to the implemented screening programme. This gradual change was encouraged by an ongoing RCT which showed that there were no differences in radiographic outcome at six years of age between children who did or did not receive abduction splinting for mild DDH from birth.[26]

The major objective of the selective US screening programme was in fact met, in that the rate of late subluxated or dislocated hips was significantly lower than those based on a previous RCT, and on historical data (0·32 vs. 1·3 and 2·6 per 1000 births, respectively).[7] The rate compares well to other studies using selective US (0·2-0·7 per 1000)[7-11] or universal US screening (0·13-0·3 per 1000).[7,10] However, to date, no screening strategy has succeeded in eliminating all late cases, suggesting that US is less than 100% sensitive or that dysplastic but stable hips at birth may progress to irreducible dislocation. The development of a clinically and sonographically normal newborn hip into later dislocation appears less likely since all but three of the late presenting cases in our survey were low-risk babies, i.e. had no US screening. The relatively low rate of late detected subluxations and dislocations in our study suggests that a universal US screening programme may not be cost-effective since it would require considerable resources both for initial screening and follow-up.[27] Most children with late detected DDH were treated for residual dysplasia without subluxation or dislocation. These children were mainly referred for asymmetry on hip abduction, which in absence of subluxation is positional due to e.g. preferred sleeping position, secondary to torticollis. The natural course of acetabular dysplasia remains unknown, but radiographic residual dysplasia has been shown to occur in 2-3% of healthy five months old children without any risk factors.[28] This suggests that at least the majority of these infants would have recovered without treatment.

The rate of a first surgical treatment of 0·38 per 1000 compares well with rates of 0·40 and 0·58 per 1000 reported for other selectively screened populations.[8,9]

The concept of ‘watchful waiting’ of mild dysplasia for at least six weeks proved helpful, as hips in four out of five infants normalised spontaneously within the first six months. One may

argue that postponing the US screening programme until six weeks of age would allow for spontaneous recovery, facilitating the identification of those in need of treatment. We suggest four arguments against delayed US screening. Firstly, treatment may be unduly delayed in newborns with clinically undetected but severe pathology on US. This was true for one in ten of those treated from birth in this study. This figure is conservative as some of the dislocatable or dislocated hips were first acknowledged at the clinical re-examination after first being identified on US. Secondly, knowledge of the baseline appearance of the newborn hip will help interpretation of clinical and sonographic development during the first six weeks, and thus allow for personalised management decisions. Thirdly, postponing hip US to six weeks or later will increase costs as all babies would have to be scheduled for out-patient US and paediatrics visits. Finally, some babies may not show up at six weeks due to lack of parental compliance.

We acknowledge several limitations of our study. Children with late detected DDH may have moved out of our catchment area. However, the migration rate is low,[18] and children with subluxated or dislocated hips would most likely have been referred back unless the family had moved to another major region of the country since our hospital has a regional service. We also performed detailed searches within hospital records in order to avoid missed cases. The strengths of this study include the prospective collection of data, and standardised and unchanged protocols for screening and management throughout the period. Finally, only six experienced paediatric radiologists performed all the US examinations, using a validated, combined ultrasound technique, and performed all the x-ray interpretations.

Conclusion

A standardised selective ultrasound screening programme for detecting DDH resulted in an early treatment rate of 3·0%; 2·3% from birth and 0·7% after initial clinical and sonographic follow-up. Another 3·3% were followed sonographically until spontaneous improvement. Rates of late subluxation/dislocation, surgical treatment and AVN were low compared to other screening programmes.

Panel: Research in context

Systematic review

Preferred screening policy for DDH in newborns is debated, and international guidelines are lacking. Extensive literature reviews emphasize the need to reach an agreement.[3,17,29] Only two large randomized controlled trials evaluating different screening strategies have been performed,[7,10] both advocating a selective strategy with ultrasound offered to those at increased risk. Recommendations published by the European Society of Pediatric radiology (ESPR) DDH task force group in 2011 endorse selective ultrasound screening in areas with a high prevalence of late DDH, and suggest that universal ultrasound screening may be considered if selective screening has no effect on the prevalence of late cases.[30] We searched PubMed, Embase, references from published papers, and the authors' personal libraries for studies of screening for DDH in newborns, with particular emphasis on ultrasound strategies. The terms searched for in PubMed were: developmental dysplasia of the hip, hip dysplasia, hip ultrasound, neonatal screening.

Interpretation

The first 16 years of a standardised selective ultrasound screening programme for DDH resulted in acceptable rates of early treatment and US follow-ups. The rates of late subluxated/dislocated hips were low, and involved mostly low-risk girls. We suggest that the applied screening programme is a reasonable approach, supporting the ESPR DDH task force group recommendations.[30]

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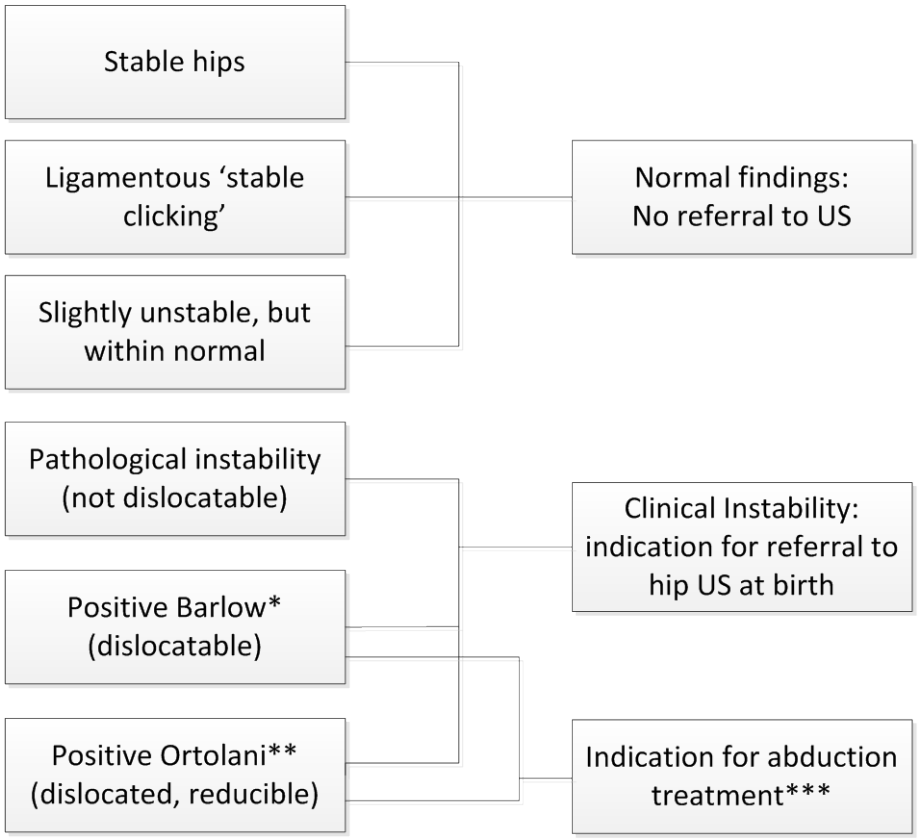
Authors' contributions

KR and TM designed the initial protocol. TM and HR have performed a substantial number of the clinical newborn examinations. LBE and KI have been involved in the surgical treatments. KR, KRB, JAB and SMA performed most of the ultrasound examinations. LBE, TGL, IØE, HD and LBL managed and checked the complete data set. LBL and KR drafted the initial manuscript. All authors critically reviewed the initial manuscript. LBL and KR were responsible for the analysis. All the authors contributed to the critical analysis of the data, interpretation of the findings, and revision of the manuscript, and all authors critically reviewed the final version of the manuscript. The corresponding author (LBL) confirms full access to all the data in the study, and final responsibility for the decision to submit for publication.

Conflict of interest: KR chairs the European Society of Pediatric Radiology (ESPR) task force group on DDH. The others declare no conflicts of interest.

Figure 1

Clinical assessment of hip stability at birth. The Barlow/Ortolani tests are performed separately in the supine child with hips flexed to 90 degrees, one hip at the time.



* Positive in cases where the femoral head can be dislocated while adducting the hip and applying backward pressure to the femoral head

** Positive in cases where a dislocated hip can be reduced into the acetabulum while abducting the hip and applying forward pressure to the head

*** If persisting on clinical re-examination irrespective of US findings. Babies referred to ultrasound due to a positive Barlow/Ortolani test were left untreated if neither the ultrasound nor the clinical re-examination fulfilled the treatment criteria. For simplicity, positive Barlow/Ortolani test on first clinical examination was considered as risk factor rather than confirmed diagnosis of DDH.

Figure 2

Sonographic assessment of hip morphology in newborns, using Grafs standard coronal view [13] and the alpha angle. Each hip was morphologically classified as a) normal (α≥60°), b) immature (50°≤ α<60°), c) mildly dysplastic (43°≤ α<50°) or d) severely dysplastic (α<43°) (Rosendahl's classification)[14].

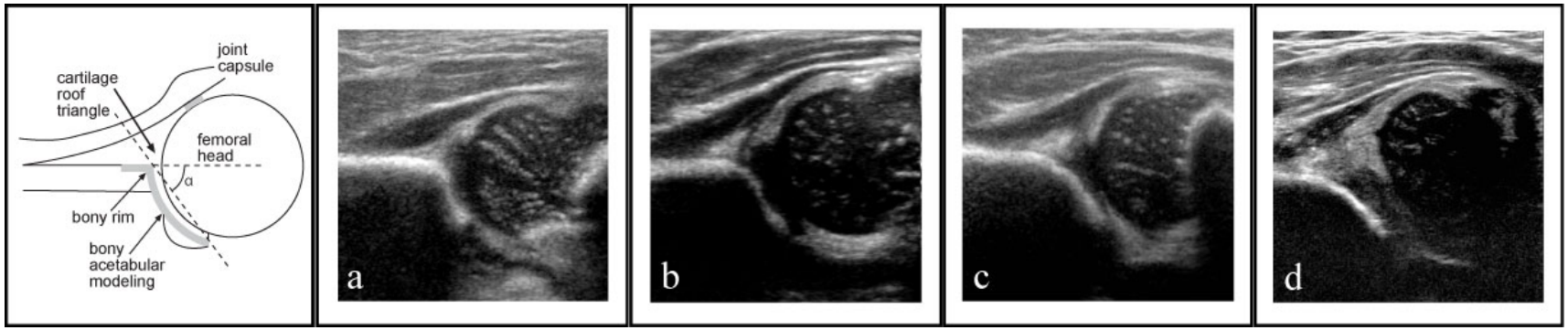


Figure 3

Sonographic assessment of hip stability in newborns. By using a modified Barlow-maneuver with the baby in the same, lateral position, hips were classified as a) stable, b) unstable (significant movement of the femoral head, but not dislocatable), c) dislocatable or d) dislocated.

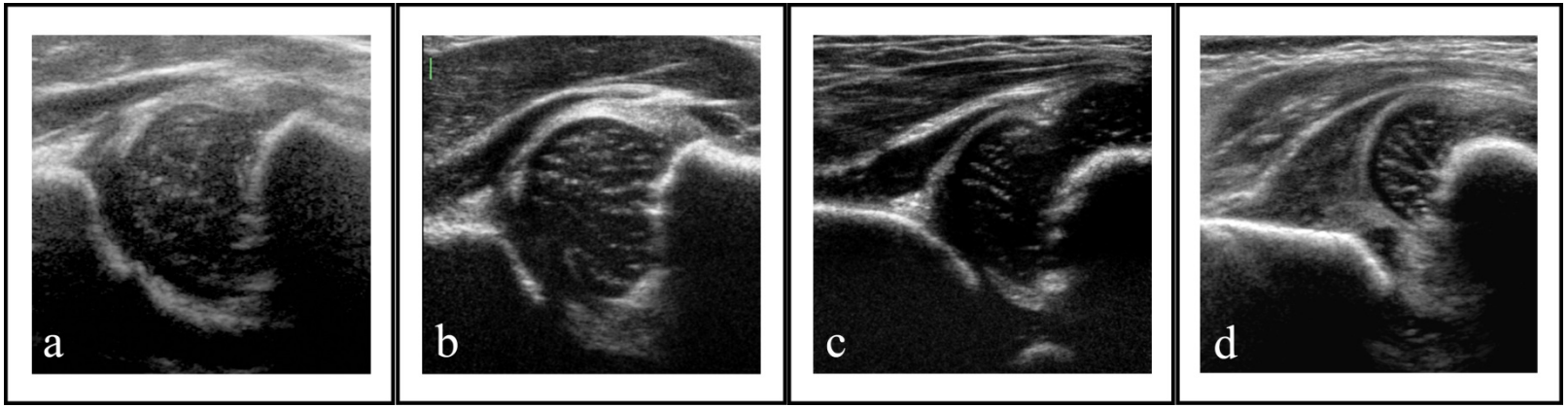
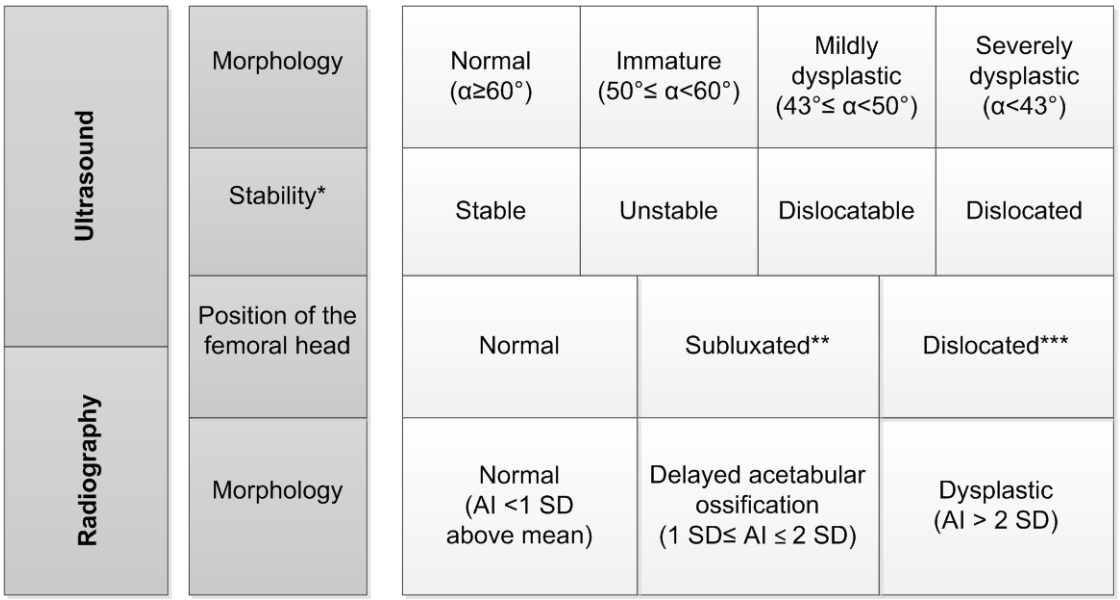


Figure 4

Radiological assessment of DDH. Ultrasound is used until the age of 4.5 months, with separate assessment of morphology and stability (Rosendahl's method)[14] during the first six weeks. Thereafter, when the hips are considered stable, the position of the femoral head is assessed, rather than stability.[20] Pelvic radiographs are used from 4.5 months onwards.



* Using a modified Barlow-maneuver for assessment of stability during the first six weeks.
** Lateral displacement of the femoral head partially out of the acetabulum
*** Femoral head lies outside the acetabulum (also called 'luxated')
α = alpha angle, AI= Acetabular index, SD= standard deviation

Figure 5

Flow of participants through the selective screening programme. The denominator for all proportions (%) is the total number of live births (81564) from January 1991 through December 2006.

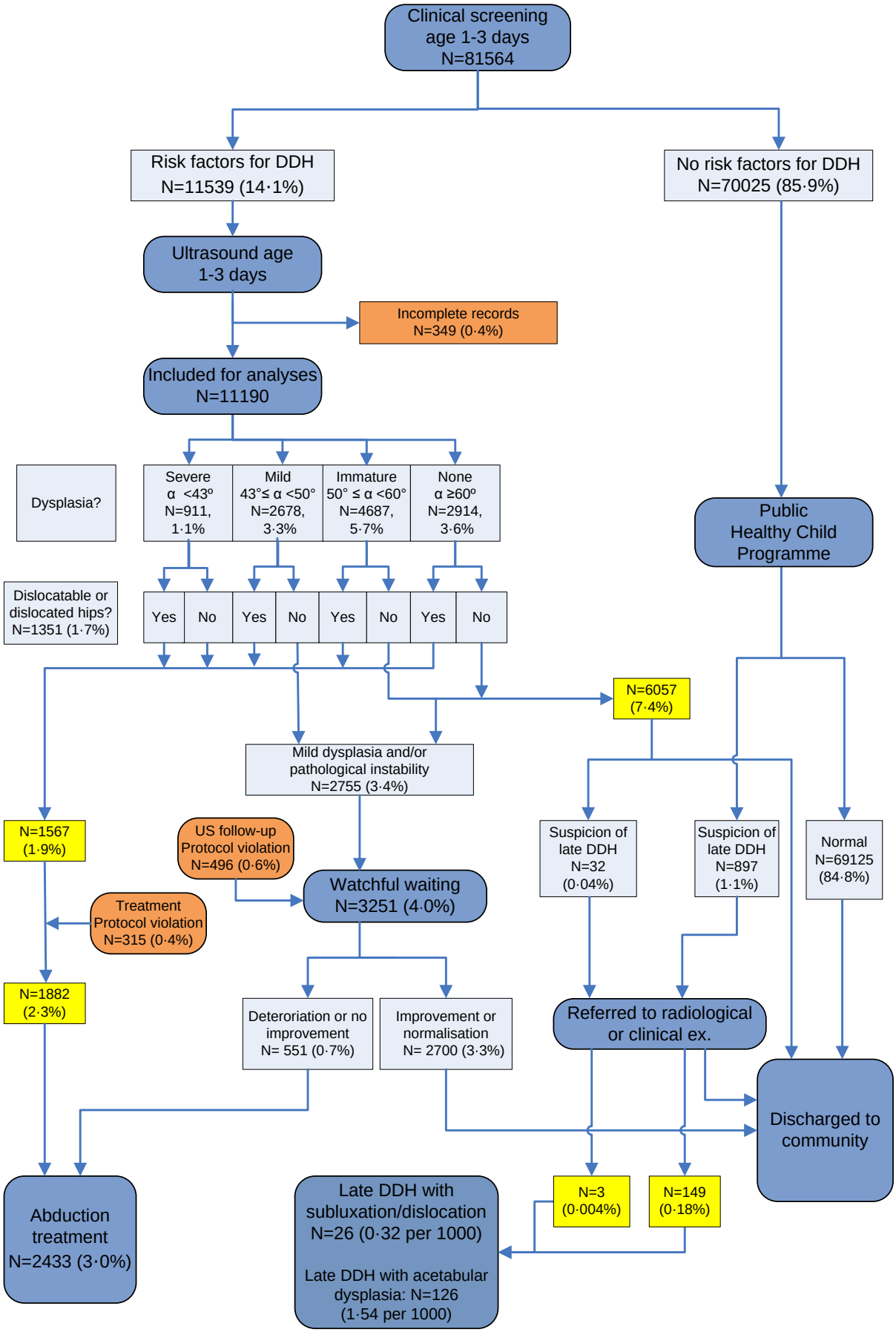

Clinical screening
age 1-3 days
N=81564
Risk factors for DDH
N=11539 (14·1%)
No risk factors for DDH
N=70025 (85·9%)
Ultrasound age
1-3 days
Incomplete records
N=349 (0·4%)
Included for analyses
N=11190
Dysplasia?
Severe
α <43º
N=911,
1·1%
Mild
43°≤ α <50°
N=2678,
3·3%
Immature
50° ≤ α <60°
N=4687,
5·7%
None
α ≥60º
N=2914,
3·6%
Public
Healthy Child
Programme
Dislocatable or
dislocated hips?
N=1351 (1·7%)
Yes
No
Yes
No
Yes
No
Yes
No
N=6057
(7·4%)
Mild dysplasia and/or
pathological instability
N=2755 (3·4%)
N=1567
(1·9%)
US follow-up
Protocol violation
N=496 (0·6%)
Suspicion of
late DDH
N=32
(0·04%)
Suspicion of
late DDH
N=897
(1·1%)
Normal
N=69125
(84·8%)
Watchful waiting
N=3251 (4·0%)
Treatment
Protocol violation
N=315 (0·4%)
N=1882
(2·3%)
Deteroriation or no
improvement
N= 551 (0·7%)
Improvement or
normalisation
N= 2700 (3·3%)
Referred to radiological
or clinical ex.
Discharged to
community
Abduction
treatment
N=2433 (3·0%)
Late DDH with
subluxation/dislocation
N=26 (0·32 per 1000)
Late DDH with acetabular
dysplasia: N=126
(1·54 per 1000)
N=3
(0·004%)
N=149
(0·18%)

Figure 6 Rates (%) of newborns who had early abduction treatment (initiated from birth or after watchful waiting the first six weeks of life), and of newborns who had ultrasound follow-up from birth without being treated, from January 1991 through December 2006.

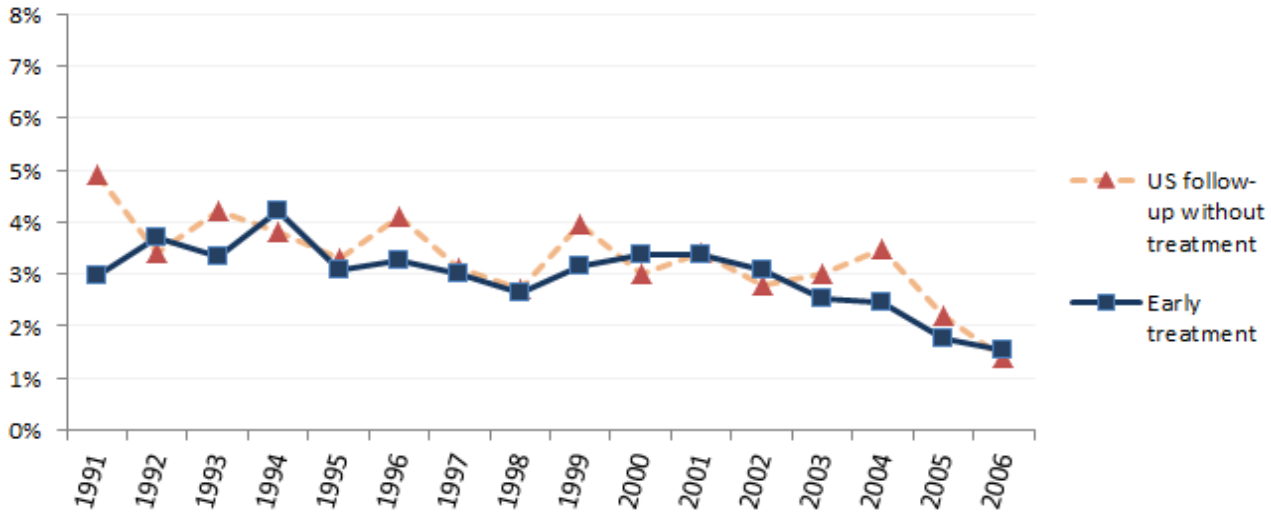


Table 1

Indications for hip ultrasound among newborns referred because of increased risk for developmental dysplasia of the hip. Figures are presented as total number and rates (%). More than one indication was possible for one infant.

Risk Factor	Total n=11190	Boys, n=4741	Girls, n=6449
Clinical hip instability on first newborn examination*	3334 (29·8)	1022 (21·6)	2312 (35·9)
Positive family history**	4739 (42·4)	2253 (47·5)	2486 (38·5)
Breech presentation at delivery	2513 (22·5)	1108 (23·4)	1405 (21·8)
Congenital foot deformity	197 (1·8)	85 (1·8)	112 (1·7)
Other reason***	1858 (16·6)	749 (15·8)	1109 (17·2)

*Includes pathological instability, dislocatable and dislocated hips. Of 3334 referred, 1351 had dislocatable/dislocated hips and were treated.

** ≥1 1st degree (sibling, parent) or ≥2 2nd degree (aunt, uncle, grand-parent) relative

***Includes slightly unstable hips, clicks, torticollis, muscular hypo/hyper tonicity or unknown

Table 2

Sonographic hip morphology at birth by sex among 11190 babies at risk for DDH based on the worst affected hip, and number (%) with clinically or sonographically dislocatable or dislocated hips according to morphology.

Hip morphology, n (%)				Number (%) with additional dislocatable / dislocated hips		
	Total	Males	Females	Total	Males	Females
Normal	2914 (26·0)	1685 (35·5)	1229 (19·1)	12 (0·4)	4 (0·24)	8 (0·65)
Immature	4687 (41·9)	2059 (43·5)	2628 (40·8)	224 (4·8)	65 (3·2)	159 (6·1)
Mild dysplasia	2678 (24·0)	829 (17·5)	1849 (28·7)	420 (15·7)	83 (9·9)	337 (18·2)
Severe dysplasia	911 (8·1)	168 (3·5)	743 (11·5)	695 (76)	125 (74·4)	570 (76·7)
Total	11190 (100)	4741 (100)	6449 (100)	1351 (12)	277 (5·8)	1074 (16·7)

Table 3 A

Rates of early abduction treatment according to clinical and sonographic findings at birth. Rates (% with 95% confidence interval (CI)) are presented with the total number of live births (81564) as the denominator

Early abduction treatment	Total	Boys	Girls	% of whole cohort, (95% CI)
Treatment from birth: Total	1882	412	1470	2·3%, (2·2-2·4)
Dislocatable or dislocated hip (clinically or sonographically) *and* severe dysplasia	695	125	570	
Dislocatable or dislocated hip (clinically or sonographically) *without* severe dysplasia	656	152	504	
Sonographically severe dysplasia, *without* dislocatable/dislocated hip	216	43	173	
Other reasons*	315	92	223	
Treatment from ≥6 weeks (after watchful waiting and repeat US)	551	116	435	0·7%, (0·6-0·8)
Total Early treatment	2433	528	1905	3·0%, (2·9-3·1)

*mildly dysplastic but stable hips, or pathologically or slightly unstable hips on clinical examination

Table 3 B

Rates of watchful waiting for babies at risk for DDH who had unstable (not dislocated/ dislocatable hips) and/or mild dysplasia as newborns. Rates (% with 95% confidence interval (CI)) are presented with the total number of live births (81564) as the denominator.

Watchful waiting from birth	Total	Boys	Girls	% of whole cohort, (95% CI)
Only ultrasound follow-up, no treatment				
Clinical or sonographic pathological instability alone	774	316	458	
Mild sonographic dysplasia alone	260	108	152	
Both pathological instability and mild dysplasia	1212	442	770	
Other reasons*	454	210	244	
Total**	2700	1076	1624	3·3%, (3·2-3·4)
Treatment after 6 weeks or longer of watchful waiting***				
Clinical or sonographic pathological instability alone	106	22	84	
Mild sonographic dysplasia alone	86	19	67	
Both pathological instability and mild dysplasia	317	63	254	
Other reasons*	42	12	30	
Total	551	116	435	0·7%, (0·6-0·8)

* immature hips on ultrasound and slightly unstable hips on clinical newborn examination

**1539 (57%) were followed until six weeks, 876 (32%) until three to four months, and the remaining 285 (11%) longer than four months before initiation of treatment.

***These children are included in the early treatment rate (table 2A).

Table 4

Children with late detected DDH diagnosed until five years of age according to low-risk or at-risk for DDH. Rates (% with 95% confidence interval (CI)) are presented with the total number of live births (81564) as the denominator

	Low-risk group* (boys+girls)	At-risk group** (boys+girls)
Late subluxation	16 (2+14)	2 (0+2)
Late dislocation	8 (0+8)	0
Total (late subluxation + dislocation)	26 (2+24)	
Rate per 1000, (95% CI)	0·32 (0·20-0·44)	
Late residual dysplasia	125 (21+104)	1 (0+1)
Total (residual dysplasia)	126 (21+105)	
Rate per 1000, (95% CI)	1·54 (1·27-1·81)	

* No risk factors and not examined by early ultrasound, ** Examined by ultrasound as newborns because of risk due to heredity, breech presentation , foot deformities or pathological instability on clinical examination

Table 5

Children undergoing a first surgical treatment performed until five years of age according to low-risk or at-risk for DDH. Rates (% with 95% confidence interval (CI)) are presented with the total number of live births (81564) as the denominator

	Low-risk group* (boys+girls)	At-risk group** (boys+girls)
Surgical treatment***		
Osteotomy	3 (0+3)	3(0+3)
Open reduction	3 (0+3)	4 (3+1)
Closed reduction	9 (0+9)	9 (2+7)
Total (0 weeks-5 years)	31 (5+26)	
Rate per 1000, (95% CI)	0·38 (0·25-0·51)	

* No risk factors and not examined by early ultrasound, ** Examined by ultrasound as newborns because of risk due to heredity, breech presentation , foot deformities or pathological instability on clinical examination ***All in need of surgery from the low-risk group were late detected cases. All from the at- risk group were detected from birth (nine had initial surgical treatment and seven were treated surgically after failure of abduction treatment).

Appendix 1: Report form for babies at risk for DDH referred to hip ultrasound at birth

Report form Referral Hip Ultrasound Referring clinician: _____

_____ _____ ☐ Girl ☐ Boy

Surname Birth date

_____ _____

Birth date mother Date of examination

Reason for referral (please indicate all reason(s)):

- ☐ Positive clinical findings
- ☐ Equivocal clinical findings
- ☐ Breech position at birth ☐ extended legs ☐ not extended legs
- ☐ Family history of DDH (siblings/parents): who _____
- ☐ Family history of DDH in at least two second grade relatives (grandparents, aunts, uncles): who: _____
- ☐ Foot deformities (pes equinovarus) or other particular reason, as indicated: _____

Tonicity:

- ☐ Hypo-tonicity- both legs fall easily until 90° of abduction
- ☐ Normal tonicity-both legs can easily be brought until 80-90° of abduction
- ☐ Hyper-tonicity- Abnormally high tonicity; 75° or less of abduction

Other clinical findings:

	Right		Left	
	yes	no	yes	no
Stable clicking (1)	☐	☐	☐	☐
Stable hips (2)	☐	☐	☐	☐
Slightly unstable, but within normal (3)	☐	☐	☐	☐
Pathological instability, not dislocatable (4)	☐	☐	☐	☐
Positive Barlow test (dislocatable) (5)	☐	☐	☐	☐
Positive Ortolani test (dislocated, reducible) (6)	☐	☐	☐	☐

Ultrasound findings: Date: _____

	Right	Left
Graf type (morphology) (Normal; Immature; Mild; Severe)	_____	_____
Stability (1-stable, 2-unstable not dislocatable, 3-dislocatable. 4-dislocated)	_____	_____

Re-evaluation: Date: _____ Clinician: _____

	Right	Left
Clinical findings (numeration as above):	_____	_____
Ultrasound:	_____	_____

Appendix 2: Protocol for management of DDH at Haukeland University Hospital

Routines for management of developmental dysplasia of the hip (DDH).
Departments of Paediatric Radiology, Paediatrics and Paediatric Orthopedic Surgery, Haukeland University Hospital

7. Screening of newborns:
   Premature babies (gestational age < 33 weeks) are not referred to hip ultrasound after breech presentation at birth, but on all other indications as for full-term born babies. Ultrasound is performed before departure from the hospital, unless the clinical circumstances require earlier examination.

8. Indication for treatment and further follow-up at 6 weeks in children that are not already under treatment:
   d. Persisting mild dysplasia (<50º): Initiate treatment with Frejka's splint. Clinical re-exam within 2-3 weeks, clinical and sonographic re-exam at 12-14 weeks.
   e. 50-55º: No treatment. New clinical re-exam at 12 weeks.
   f. ≥55º: No re-exam, unless siblings with late presenting DDH. If it is the case, a re-exam should be performed at 12 weeks, unless the alpha angle is ≥60º at 6 weeks.

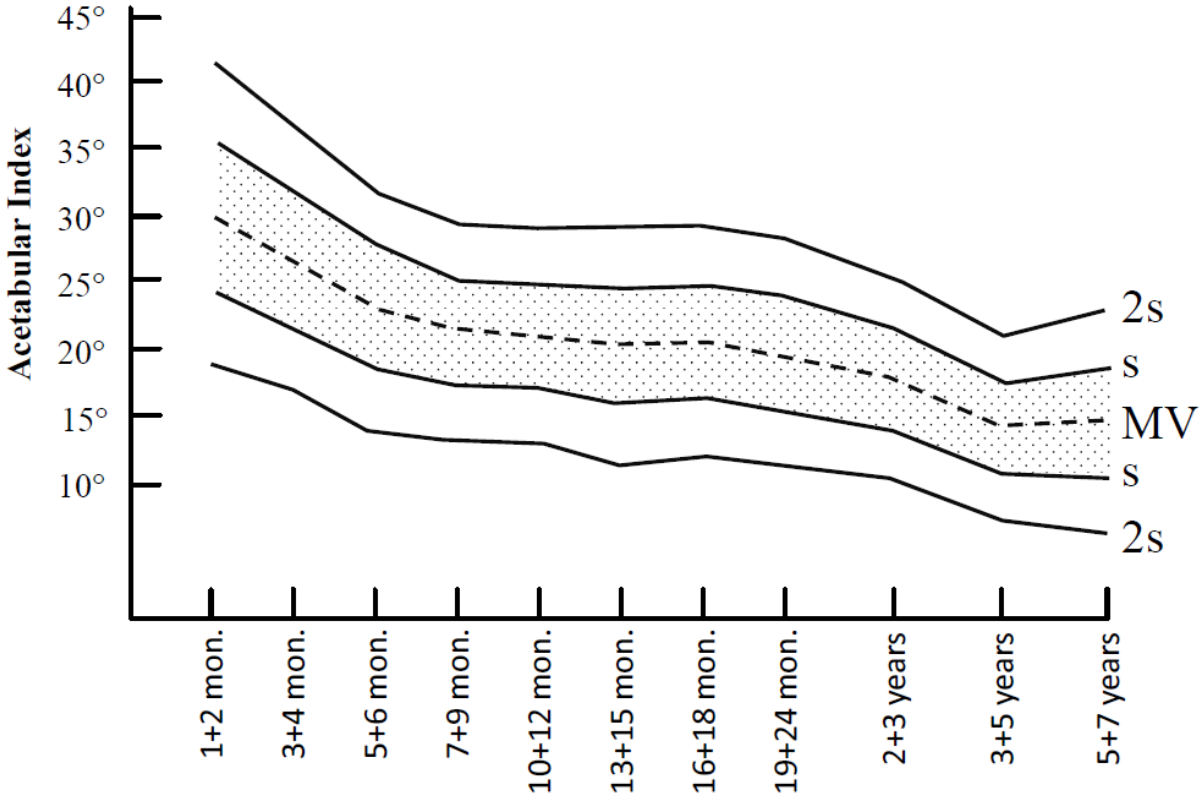
9. Indication for treatment and further follow-up at 3 months in children that are not already under treatment:
   d. No improvement from 6 weeks of age (50-55º): Orthosis
   e. 55-58º: Radiograph at 5 months
   f. ≥58º: No re-exam.

10. Indication for continuation of treatment at 3 months in children with abduction treatment:
   d. <55º: Continuation of treatment for 1-2 months, followed by radiograph
   e. 55-58º: Continuation of Frejkas splint treatment for 1 month. Parents stop treatment alone at home. New re-exam and radiographs at 6 months.
   f. ≥58º: Stop treatment. Re-exam with radiograph at 6 months of age.

11. Indication for later follow-up and treatment (after 3 months of age) (confer figure):
e. Dysplasia: Acetabular index (AI) > 2 standard deviations (SD) above mean: Orthosis
f. Delayed acetabular ossification (1 SD≤AI≤2 SD): new radiograph within 2-4 months
g. Normal (AI <1 SD above mean)
h. Children who are followed until 10-11 months of age due to unsatisfactory AI: Last radiograph at 18-24 months of age.

12. Late presenting DDH in need of treatment:
d. All cases where traction is considered: referral to orthopaedic surgeon
e. Older than 6 months of age and newly detected: referral to a paediatric orthopaedic surgeon.
f. Younger than 6 months of age, and in some cases older than 6 months but already followed some time at the paediatric radiology department: continuation of treatment managed by the paediatric radiology department.

Age-adapted mean values of the acetabular index (AI) with one and two standard deviations (SD) indicated. (with permission. Tönnis, Brunken 1968[19])



Appendix 3 First surgical treatment, including osteotomies, open and closed reductions, for children considered to be at risk and at low risk for DDH at birth, respectively. Cases of avascular necrosis of the femoral head are also presented for both risk groups. All cases marked with asterisks are included in the rate of a first surgical treatment performed until five years of age.

Patient	Age at diagnosis, m-months, y-years	Diagnosis	Initial treatment, start-end in w-weeks	First surgical treatment, start-end in m-months	Age at first surgical treatment, m-months, y-years	AVN, side, age in y-years
At-risk group						
Girl**	0m	Left subluxation severe bilateral dysplasia	Frejka 0-16w, orthosis 32-40w	Salter Osteotomy	24 m	
Girl**	0m	Bilateral subluxation	Frejka 0-12w	Salter Osteotomy	36m	
Girl**	0m	Right subluxation	Frejka 0-16w	Salter Osteotomy	36 m	
Girl	0m	Mild dysplasia and Bilateral instability	Frejka 0-18w, orthosis 18-24w	Salter Osteotomy	6 y	Left, 4y
Girl[¶]	0m	Mild dysplasia at birth, residual dysplasia at 16 years	Frejka 0-12w	PAO	16 y	
Girl[¶]	0m	Mild dysplasia at birth, residual dysplasia at 18 years	Frejka 0-12w	PAO	18 y	
Girl**	0m	Right dislocation	Frejka, 0-12w	Open reduction, cast	3m	
Girl*	0m	Bilateral immature and pathologically unstable hips. At 8 weeks mild dysplasia and subluxated left hip.	Ultrasound surveillance 0-8w	Closed reduction, cast	2 m	
Girl**	0/3 m	Bilateral dysplasia at birth. Left dislocation at 3 weeks	Frejka 0-3w	Closed reduction, cast 1-3m	1 m	Right, 3y
Girl*	0m	Dislocated and severely dysplastic hips	-	Closed reduction, cast	0m	
Girl*	0m	Dislocated and severely dysplastic hips	-	Closed reduction, cast 0-1m, orthosis 1-8m	0m	
Girl*	0m	Right dislocation	-	Closed reduction, cast	0m	
Girl*	0m	Left dysplasia	-	Closed reduction, cast, orthosis	0m	
Girl*	0m	Right dysplasia	-	Closed reduction, cast	0m	
Girl[#]	0m	Left dislocation and severe bilateral dysplasia at birth (32^{nd} gestational week)	Frejka 0-12w	None	-	Left, 4y
Boy	0m	Left dislocation, right subluxation	Frejka 0-16w	Salter Osteotomy	10 y	
Boy*	0m	Bilateral subluxation	-	Open reduction and cast (birth), orthosis 0-12m, Salter	0 m	Right, 4y

				Osteotomy 36 m		
Boy*	0m	Left dislocation	-	Open reduction, cast (birth), Salter Osteotomy at 10 years	0m	
Boy**	0m	Left dislocation	Frejka 0-12w	Open reduction, cast	48m	
Boy**	0m	Left dislocation	Frejka 0-12w	Closed reduction, cast	3m	
Boy*	0m	Right dislocation	-	Closed reduction, cast 0-3m	0m	
Low-risk group						
Girl***	36 m	Late right subluxation	-	Salter Osteotomy	48 m	
Girl***	15 m	Late right subluxation	-	Salter Osteotomy	60 m	
Girl***	10 m	Late restricted abduction right	-	Salter Osteotomy	36 m	
Girl[¶]	17 y	Residual dysplasia at 17 years	-	PAO	17 y	
Girl***	7 m	Late left dislocation	-	Traction, open reduction, adductor tenotomy	7m	Left, 3y
Girl***	18 m	Late right dislocation	-	Open reduction	18m	
Girl***	2 m	Late right subluxation	-	Open reduction, adductor tenotomy, cast, orthosis 2-21m	2 m	Right, 3·5y
Girl***	5 m	Late left dislocation	-	Traction, closed reduction, cast, orthosis 6-12m	5m	Left, 3y
Girl***	8 m	Late left dislocation	-	Closed reduction, cast	8m	
Girl***	7 m	Late left irreducible dislocation	-	Closed reduction, cast	7m	
Girl***	2 m	Late left subluxation	Orthosis 8-76w	Traction, closed reduction, cast	18m	
Girl***	12 m	Late left subluxation	-	Traction, closed reduction, cast	12m	
Girl***	3 m	Late left subluxation	-	Traction, closed reduction, cast	3m	
Girl***	1·5 m	Late right dislocation	-	Traction, closed reduction, cast	1·5 m	
Girl***	6 m	Late right dislocation	-	Closed reduction, cast	6m	
Girl***	6 m	Late left subluxation	-	Traction, closed reduction	6m	
Boy	48 m	Late bilateral dysplasia	-	Salter Osteotomy	7+8 y	
Boy[¶]	8 y	Residual dysplasia at 8 years	-	Salter Osteotomy	8 y	
Boy[¶]	19 y	Residual dysplasia at 19 years	-	PAO	19 y	

PAO: Periacetabular osteotomy; AVN: avascular necrosis of the hip
* Initial surgical treatment the first weeks of life
** Surgical treatment after failure of initial abduction treatment
*** Surgical treatment due to late detected DDH
[#] Included due to AVN, did not have any surgical treatment
[¶] The five additional cases of late DDH detected after five years of age

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Screening Strategies for Hip Dysplasia: Long-term Outcome of a Randomized Controlled Trial

Lene B. Laborie, Ingvild Ø. Engesæter, Trude G. Lehmann, Deborah M. Eastwood, Lars B. Engesæter and Karen Rosendahl

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Screening Strategies for Hip Dysplasia: Long-term Outcome of a Randomized Controlled Trial

WHAT'S KNOWN ON THIS SUBJECT: Only 2 randomized controlled trials have addressed effects of ultrasound screening for developmental hip dysplasia. Both concluded that adding universal or selective ultrasound to routine clinical examination gave a nonsignificant reduction in rates of late presenting cases, but higher treatment rates.

WHAT THIS STUDY ADDS: This maturity review assesses long-term outcome of one of these trials. Rates of radiographic findings indicating acetabular dysplasia and degenerative change were similar across the 3 screening groups in young adulthood. Increased treatment rates were not associated with avascular necrosis.

abstract

OBJECTIVE: Screening for hip dysplasia is controversial. A previous randomized controlled trial revealed that adding universal or selective ultrasound to routine clinical examination gave a nonsignificant reduction in rates of late presenting cases, but with higher treatment rates. This study assesses differences in outcome at skeletal maturity for the 3 newborn screening strategies in terms of radiographic markers of acetabular dysplasia and early degenerative change and avascular necrosis (AVN) secondary to neonatal treatment.

METHODS: From the initial trial including 11 925 newborns, a population-based sample of 3935 adolescents was invited for follow-up at age 18 to 20 years. A standardized weight-bearing anteroposterior view was obtained. The outcomes evaluated were the radiographic findings of dysplasia (center-edge angle, femoral head extrusion-index, acetabular depth-width ratio, Sharp's angle, subjective evaluation of dysplasia) and degenerative change (joint-space width). Signs of AVN were documented.

RESULTS: Of the 3935 subjects invited, 2038 (51.8%) attended the maturity review, of which 2011 (58.2% female patients) were included: 551, 665, and 795 subjects from the universal, selective, and clinical groups, respectively. Rates per group of positive radiographic findings associated with dysplasia or degenerative change varied depending on radiographic marker used. No statistically significant differences were detected between groups. No AVN was seen.

CONCLUSIONS: Although both selective and universal ultrasound screenings gave a nonsignificant reduction in rates of late cases when compared with expert clinical programs, we were unable to demonstrate any additional reduction in the rates of radiographic findings associated with acetabular dysplasia or degenerative change at maturity. Increased treatment rates were not associated with AVN. *Pediatrics* 2013;132:492–501

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KEY WORDS

hip dysplasia, ultrasound, randomized controlled trial, follow-up studies, neonatal screening

ABBREVIATIONS

ADR—acetabular depth-width ratio
AVN—avascular necrosis
CE—centre-edge
DDH—developmental dysplasia of the hip
FHEI—femoral head extrusion index
RCT—randomized controlled trial

Dr Laborie collected the data material at follow-up, was responsible for the linkage of data from the initial trial and from the follow-up study, performed the radiographic digital measurements, drafted the initial manuscript and was responsible for the statistical analyses, and revised the manuscript; Dr Engesæter collected the data material at follow-up, performed the radiographic digital measurements, and critically reviewed and revised the manuscript; Dr Lehmann collected the data material at follow-up, performed the radiographic digital measurements, and critically reviewed and revised the manuscript; Ms Eastwood offered help and advice regarding study design and data collection, contributed to the preliminary statistical analyses, and critically reviewed and revised the manuscript; Dr Engesæter conceptualized and designed the follow-up study, coordinated and participated in collection of the data material at follow-up, and reviewed and revised the manuscript; Dr Rosendahl conceptualized and designed the initial randomized controlled trial and also the follow-up study, collected all data and performed all ultrasounds for the initial trial, interpreted all radiographs at skeletal maturity by gross vision, contributed to the statistical analyses, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

This trial has been registered at www.clinicaltrials.gov (identifier NCT01818934).

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Developmental dysplasia of the hip (DDH) represents an important health issue and is the underlying cause of 1 in 4 total hip replacements in patients under the age of 40.[1] The reported prevalence varies from 0.15% to 4% according to definition used, age, ethnicity, and method of ascertainment.[2–5] Clinical neonatal screening with early treatment of those testing positive was introduced ~6 decades ago. It has, however, not been as efficient in reducing the rates of late presenting cases and their need for surgery as first expected,[6–8] due perhaps to poorly organized screening programs, inexperienced examiners, and/or insufficient follow-up.[9,10] This led to the widespread use of hip ultrasound throughout Europe, with implementation of universal or selective ultrasound screening before 6 weeks of age, associated with treatment rates as high as 7.7% after universal ultrasound.[11–15] The rate of late presenting DDH is commonly used as outcome measure in the evaluation of a screening program. However, the age definition of a "late case" ranges from 4 weeks of age to 6 months of age and more, making the interpretation of the literature difficult. Screening policies have been influenced by a number of studies, including 2 randomized controlled trials (RCTs), which both advocate a selective ultrasound approach, in addition to high-quality clinical screening.[16,17] One of the RCTs, performed at our institution,[16] evaluated the effect of 3 different ultrasound screening strategies for DDH in newborns. It demonstrated a nonsignificant reduction in the rates of late presenting (ie, after 4 weeks of age) subluxated or dislocated DDH in the universally and selectively screened groups as compared with the group receiving clinical examination alone ($P = .11$), but also higher treatment rates for the universal group ($P < .001$) (Table 1).

Results from a maturity review of a population-based sample drawn from the initial RCT have previously shown that the prevalence of radiographic findings associated with hip dysplasia in young adulthood (based on at least 1 affected hip) ranged from 1.7% to 20% depending on the radiographic measurement and on their corresponding cutoff values used.[18] This wide range highlights the challenge of defining acetabular dysplasia. Based on the original RCT, we hypothesized that at skeletal maturity there would be no difference between the 3 trial groups in the rates of radiographic findings associated with acetabular dysplasia or early degenerative change. Avascular necrosis (AVN) of the femoral head described as a medial flattening of the femoral head was documented for the 3 groups as a potential adverse effect of neonatal treatment.

TABLE 1 Rates of Abduction Treatment, Ultrasound Follow-up and Late Detected Cases by Screening Group During the Initial RCT in 1988–1990 Comprising 11 925 Newborns

Variable	Universal Ultrasound Screening ($n = 3613$)	Selective Ultrasound Screening ($n = 4388$)	No Ultrasound Screening ($n = 3924$)	Prestudy Period 1983–1987
Treatment rate (%)	123 (3.4)	89 (2.0)	71 (1.8)	2.0
Ultrasound follow-up rate (%)	470 (13.0)	78 (1.8)	—	14–20[a]
Rate of late cases[b] (per 1000)	1 (0.3)	3 (0.7)	5 (1.3)	2.6

[a] Pelvic radiograph at 4.5 months.
[b] Subluxated or dislocated hips.

METHODS:

Study Population and Design

The current study is a maturity review of a population-based sample drawn from the initial RCT.[16] The original RCT study included 11 925 infants born during January 1988 to June 1990 at the maternity hospital in Bergen, Norway. The infants studied were assigned to universal ultrasound screening ($n = 3613$), selective ultrasound screening ($n = 4388$), or clinical screening alone ($n = 3924$). The "1989 Bergen Birth Cohort Hip Study" was defined as all newborns from 1989 included in the initial RCT except those whose mother lived outside the hospital catchment area ($n = 296$) (Fig 1). Of these, 3935 were invited by postal letter to participate in this review (Fig 1), performed at the pediatric radiology department between March 2007 and March 2009.

Original RCT Performed During 1988–1990

This RCT[16] was published in 1994 and is described in detail in the Appendix. All newborns were assessed for known risk factors for DDH (breech presentation and/or family history of DDH). All infants had a clinical assessment, including hip stability (Barlow/Ortolani tests).[19,20] In addition, high-risk infants (ie, at least 1 risk factor, and/or clinical hip instability) from the selectively screened group and all infants from the universally screened group were offered a single examiner hip ultrasound (Rosendahl's method) at birth (Fig 2).[21] Rates of abduction treatment, ultrasound follow-up, and late detected (ie, after 4 weeks) cases by screening group are shown in Table 1. There were 6 late detected subluxated hips and 3 late detected dislocated hips among the original 11 925 participants. All 9 received traction followed by cast and/or orthotic treatment: the 3 dislocated hips also had a closed (2) or open (1) reduction. None of the 3 dislocated cases had had an ultrasound performed: 2 came from the clinical screening group, and 1 was classified low-risk from the selectively screened group. Of the 6 cases with subluxation, 5 were low-risk cases from the clinical (3) and the selectively screened (2) groups, and thus did not have a newborn hip ultrasound. The final case was low-risk

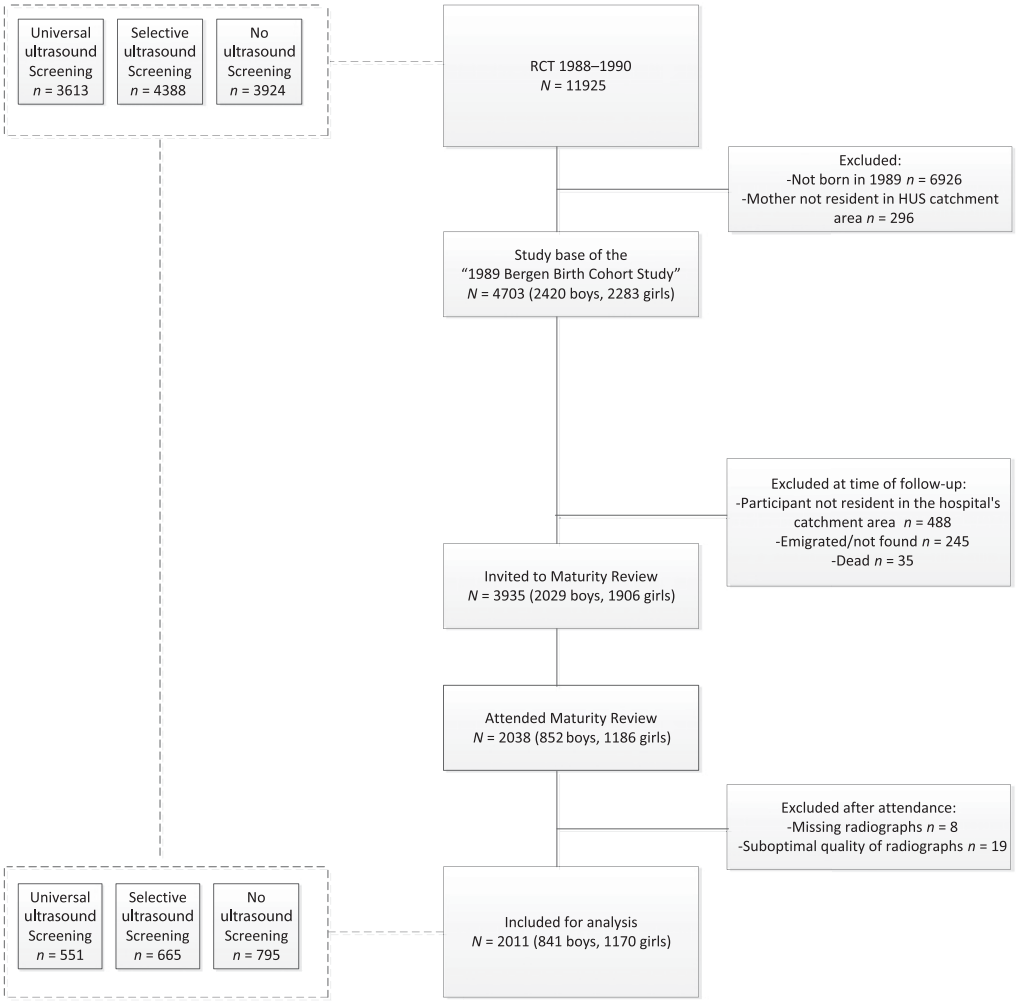

FIGURE 1
Flowchart of participants included in the original RCT (1988–1990) and who later attended the maturity review (2007–2009).

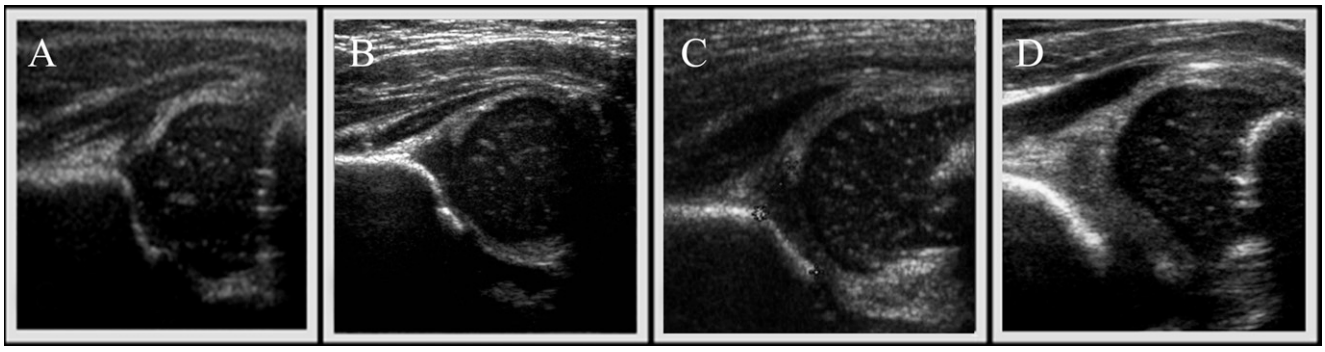

FIGURE 2
Graf's coronal standard section through the midacetabulum revealing normal (A), immature (B), mild (C), and severe dysplasia (D) in a newborn hip.

but in the universally screened group, with a reportedly normal ultrasound at birth. There were no signs of AVN at the conclusion of the original RCT at a minimum 27 months of age.

Data Collection at Maturity Review

The follow-up study aimed to assess radiographic and clinical features related to acetabular dysplasia and early degenerative change at skeletal maturity. The participants were asked about weekly hours of physical activity and self-reported hip discomfort in either hip during the preceding 3 months. The clinical assessment included height,

weight, and hip range of motion in all planes. All examiners were unaware of the original screening group. Exclusion criteria were radiographs of suboptimal technical quality, including excessive pelvic rotation as assessed by a foramen obturator index beyond the range 0.6 to 1.8,[22] or missing radiographs (uncertain pregnancy status or examination refused). Searches within the database of our hospital and of the only other orthopedic hospital in the area detected no additional cases of late presenting DDH or of surgery among the nonresponders. At follow-up, baseline characteristics from the original RCT including gender, birth weight, positive clinical findings (Barlow/Ortolani), positive family history, and breech presentation were compared between the 3 sample groups.

The weight-bearing, anteroposterior view (Fig 3) was obtained according to a standardized protocol, by 1 specifically trained radiographer. All radiographs were obtained with a low-dose digital radiography technique (Digital Diagnost System, version 1.5, Philips Medical Systems, Best, Netherlands). The film/focus distance was 1.2 m and centered at 2 cm proximal to the symphysis. A tube containing a contrast medium was placed in the radiograph field to give the true horizontal level for leg length measurement. The radiographer ensured that hips were kept in a neutral abduction-adduction position with toes pointing forward.[5,23] All male patients were offered gonadal shields. The radiographs were measured in the digital measurement program "Adult DDH" (University of Iowa Hospitals and Clinics, Iowa City, IA),[24] by 3 of the authors (Drs Laborie, Engesæter, and Lehmann), unaware of original screening group. Detailed descriptions of the digital measurement program, of its accuracy and of the measurements included have been reported previously.[25,26] The following measurements were performed digitally. Markers for acetabular dysplasia (Fig 4 A–D): The center-edge (CE) angle of Wiberg,[27] the femoral head extrusion index (FHEI),[28] the acetabular depth-width ratio (ADR),[29] and Sharp's angle.[30] Minimum joint space width (JSW) as a marker for early degenerative change was measured digitally at 3 locations: laterally, centrally, and medially (Fig 5).[31,32] There is no clear consensus on the definition of acetabular dysplasia at skeletal maturity.[18] To perform a group comparison of acetabular dysplasia as a long-term outcome, we chose to assess the most common radiographic measurements and findings associated with acetabular dysplasia. For the CE angle, we also calculated the rates of the often used borderline group, for detection of differences at a level in between normal and dysplastic hips. As the definition of acetabular dysplasia is unclear, we also created an individual variable corresponding to ≥1 positive dysplasia finding based on categorization of the angle measurements. We then compared the results at a group level. All angle measurements were performed digitally. Subjectively assessed findings and leg length discrepancy were not part of the digital program and thus assessed manually in the IMPAX (Agfa IMPAX Web1000, version 5.0, Agfa Gaevert, Mortsel, Belgium). The shape of the lateral acetabular roof, namely the subchondral bony condensation known as the "sourcil" was evaluated subjectively as normal, immature, or mildly

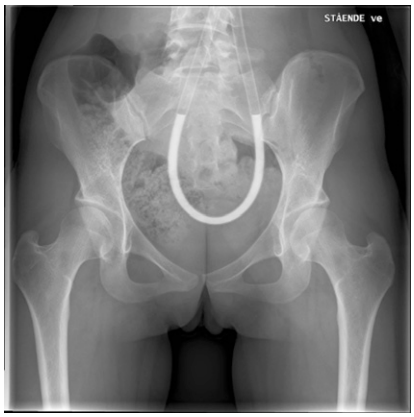

FIGURE 3
A weight-bearing anteroposterior radiograph of a study participant at skeletal maturity, revealing bilateral moderate dysplasia.

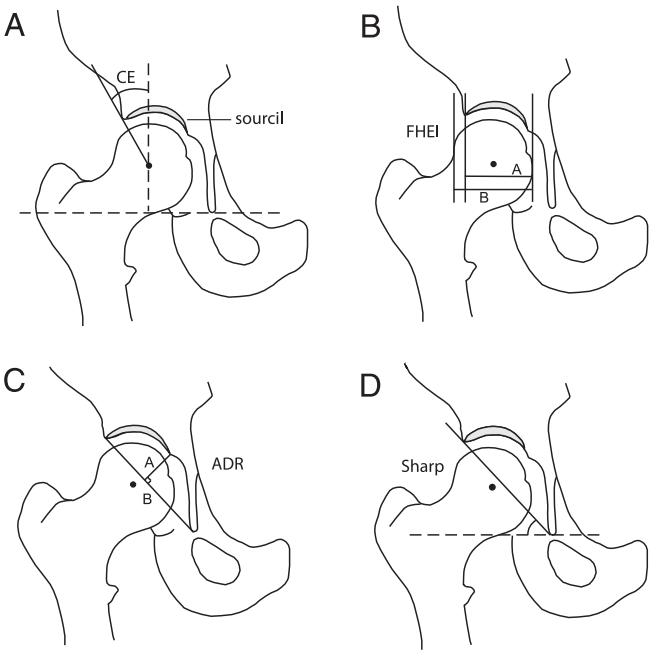

FIGURE 4
Measurements describing the position of the femoral head relative to the acetabular cavity: CE angle of Wiberg (A) and FHEI (B). Measurements describing the acetabular anatomy: ADR ([A/B]*1000) (C) and Sharp's angle (D).

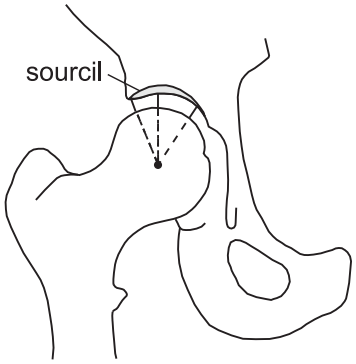

FIGURE 5
JSW at the medial, central, and lateral position in the hip joint.

or moderately dysplastic.[33] This subjective assessment of dysplasia was performed by a musculoskeletal radiologist with more than 25 years of experience (Dr Rosendahl), and was included as an alternative and complementary assessment of acetabular dysplasia. Subjective evaluation of medial flattening of the femoral head indicative of AVN as a possible complication of treatment was also performed by the senior author (Dr Rosendahl).[34] Leg length discrepancy was measured manually by one author (Dr Laborie), by drawing a true horizontal line through the tube at the 2 top levels of liquid contrast (Fig 3), and thereafter measuring perpendicularly down to the top of the caput on each side. A difference of >5 mm was considered a positive finding.

Ethics

The research protocol, including analyses of the nonresponders, was approved by the Regional Ethical Committee for Medical and Health Research (number 018.06). All participants of the follow-up study gave written informed consent according to the 1964 Declaration of Helsinki.

Statistical Analysis

Data for the radiologic outcome measures were summarized by using mean and SD, or number and percentage, as appropriate. The radiographic measurements were compared as continuous variables, and also categorized as normal or dysplastic, based on previously published gender-specific cutoff values (CE angle <21°/<20°, Sharp's angle >46°/>47°, FHEI <74%/<73%, and ADR <235‰/<233‰ for male and female patients, respectively).[26] In addition, an intermediate borderline group (<25°) for the CE angle as a categorical variable was calculated.[18] A categorical variable corresponding to at least 1 positive radiographic marker was created, consisting of the CE angle (dysplastic values only), FHEI, ADR, and Sharp's angle. Subjective evaluation of the sourcil was a categorical variable. JSW was assessed both as a continuous variable and also categorized as normal or pathologic, defined as minimum JSW ≤ 2 mm in at least 1 position.[5,35]

A general regression model was performed, adjusted by side, gender, family history, and breech and taking into account clustering of hips within a subject to compare the 3 screening groups. Univariate (crude) and multivariate (adjusted) *P* values are presented. No correction for multiple comparisons was performed. All *P* values were 2-tailed. To adjust for nonresponders when comparing the 3 screening groups we calculated inverse probability weights[36] based on a logistic regression model including gender, ultrasound performed at birth (yes/no), and DDH treatment received (yes/no) as covariates. Statistical analyses were performed in IBM SPSS Statistics, version 20.0 (Armonk, NY) and in Stata Statistical Software (Release 11, Stata Corp, College Station, TX).

RESULTS

Of the 3935 subjects invited, 2038 (51.8%) attended the follow-up, of which 2011 (1170 [58.2%] female participants) were included for further analyses, predominantly ethnic Norwegians.

This population-based sample of 2011 participants represented equal proportions of the 3 original RCT screening groups: 551/3613 (15.3%), 665/4388 (15.2%), and 795/3924 (20.3%) subjects originated from the initial universal ultrasound, selective ultrasound, and clinical only screening groups, respectively (Fig 1). Mean age was 18.6 years (SD 0.6, range 17.2–20.1 years) for both genders. The 3 groups were similar at time of follow-up with respect to gender distribution (*P* = .56), BMI (kg/m^2) (*P* = .83), weekly hours of physical activity (*P* = .80), leg length discrepancy (*P* = .85), and hip range of motion in all planes (all *P* values > 0.20). Hip discomfort during the preceding 3 months were similarly distributed between groups for right and left side (*P* = .81 and *P* = .75, respectively). The 3 groups also demonstrated similar baseline characteristics from the RCT with respect to birth weight, positive clinical findings (Barlow/Ortolani), and positive family history (*P* = .37, *P* = .44, *P* = .57, respectively). Similar to the initial universal group, breech presentation was slightly higher in the corresponding follow-up group as compared with the 2 other groups (6.4% vs 3.6% and 3.7% at follow-up, *P* = .03). Among the 2011 subjects who attended the follow-up, 39/551 (7.1%), 33/665 (4.9%), and 30/795 (3.8%) had received abduction treatment in the universal, selective, and no ultrasound screening groups, respectively.

Radiologic Outcome Measures

The rates per screening group of radiographic findings associated with left- or right-sided acetabular dysplasia varied depending on the measurement used: The CE angle, FHEI, ADR, Sharp's angle, and subjective evaluation of the sourcil shape. Dysplastic rates based on the 4 angle measurements ranged from 1.1% (FHEI in the universal group) to 3.4% (CE angle in the no ultrasound group). The total rate when including those with at least 1 positive dysplastic findings

based on the 4 categorical angle measurements ranged from 5.7% to 7.6% for the left side, and from 5.4% to 7.6% for the right side. Rates based on a borderline CE angle <25° ranged from 9.3% to 13.3% on left and right side separately. No statistically significant differences in acetabular dysplasia, as assessed by the CE angle, FHEI, ADR, Sharp's angle, or subjective evaluation of the sourcil shape could be found between the 3 groups at skeletal maturity (Tables 2 and 3).

On subjective evaluation of the sourcil shape, 6 hips (4 girls) were classified as moderate dysplasia (Fig 3). Two left (0.25%) and 3 right (0.38%) hips (1 unilateral and 2 bilateral cases) came from the no ultrasound group and 1 left (0.15%) hip from the low-risk arm (ie, no ultrasound) of the selective group (Table 3). The 1 unilateral case from the clinically screened group had a late detected left dislocated hip and received a closed reduction in infancy. One of the persons from the no ultrasound group, with bilateral moderate dysplasia as assessed both subjectively and by the angle measurements, was referred to an orthopedic surgeon.

The rates of a positive minimum JSW as an indicator for early degenerative change ranged from 3.1% to 4.7% and from 1.9% to 3.0% for left and right side, respectively, without any detectable differences between groups (Table 4). None of the study participants had a flattening of the medial aspect of the femoral head interpreted as a sign of AVN.

TABLE 2 Radiographic Findings (Mean [SD]) at Time of Follow-up of the 2011 Participants, According to Newborn Screening Group During the RCT

Variable	Screening Strategy			*P*	
	Universal Ultrasound (*n* = 551), Mean (SD)	Selective Ultrasound (*n* = 665), Mean (SD)	No Ultrasound (*n* = 795), Mean (SD)	Crude	Adjusted[a]
CE angle of Wiberg (°)					
Left	31.8 (5.9)	31.8 (5.9)	32.3 (6.0)	.12	—
Right	31.3 (6.0)	31.2 (6.1)	31.7 (6.2)	.25	.28
FHEI (%)					
Left	86.7 (6.3)	86.6 (6.5)	87.1 (6.4)	.24	—
Right	85.4 (6.3)	85.6 (6.6)	86.0 (6.5)	.21	.40
ADR (‰)					
Left	300.0 (35.4)	296.8 (34.7)	299.9 (34.6)	.17	—
Right	297.2 (34.4)	295.3 (35.5)	296.6 (36.1)	.63	.25
Sharp's angle (°)					
Left	40.1 (3.5)	39.8 (3.7)	39.9 (3.8)	.25	—
Right	39.9 (3.6)	40.0 (3.7)	39.8 (3.6)	.73	.56

[a] Estimated by using a general regression model, adjusted by side, gender, family history and breech, and taking into account clustering of hips within a subject.

DISCUSSION

The wide variety of management strategies used for DDH reflects our poor understanding of its natural course and the short- and long-term effects of different treatment and follow-up programs. To date, only 2 RCTs addressing these issues have been performed; both concluded that universal and selective ultrasound screening tended to reduce the rates of late cases during infancy and early childhood but at the cost of higher treatment rates. Ultrasound is able to identify newborns with dysplastic hips in need of early treatment, thus reducing the number of late subluxed or dislocated cases in early childhood. Its ability to prevent acetabular dysplasia at skeletal maturity, however, has not been demonstrated. Several authors have emphasized the need for outcome studies at skeletal maturity for the different screening policies.[37–39]

Our study confirms that in a Norwegian population, all 3 screening programs studied resulted in similar rates of all radiographic findings associated with acetabular dysplasia or early degenerative change at skeletal maturity. Offering universal hip ultrasound, and treating those testing positive, had thus no additional impact at a group level at skeletal maturity. A universal strategy with higher treatment rates did not seem to cause higher rates of AVN even though abduction treatment may place hips at risk. We have previously shown that based on existing cutoff values the prevalence of acetabular dysplasia (ie, at least 1 hip) ranges from 1.7% to 20% in this cohort,[18] with the lowest value based on the subjective assessment of the sourcil shape, and the highest value based on the borderline CE angle. The prevalence based on the dysplastic CE angle was 3.3%. These previous findings confirm the challenge in diagnosing acetabular dysplasia. Assessment of acetabular dysplasia at skeletal maturity is important as it is associated with early onset hip osteoarthritis.[5,40] Several radiographic measurements are used to describe and define the condition, with presumably varying clinical validity as to which extent they are indicators for early degenerative change. Significant relationships between radiographic osteoarthritis discriminators including minimum JSW, and dysplasia discriminators including the CE angle, FHEI, and ADR were shown in a Danish study.[5] We chose to assess the most common quantitative measurements (ie, CE angle, FHEI, ADR, and Sharp's angle), and also a subjective evaluation of dysplasia.[18]

The strengths of our study include a large original RCT (11 925 infants) as the basis for this follow-up study, with standard protocols that remained unchanged throughout the whole RCT period. This maturity review also followed a highly standardized radiographic protocol. One specifically trained radiographer performed all the radiographs and ensured correct posture to avoid pelvic tilting and rotation.[41] Moreover, each of the 3

TABLE 3 Radiographic Findings (*N* [%]) at Time of Follow-up of the 2011 Participants, According to Newborn Screening Group During the RCT

Variable	Screening Strategy			*P*	
	Universal Ultrasound (*n* = 551), *n* (%)	Selective Ultrasound (*n* = 665), *n* (%)	No Ultrasound (*n* = 795), *n* (%)	Crude	Adjusted[a]
CE angle of Wiberg					
Left borderline	57 (10.3)	73 (11.0)	74 (9.3)	—	—
Dysplasia	10 (1.8)	15 (2.3)	16 (2.0)	.83	—
Right borderline	73 (13.3)	77 (11.6)	84 (10.6)	—	.54
Dysplasia	10 (1.8)	20 (3.0)	27 (3.4)	.28	.20
FHEI					
Left	6 (1.1)	14 (2.1)	12 (1.5)	.36	—
Right	10 (1.8)	20 (3.0)	18 (2.3)	.38	.71
ADR					
Left	13 (2.4)	22 (3.3)	12 (1.5)	.08	—
Right	10 (1.8)	18 (2.7)	24 (3.0)	.38	.44
Sharp's angle					
Left	16 (2.9)	20 (3.0)	25 (3.1)	.97	—
Right	12 (2.2)	19 (2.3)	18 (2.3)	.69	.70
Dysplasia score[b]					
Left ≥1 positive findings	36 (6.6)	50 (7.6)	45 (5.7)	.36	—
Right ≥1 positive findings	30 (5.4)	50 (7.6)	55 (6.9)	.34	.36
Subjectively assessed dysplasia					
Left normal	491 (89.1)	597 (89.8)	716 (90.1)	—	—
Immature	55 (10.0)	55 (8.3)	70 (8.8)	—	—
Mild	5 (0.9)	12 (1.8)	7 (0.9)	—	—
Moderate	—	1 (0.15)	2 (0.25)	.52	—
Right normal	491 (89.1)	594 (89.3)	721 (90.7)	—	—
Immature	56 (10.2)	61 (9.2)	64 (8.1)	—	.15
Mild	4 (0.7)	10 (1.5)	7 (0.9)	—	.26[c]
Moderate	—	—	3 (0.38)	.30	—

[a] Estimated by using a general regression model, adjusted by side, gender, family history and breech, and taking into account clustering of hips within a subject.
[b] Dysplasia score based on positive CE (dysplastic), FHEI, ADR, and Sharp values.
[c] Combined *P* value for mild and moderate score, due to few cases of moderate dysplasia.

TABLE 4 Minimum Joint Space Width (Mean [SD] and *N* [%]) Indicating Early Degenerative Change at Time of Follow-up of the 2011 Participants, According to Newborn Screening Group During the RCT

Variable	Screening Strategy			*P*	
	Universal Ultrasound, *n* = 551	Selective Ultrasound, *n* = 665	No Ultrasound, *n* = 795	Crude	Adjusted[a]
JSW, mean (SD), mm					
Lateral left	5.3 (1.1)	5.3 (1.1)	5.3 (1.1)	.87	—
Right	5.4 (1.1)	5.4 (1.2)	5.5 (1.1)	.29	.31
Central left	3.6 (0.9)	3.6 (0.9)	3.5 (0.8)	.53	—
Right	3.7 (0.8)	3.7 (0.8)	3.7 (0.8)	.57	.88
Medial left	4.4 (1.3)	4.5 (1.4)	4.5 (1.4)	.44	—
Right	4.4 (1.2)	4.5 (1.3)	4.4 (1.3)	.82	.53
JSW, *n* (%)[b]					
Left	26 (4.7)	31 (4.7)	25 (3.1)	.23	—
Right	13 (2.4)	20 (3.0)	15 (1.9)	.38	.12

[a] Estimated by using a general regression model, adjusted by side, gender, family history and breech, and taking into account clustering of hips within a subject.
[b] Less than or equal to 2 mm in at least 1 position.

groups had a similar participation rate at follow-up.

We acknowledge several limitations to our study. We have only reviewed 2038 young adults, corresponding to 17% of the 11 925 included in the original RCT. This weakens the power of the study as the original trial was not designed to detect such differences between the 3 groups at time of follow-up. An undetected difference (type II error) can therefore not be excluded. Based on the population-based sample invited, there was a moderate follow-up rate of 51.8%. Previous analyses based on height and weight measured at birth, 7 and 19 years of age revealed no differences between the responders and the nonresponders except for the gender distribution.[42] The treatment rate for each group was higher in the maturity sample than in the original RCT, most likely due to a selection bias reflecting that those who received treatment of DDH were more prone to participate at follow-up. We therefore calculated inverse probability weights taking into account gender, hip ultrasound at birth, and treatment of DDH to adjust for nonresponders when comparing the 3 screening groups.

CONCLUSIONS

Although both selective and universal ultrasound screenings gave a nonsignificant

reduction in the rates of late cases in infants and young children when compared with expert clinical programs, we were not able to demonstrate any additional reduction in rates of radiographic findings associated with acetabular dysplasia or early degenerative change at maturity, thus confirming our hypothesis. Increased treatment rates were not associated with AVN.

APPENDIX: ADDITIONAL INFORMATION REGARDING THE ORIGINAL RCT PERFORMED DURING 1988–1990

The original study base of the RCT included 11 925 infants born during January 1988 to June 1990 at the maternity hospital in Bergen, Norway, after exclusion of those with birth weight <1500 g, with severe disease/malformations or who died within the first month after birth (n = 103).[16] The infants studied were randomly assigned to universal ultrasound screening (n = 3613), selective ultrasound screening (n = 4388), or clinical screening alone (n = 3924). The details regarding the randomization process is described in the original article presenting the RCT.[16] The maternity unit in Bergen consists of 3 equally sized nursery units, separate from the delivery ward. The 3 units received patients in a random sequence according to available beds. One of the units (unit 2) received some more women recovering from cesarean deliveries due to the availability of a few single-patient rooms, and thus a slightly higher rate of breech presentation deliveries was expected at this unit. The staff at the delivery unit did not receive any information on the ongoing trial. The general screening group represented unit 2 and half of unit 3, and the selective screening group represented the other half of unit 3, and unit 1. Infants born when ultrasound was not available comprised the clinical only group and represented all 3 units. Unavailability occurred in periods of 1 to 3 weeks spread unsystematically throughout the year. Randomization was area-based (cluster randomization), to keep mothers separate (ie, to avoid recall bias with respect to risk factors). This decision was based on experiences from 1987, when all girls and boys at risk were offered ultrasound screening. The mothers of the participants and the ultrasound examiner were aware of group assignment when the ultrasound was performed.

The aim of the RCT was to determine more appropriate criteria for treatment and to determine whether the addition of a universal or selective ultrasound screening program resulted in a reduced prevalence of late DDH (ie, after 4 weeks of age) compared with clinical examination alone. Cases of AVN of the femoral head were also reported.

All newborns were assessed by means of known risk factors for DDH (breech presentation at delivery, and/or family history [first or second grade] of DDH) and by means of clinical hip examination, including hip stability. The infant was classified as high-risk if at least 1 risk factor and/or clinical hip instability (ie, pathological instability without dislocatability, dislocatability [positive Barlow test] and dislocation [positive Ortolani test]) were present. High-risk infants from the selectively screened group and all infants from the universally screened group were offered a single examiner hip ultrasound (Rosendahl's method).[21] The ultrasound method is based on Graf's coronal standard section through the midacetabulum, and each hip is classified according to morphology and stability, separately.[43] The ultrasound examination was thoroughly standardized before the RCT.[44] All high-risk infants with normal hips at birth had a hip-radiograph at age 4.5 months, regardless of screening group. Indications for treatment were persistent dislocatable/dislocated hips on a repeated, single-examiner clinical examination or severe, sonographic dysplasia irrespective of clinical or sonographic stability. Hips with a mildly dysplastic morphology ($43° \leq \alpha < 50°$) were treated if they were also clinically or sonographically dislocatable/dislocated. Sonographically immature ($50° \leq \alpha < 60°$) or mildly ($43° \leq \alpha < 50°$) dysplastic but clinically stable hips had sonographic and clinical surveillance every fourth week until normalization or until treatment was instigated due to lack of improvement. Moreover, all children in Norway have clinical examinations performed regularly during their first 2 years as a part of the national health program, with referral to a specialist if any clinical suspicion of DDH is noted. Routines for abduction treatment included a Frejka's pillow splint from birth until 3 to 4 months of age. If further treatment was necessary, an age-adapted orthosis was used. Late detected cases (ie, after the first month of age) were defined as subluxated or dislocated hips and/or mildly or severely dysplastic hips on ultrasound, or as an acetabular index[45] >2 SDs above mean for age and/or femoral head position (classified as dysplasia, dysplasia with subluxated hip, or dysplasia with dislocated hip) on radiographs.[46,47] Outcome measures in the RCT were (1) rates of late detected DDH, rates of (2) ultrasound follow-up, and (3) abduction treatment.

During the years of clinical screening before the RCT, the prevalence of late detected cases was 2.6 per 1000 live births. To detect a sixfold reduction in prevalence in a group subjected to screening, the 2 groups would have to include ~3000 infants each (80% power, 5% significance level). In the original trial, differences in prevalence rates were tested by χ^2 tests. An exact test for linear trend in the prevalence of late DDH with the groups ordered according to the degree of ultrasound screening from the no-screening group to the selective group and to the universal screening group was used. All reported P values

were 2-sided. Intention-to-treat-analysis was applied.

The baseline demographic and clinical characteristics of each group are reported in the original article.[16] There were no statistically significant differences in gender distribution or in the prevalence of positive Barlow/Ortolani tests between the 3 study groups or in the total number of infants with risk factors between the 2 groups subjected to ultrasound screening. The number of infants born in the breech position and with a family history of DDH was significantly higher in the universally than in the selectively screened group.

In brief, the RCT demonstrated lower rates of late presenting subluxated or dislocated DDH in the universally and selectively screened groups as compared with the group receiving clinical examination alone (0.3 and 0.7 vs 1.3 per 1000) ($P = .11$, test for trend).[16] Treatment rates were, however, higher for the universally screened group as compared with the selectively or nonscreening groups; 3.4% vs. 2.0 and 1.8 ($P < .001$). When compared with the prestudy period, the rates of late cases were significantly lower (eg, 0.3 and 0.7 per 1000 vs 2.6 per 1000 live newborns).

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Radiographic measurements of hip dysplasia at skeletal maturity—new reference intervals based on 2,038 19-year-old Norwegians

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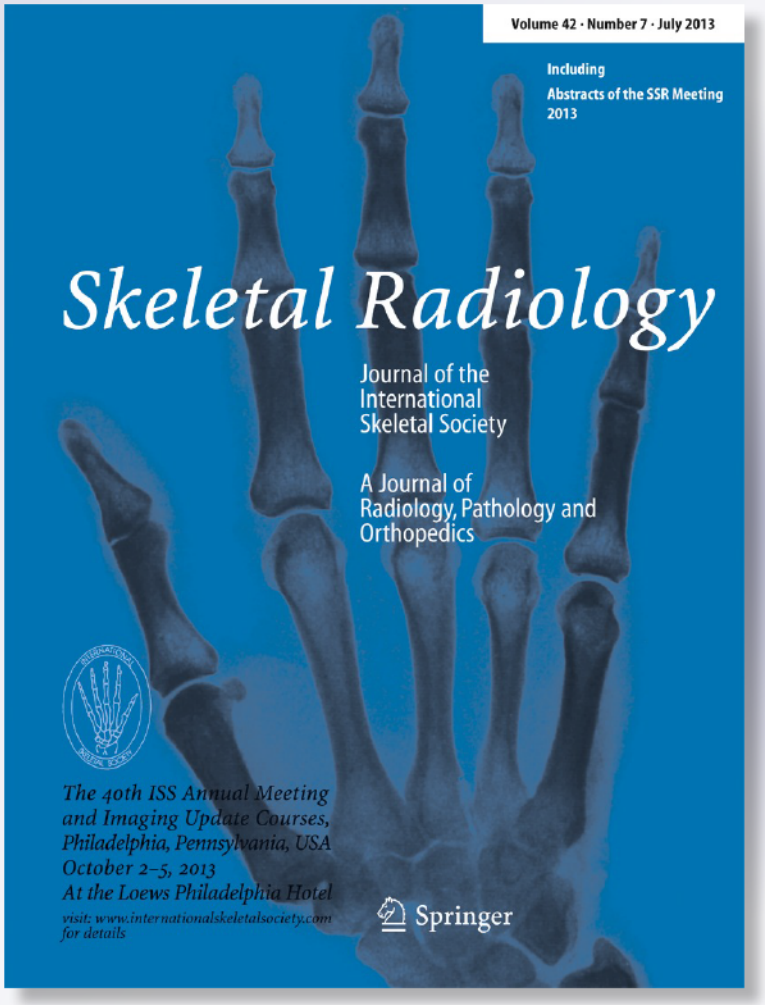

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SCIENTIFIC ARTICLE

Radiographic measurements of hip dysplasia at skeletal maturity—new reference intervals based on 2,038 19-year-old Norwegians

Lene Bjerke Laborie · Ingvild Øvstebø Engesæter · Trude Gundersen Lehmann · Francesco Sera · Carol Dezateux · Lars Birger Engesæter · Karen Rosendahl

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Abstract
Objective Normative references for radiographic measurements commonly used in the diagnosis of developmental dysplasia of the hip at skeletal maturity are incomplete. The present study therefore aimed to establish new gender-specific standards for measurements reflecting the acetabular morphology, namely Sharp's angle, the acetabular roof angle of Tönnis (AA) and the acetabular depth-width ratio (ADR), and measurements reflecting the position of the femoral head related to the acetabulum, namely the center-edge (CE) angle of Wiberg, the refined CE angle of Ogata, and the femoral head extrusion index (FHEI). The joint space width (JSW) is also reported.
Materials and methods The population-based 1989 Bergen Birth Cohort (n=3,935) was invited at age 19 years to a follow-up during 2007–09, of which 2,038 (52 %) attended. A standardized antero-posterior radiograph was assessed. The normative references are presented as mean ± standard deviation (SD) and 2.5–97.5 percentiles with 95 % confidence intervals.
Results A total of 2,011 (841 males, 1,170 females, mean age 18.6 (SD 0.6)) radiographs were analyzed. Sharp's angle was 38.8°±3.5° in males and 40.7°±3.5° in females, with 97.5 percentiles of 46° and 47°, respectively. The CE angle was 32.1°±6.1° in males and 31.0°±6.1° in females, with 2.5 percentiles of 21° and 20°, respectively. The FHEI was 86.0 %±6.3 % in males and 85.6 %±6.6 % in females, with 2.5 percentiles of 74° and 73°, respectively.
Conclusions Updated gender-specific reference ranges for radiographic measurements commonly used for hip dysplasia at skeletal maturity are reported, similar to or slightly wider than those described in the literature. Statistically significant gender differences have been confirmed for most of the measurements.

Keywords Hip dysplasia · Adult hip · Normative references · Radiographic measurements

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Introduction

Morphological abnormalities of the acetabulum and of its relationship to the femoral head are important contributing factors in developmental dysplasia of the hip (DDH) [1, 2]. They also

play an equally important role in the etiology of femoroacetabular impingement (FAI) [3–6]. Pathophysiological mechanisms involving chondral damage and subsequent labral injury of the hip joint are present in both DDH and FAI, and both conditions are assumed to be predisposing etiological factors of premature osteoarthritis of the hip (OA) [6–17]. Careful clinical examination and a standardized radiographic protocol ensuring high-quality pelvic radiographs are important in the diagnostic work-up of DDH. The adult acetabular anatomy varies according to sex, age, and ethnicity [18–22]. Furthermore, the diagnosis of DDH depends on the radiographic measurement, as well as of the cut-off values used. Several radiographic measurements are commonly used in the diagnosis of DDH (Fig. 1a-d). In the assessment of the acetabular morphology, Sharp's angle [23], the acetabular roof angle of Tönnis (AA) [1, 24], and the acetabular depth-width ratio (ADR) [8, 25] are often used. The relation between the femoral head and the acetabulum is commonly described by the center-edge (CE) angle of Wiberg [26, 27], the refined CE angle of Ogata [28], and the femoral head extrusion index (FHEI) [29]. Often, a combination of these radiographic findings is recommended in order to confirm the DDH diagnosis. The joint space width (JSW) (Fig. 2) as a discriminator of OA is also reported [30]. Existing reference values for DDH on plain radiographs at skeletal maturity are incomplete, and the present study therefore aimed to establish new gender-specific references based on a population-based cohort of 2,038 healthy 19-year-old Norwegians.

Patients and methods

Study population and design

The population-based 1989 Bergen Birth Cohort follow-up study was carried out from February 2007 to March 2009 as a long-term clinical and radiological follow-up study focusing on hip dysplasia. This study originated from a large, randomized controlled trial undertaken at this hospital in 1988–1990, designed to assess different ultrasound screening strategies in newborns [31]. A total of 4,703 subjects constituted the study base of the 1989 Bergen Birth Cohort, after exclusion of low birth weight <1,500 g (n=34), death within first month of life (n=14) and of subjects whose mother did not live in the catchment area of the hospital (n=296). Exclusion criteria applied before invitation at the time of follow-up were postal address outside the hospital catchment area at time of follow-up (n=488), emigrated or not found persons (n=245), and death (n=35). Thus, from the 1989 Bergen Birth Cohort, a total of 3,935 were invited by postal letter to participate in the follow-up (Fig. 3). A total of 2,038/3,935 (52 %) were enrolled, predominantly ethnic Norwegians. Further exclusion criteria after attendance were missing radiographs due to possible pregnancy (n=6) or to radiographs not obtained for other reasons (n=2). Radiographs of suboptimal quality and excessive pelvic rotation as assessed by a foramen obturator index beyond range of 0.6–1.8 [1] were also excluded from the analyses (n=19); 102/2,011 (5.1 %) of the subjects were treated for DDH as newborns; 21/841 (2.5 %) of the males and 81/1,170 (6.9 %) of the females. The follow-up study consisted of questionnaires, clinical examination, radiographs and salivary sampling for later genetic analysis. The research protocol was approved by the medical research ethics committee of the western region of Norway, who also approved further analyses regarding the non-responders. Data on sex, age, birth weight, weight, and height (body mass index (BMI), kg/m^2) at 7 years (±3 months) were collected from the community health care centers in Bergen and suburbs for all those born during the study period, including the non-responders. All participants gave written informed consent according to the 1964 Declaration of Helsinki. The study was conducted in accordance with the ethical standards given by the Regional Ethical Committee for Medical and Health Research. Fifteen subjects presenting with uncertain or severe clinical and/or radiographic findings related to hip, back, or pelvic pathology were immediately scheduled for a radiological follow-up consultation (KR) and/or for a consultation with a senior pediatric orthopedic surgeon (LBE) as appropriate.

Radiological examination

All radiographs were recorded in the pediatric unit of the radiology department using a low-dose digital radiography technique (Direct Digital Radiography, Digital Diagnost System, version 1.5, Philips Medical Systems, Best, The Netherlands).

Gonadal shields were offered for males. The total mean radiation dose for the two obtained radiographs together was 0.5 Gycm^2. One weight-bearing, anteroposterior (AP) view and one supine frog-leg view were obtained following a strictly standardized protocol, performed by one specifically trained radiographer. For the AP view, hips were kept in a neutral abduction-adduction position, toes pointing forwards [32, 33]. The radiographer ensured correct posture during the exposures. The film/focus distance was 1.2 m and centered at 2 cm proximal to the symphysis for the AP view.

Image evaluation and radiographic measurements

All radiographs were stored in the PACS (Picture Archiving Communication System) of the hospital, and retrieved as DICOM (Digital Imaging and Communications in Medicine) files and stored at a local computer. The digital measurement program "Adult DDH" (University of Iowa Hospitals and Clinics, Iowa City, IA, USA) was used to assess all the radiographic parameters on the AP view [34]. All measurement results were automatically transferred to an Excel spreadsheet

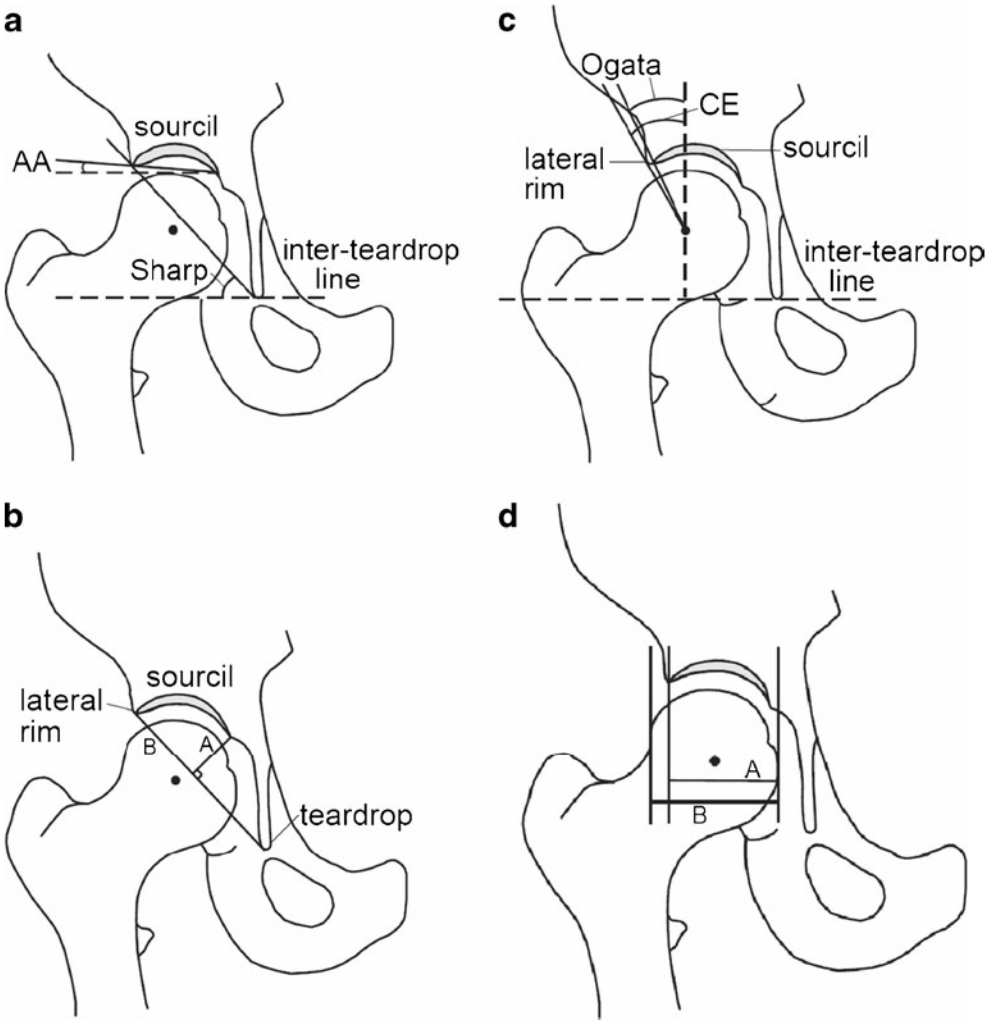

Fig. 1 **a** and **b** describe the morphology of the acetabulum: *Sharp's angle* describes the angle formed between the inter-teardrop-line and the line connecting the inferior tip of the teardrop to the lateral acetabular rim (Fig. 1a). *The acetabular roof angle of Tönnis* (*AA*) is the angle between a line intersecting the inferior part of the medial sourcil parallel to the inter-teardrop-line and a line running from the inferior part of the medial sourcil until the lateral acetabular rim (Fig. 1a). The *acetabular depth-width ratio* (*ADR*) is the depth of the acetabulum divided by the width of the acetabulum, multiplied by 1,000, presented as a ratio: (A/B)*1,000 (Fig. 1b). The width is measured from the inferior end of the teardrop to the lateral rim of the acetabulum, and the depth is measured perpendicularly from the midpoint of the width line. **c** and **d** describe the relation between the femoral head and the acetabulum: The *CE angle of Wiberg* is formed by a vertical line through the center of the femoral head and perpendicular to the transverse axis of the pelvis (inter-teardrop-line), and a line joining the head center with the lateral rim of the acetabulum (Fig. 1c). The *refined CE angle of Ogata* uses the lateral end of the sourcil, i.e., the weight-bearing area of the acetabulum, rather than the lateral rim of the acetabulum (Fig. 1c). The *femoral head extrusion index* (*FHEI*) quantifies how much of the femoral head is covered by the acetabulum, i.e., lies medial to the lateral edge of the acetabulum (A/B×100) (Fig. 1d)

[35]. The radiographs were measured by one of three of the authors (LBL, TGL, IØE). The accuracy of the digital program has been reported previously [36]. In order to perform the standardized measurements as precisely as possible, a detailed common understanding of important pelvic landmarks and of all the measurements was ensured prior to the analyses. The radiographic teardrop is a landmark seen on the AP view. Its medial surface consists of the cortical surface of the pelvis, and its lateral border consists of the cortical surface of the middle third of the acetabular fossa [37]. The inter-teardrop-line, connecting the inferior tip of both teardrops was used as the transverse axis of the pelvis. This is consistent with work published by others [32, 38]. The most lateral point of the bony acetabulum roof is referred to as the lateral acetabular edge. In normal hips, both the posterior and the anterior acetabular rim will run downwards from the lateral edge point. The "sourcil cotyloïdien" (sourcil: French for eyebrow) represents the weight-bearing bony area of the hip joint, seen as a hyperdense arched line along the acetabular roof. In a normal hip joint, this line is horizontal or somewhat curving downward, whereas it has an upward orientation in the dysplastic hip [28]. The lateral edge of the roof can be located more laterally than the lateral point of the sourcil. Measurements of both the acetabular morphology and of the position of the femoral head

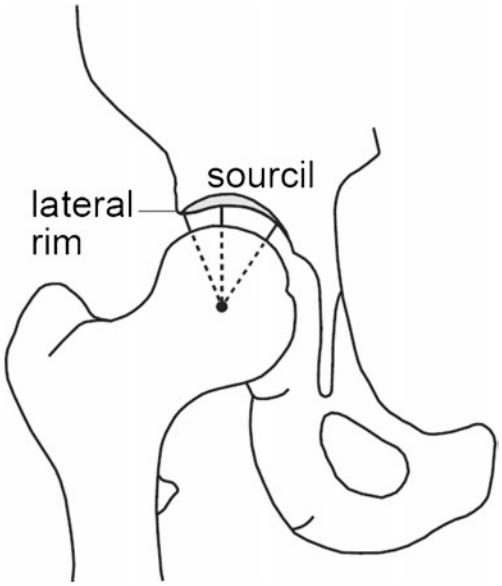

Fig. 2 The joint space width (JSW) was measured radially at three locations within the joint: namely medially (at the medial margin of the weight-bearing surface), in the middle (determined by a vertical line through the center of the femoral head), and laterally (at the lateral margin of the subchondral sclerotic line)

in the acetabulum were assessed (Fig. 1a-d). *Sharp's angle* (Fig. 1a) was originally described as "angle of inclination of the acetabulum"-"the acetabular angle" by Sharp [23]. It has occasionally been referred to as "*AA*" in the literature. However, "*AA*" is more commonly used to designate the *acetabular roof angle of Tönnis* (*AA*) (Fig. 1a) [1, 24]. This angle also has various synonyms, including "horizontal toit externe" (HTE) [39, 40], "acetabular roof obliquity" (ARO) [41, 42], and also "acetabular index" (AI), a term originally proposed as a measurement in children with open triradiate cartilage, where the inter-triradiate-line (Hilgereiners line) is used instead of the inter-teardrop line [43]. In the *acetabular depth-width ratio* (*ADR*) (Fig. 1b), the depth was originally measured along a line running perpendicularly from the width line to the deepest point of the medial sourcil arc [8, 25]. The depth of this present study was measured slightly different to the original, corresponding to the perpendicular depth at the midpoint of the width, rather than the depth given by the deepest medial sourcil point, although they often coincidence. Another depth-width ratio is also proposed in the literature, that of Heyman and Herndon from 1950 [29], using the inferiolateral point of the acetabulum rather than the teardrop tip, and the ratio is multiplied by 100 instead of by 1,000. The *center-edge* (*CE*) *angle of Wiberg* [26] (Fig. 1c) has become one of the most used parameters in the diagnosis of hip dysplasia. Wiberg initially proposed that the transverse axis be formed by an inter-center line between the two femoral heads, although the inter-teardrop line is often used for this purpose [32], including in this paper for both the CE angle and the *refined CE angle of Ogata* [28] (Fig. 1c). The *femoral*

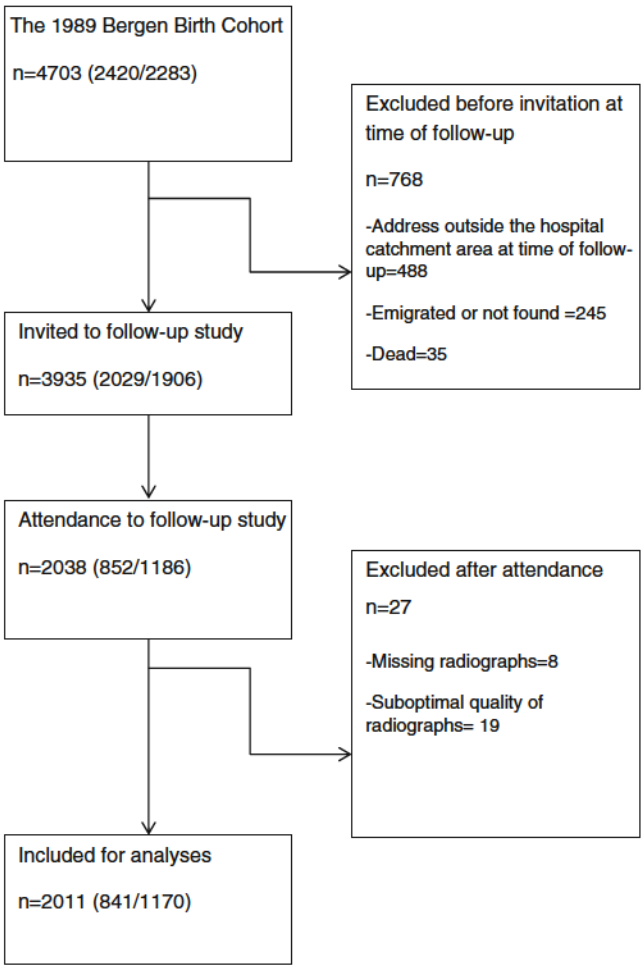

Fig. 3 Flowchart of exclusion criteria of the 1989 Bergen Birth Cohort (n=4,703) at follow-up

head extrusion index (*FHEI*) [29, 44] (Fig. 1d) is also called "femoral head coverage" or "acetabular head index" [18]. Some authors use the FHEI to describe the opposite, i.e., how much of the femoral head lies laterally to the acetabular edge [45], also termed "migration index" [32]. Measuring the *minimum joint space width* (*JSW*) radially is a well-accepted method for quantitative assessment of osteoarthritis (OA) [30, 46–48]. The JSW was measured at three locations, namely medially, in the middle, and laterally (Fig. 2) [49]. All three values are reported, rather than just the smallest value for each subject.

Statistics

The distribution of sex, birth weight, weight, and BMI at 7 years was compared among attenders and non-attenders to follow-up using Chi-square and t tests. Mean values ± standard deviation (SD) as well as empirical 2.5 and 97.5 percentiles with their corresponding 95 % confidence intervals (CI) were calculated for both sex and sides separately for each radiographic measurement [50]. CIs were obtained using the binomial method

[51]. To take into account possible non-independence of radiological markers measured on right and left hip within each subject, repeated measures analysis of variance was used [52]. To evaluate the effects of sex and side on radiological markers, subject was considered as random term, side as within subject and sex as between subject factors. A significance level of 0.05 was decided a priori, and all the reported p values are two-tailed. No correction for multiple comparisons was performed. All calculations were performed using Stata® Statistical Software, Release 11 (StataCorp LP®, College station, TX, USA) [53].

Results

Of the 2,038/3,935 (52 %) participants who attended the follow-up, a total of 2,011 (841 males, 1,170 females) were included for further analyses (Fig. 3). Mean age was 18.6 (SD 0.6), range 17.2–20.1 years for both males and for females. The baseline characteristics of the participants compared to those that declined the follow-up invitation are reported (Table 1). A similar table has previously been reported from this study group [54]. The results for each radiographic measurement are presented (Table 2). The gender difference was statistically significant for Sharp's angle, Wiberg's CE angle, Ogata's refined CE angle (all $p<0.0001$), and for the acetabular depth-width ratio (ADR) ($p=0.036$), but not for the acetabular angle of Tönnis (AA) and for the femoral head extrusion index (FHEI). The side difference was statistically significant for CE, Ogata, ADR, and FHEI (all $p<0.0001$), but not for the AA and for Sharp's angle. For the CE, Ogata, ADR, and FHEI, higher rates of values indicating dysplasia were seen in the right compared to the left hip, for both sexes. The gender-specific reference ranges based on 2.5 and 97.5 percentiles and corresponding cut-off values are reported for right and left hip, respectively (Table 3). Based on the right hip, reference ranges of Sharp's angle were 31.6–45.6° in males and 33.3–47.3° in females, with upper cut-off values of 46° and 47°, respectively. For the CE angle, reference ranges were 20.8–45.0° in males and 19.6–43.4° in females, with lower cut-off values of 21° and 20°, respectively. The descriptive statistics of the joint space width (JSW) measured on three locations are summarized for the right and the left hip in males and females (Table 4), with lowest values for the middle position and highest values for the lateral position in both sides and for both genders. Males had statistically significant higher values in all three positions than females.

Discussion

Updated gender-specific normative references for common radiographic measurements used in the diagnosis of DDH at skeletal maturity, based on a birth cohort of 2,038 healthy 19-year-old Norwegians have been presented. Overall, similar or slightly wider reference intervals based on the appropriate 2.5/97.5 percentiles were found, as compared to cut-off values often used in the literature. The gender difference was statistically significant for all measurements except the FHEI and the AA, emphasizing the need for gender-specific ranges. All of the most common DDH radiographic measurements, including Sharp's angle, the acetabular roof angle of Tönnis (AA), the CE angle, the refined CE angle (Ogata), and the femoral head extrusion index (FHEI), except for the acetabular depth-width ratio (ADR), yielded mean values more towards the dysplastic cut-off values for females than for males. Knowledge of these reference intervals is important when interpreting radiographs performed at skeletal maturity. Values outside these percentile-based ranges are not, however, necessarily pathological, but rather values in the top or bottom 2.5 % extremities of the normal ranges. None of the results were altered significantly when similar analyses were performed excluding the 102 subjects who received treatment for DDH as newborns. Measurement values obtained in clinical practice should also be interpreted in the light of the varying intra- and inter-observer variations related to each of the measurements [36].

For Sharp's angle, the mean values of 38.8° in males and 40.7° in females are slightly higher than several of the other

Table 1 Baseline characteristics by group of attendance and non-attendance for 3,935 subjects invited to a long-term clinical and radiological follow-up

Variables	Attendance n=2,038	Non-attendance n=1,897	p value
Study 2007–09			
Boys, n (%)	852/2,038 (41.8)	1,177/1,897 (62.0)	<0.001
Girls, n (%)	1,186/2,038 (58.2)	720/1,897 (38.0)	
Birth weight (g), mean (SD)	3,529.1 (539.4)	3,520.8 (536.1)	0.630
Age (years), mean (SD)	18.6 (0.6)	NA	
BMI kg/m^2, mean (SD)	23.1 (4.0)	NA	
Growth data available at 7 years (%)	835/2,038 (41.0)	633/1,897 (33.4)	
Boys, n (%)	363/835 (43.5)	383/633 (60.5)	<0.001
Girls, n (%)	472/835 (56.5)	250/633 (39.5)	
Weight at 7 years, mean (SD)	26.5 (4.7)	26.6 (4.8)	0.775
BMI at 7 years, mean (SD)	16.4 (2.1)	16.4 (2.1)	0.590

NA not available

Table 2 Descriptive statistics of commonly used DDH measurements in right and left hip in 841 males and 1,170 females, presented as mean ± standard deviation (SD) and range. *p* values are related to differences between sex and side

Variable	Males		Females		P sex	P side
	Right	Left	Right	Left		
Sharp	38.8±3.5, 25.0; 49.2	38.7±3.5, 23.2; 49.1	40.7±3.5, 27.4; 51.0	40.8±3.6, 27.4; 56.2	<0.0001	0.860
AA	5.6±4.8, −11.1; 21.8	5.4±5.0, −13.0; 20.9	5.8±4.9, −13.9; 21.4	5.9±5.2, −11.1; 28.0	0.064	0.434
ADR	294.5±34.9, 193.7; 457.7	297.2±32.2, 192.5; 435.3	297.7±35.8, 165.2; 486.7	300.1±35.3, 156.3; 428.6	0.036	<0.0001
CE	32.1±6.1, 12.3; 58.5	32.8±5.8, 15.8; 52.6	30.1±6.1, 11.1; 53.1	31.4±6.0, 4.9; 54.1	<0.0001	<0.0001
Ogata	30.4±6.3, 8.2; 58.1	31.5±6.0, 15.1; 49.9	29.1±6.3, 3.7; 51.8	29.9±6.2, 4.9; 54.5	<0.0001	<0.0001
FHEI	85.6±6.3, 63.9; 108.4	86.9±6.0, 69.1; 107.5	85.6±6.6, 66.8; 113.7	86.8±6.7, 62.2; 111.4	0.372	<0.0001

Sharp Sharp's angle; *AA* acetabular roof angle of Tönnis; *ADR* acetabular depth-width ratio; *CE* center-edge angle of Wiberg; *Ogata* refined center-edge angle of Ogata; *FHEI* femoral head extrusion index

studies performed on AP radiographs [32, 55] (Table 5), and reference intervals for both males and females are slightly wider than earlier presented in the literature (Table 3). Cut-off values of >42.3°, ≥43° and ≥45° have been proposed [8, 24, 56]. Sharp initially proposed a normal range of 33–38°, with 39–42° as an upper normal limit [23]. For the AA angle of Tönnis, mean values of 5.6 and 5.8 for males and females separately are presented, with corresponding 97.5 % cut-off values of 14.8 and 15.6. Other studies report varying results with mean values ranging from around 3 to 10° [55, 57]. Tönnis supported findings by Lequesne, and proposed 10° as an approximate upper normal limit, based on extensive work on AA in children and corresponding measurements in adult hips [1, 40] (Table 3). Interestingly, the results of the present study compare better with a cut-off value of 15 found by Nakamura [56], although ethnic differences in DDH risk and pelvic configuration must be kept in mind when comparing an ethnic Norwegians with a Japanese population. Earlier published data have shown a non-negligible intra- and inter-observer variation in relation to the AA measurement [36]. As for the ADR, mean values of 294.5 and 297.7 for males and females, respectively, were found, giving 2.5 % cut-off values of 235 and 233‰. The most used cut-off value in the literature has been <250‰ [25]. The CE of Wiberg had mean values of 32.1 and 31.0, with corresponding cut-off values of 20.8 and 19.6 for males and females, respectively. The CE angle was originally described in 100 (50 males/50 females) healthy Swedish subjects, and reported to have a physiological range of 20–40, with cut-off values of <20 indicating dysplasia, 20–25 indicating borderline cases, and >25 indicating normal hips [26]. These cut-off values have been confirmed by others [8, 58–60]. The mean values of the present study compare well with other studies [55, 56, 61, 62]. The Danish study used the lateral margin of the subchondral sclerotic "sourcil" as the lateral point when measuring the CE angle, identical to the modified CE angle of Ogata, favored by Ömeroglu et al. [63]. The Danish study reported median values of 35 for both males and females, respectively. In the present study, the Ogata angle had mean values of 30.4±6.3 and 29.1±6.3, with corresponding cut-off values of 18.4 and 17.1 for males and females, respectively.

Table 3 Updated gender-specific reference ranges and cut-off values (based on right hip) for DDH at skeletal maturity based on 2.5 and 97.5 percentiles with 95 % confidence intervals (CI) for each of the percentiles

Measurement	Gender	2.5 percentile (95 % CI)	97.5 percentile (95 % CI)	Confirmed or updated cut-off values	Cut-off values reported in the literature
Sharp (°)	M	31.6 (30.6; 32.1)	45.6 (45.2; 46.3)	>46	>42.3 [24]; ≥43 [8]; ≥45 [56];
	F	33.3 (32.6; 33.9)	47.3 (46.9; 47.8)	>47	
AA (°)	M	−4.7 (−6.5; −3.35)	14.8 (14.3; 15.6)	>15	>10 [1, 40], >15 [56]
	F	−4.1 (−4.8; −3.0)	15.6 (14.8; 16.5)	>16	
ADR (‰)	M	234.6 (225.1; 237.8)	374.6 (362.1; 385.8)	<235	<250 [25]
	F	233.1 (227.4; 237.8)	370.2 (364.8; 378.8)	<233	
CE Wiberg (°)	M	20.8 (19.9; 21.7)	45.0 (43.1; 46.0)	<21	<20 [26]
	F	19.6 (18.6; 20.5)	43.4 (42.2; 45.0)	<20	
Ogata (°)	M	18.4 (16.4; 19.2)	42.8 (41.9; 44.2)	<18	NA
	F	17.1 (16.3; 17.7)	42.0 (41.2; 43.8)	<17	
FHEI (%)	M	73.8 (72.9; 74.8)	99.1 (97.9; 101.0)	<74	<70 [29], <75 [25]
	F	73.4 (72.3; 74.3)	100.1 (98.3; 101.7)	<73	

NA not available

Table 4 Descriptive statistics of joint space width (JSW) measurements in right and left hip in 841 males and 1,170 females, presented as mean ± standard deviation (SD), range and 2.5–97.5 percentiles. *p* values are related to differences between sex and side

JSW (mm)	Males		Females		P sex	P side
	Right	Left	Right	Left		
Medial	4.6±1.4, 1.6; 10.9, 2.37; 7.81	4.6±1.4, 1.2; 10.0, 2.4; 7.8	4.3±1.2, 1.0; 9.8, 2.3; 7.0	4.4±1.4, 1.1; 10.3, 2.3; 7.8	<0.0001	0.138
Middle	3.8±0.9, 0.2; 6.9, 2.06; 5.60	3.7±0.9, 0.7; 6.7, 1.8; 5.5	3.6±0.8, 0.8; 6.8, 2.2; 5.2	3.5±0.8, 0.7; 7.5, 1.9; 5.1	0.0002	<0.0001
Lateral	5.6±1.13, 1.6; 11.6, 3.5; 8.0	5.5±1.1, 1.4; 9.0, 3.1; 7.8	5.3±1.1, 2.3; 9.9, 3.3; 7.5	5.2±1.1, 2.3; 9.3, 3.2; 7.5	<0.0001	<0.0001

These figures are lower than figures found in the Danish study. However, Park et al. have shown that the CE angle increases with age, and it is possible that age-related alterations in the sourcil-shaped weight bearing zone could partly explain this difference, as the Danish study group ranges from 22 to 93 years [22]. The femoral head extrusion index (FHEI) was originally presented with a normal range of 70–100 %, with an average of 90 % [29], with reference to the amount of femoral head covered by the acetabular roof. A cut-off value of 75 % was later proposed [25]. This has been supported by findings by the Danish group, presented as an inverse index, called the *lateral migration index*, with values above 25 % being indicative of dysplasia [32]. The results of the present study compare well with previous findings [64], with cut-off values of 73.8 and 73.4 % for males and females, respectively. Overall, the findings of the present study compare well with previous findings, also in terms of sex and age.

The joint space width (JSW) is well accepted as a radiographic discriminator of hip osteoarthritis (OA) [30, 47, 48, 65]. Fredensborg originally measured JSW both vertically and horizontally radiating from the head center, and he also obtained an integral JSW, based on the average from nine measurements in the superior part of the joint. He concluded that the vertical JSW was a good measurement used alone, and that the normal value varied between 3 and 5 mm, on average slightly above 4 mm [30]. Lanyon et al. measured the JSW at

Table 5 Mean and standard deviation (SD) values for common DDH measurements on AP pelvic radiographs in males and females, compared to other studies

Radiographic measurement	Authors, year	Country, sex (M/F), age, side (R/L/R+L[b])	Mean ± SD, males	Mean ± SD, females
Sharp's angle (°)				
	Jacobsen'05 [32]	Denmark, 1,429 M, 2,430 F 22–93 years, R	37.0[a]±3.5	39.1[a]±3.7
	Jeremic'11 [55]	Serbia, 170 M, 150 F, 21–65 years, R+L	37.5±3.6	38.5±3.9
	Laborie '12	Norway, 841 M, 1,170 F, 19 years, R	38.8±3.49	40.7±3.52
AA of Tönnis (°)				
	Jeremic'11 [55]	Serbia, 170 M, 150 F, 21–65 years, R+L	6.2±4.9	9.0±6.0
	Laborie '12	Norway, 841 M, 1,170 F, 19 years, R	5.64±4.8	5.84±4.9
ADR (‰)				
	Jacobsen'05 [32]	Denmark, 1,429 M, 2,430 F 22–93 years, R	293[a]±38	304[a]±41
	Laborie '12	Norway, 841 M, 1,170 F, 19 years, R	294.5±34.9	297.7±35.8
CE Wiberg (°)				
	Shi'10 [62]	China, 45 M, 55 F, 19–30 years, R+L	31.7±6.1	30.0±5.2
	Jeremic'11 [55]	Serbia, 170 M, 150 F, 21–65 years, R+L	33.6±5.8	31.3±6.9
	Laborie '12	Norway, 841 M, 1,170 F, 19 years, R	32.1±6.1	31.0±6.1
Ogata (°)				
	Jacobsen'05 [32]	Denmark, 1,429 M, 2,430 F, 22–93 years, R	35[a]±7.3	35[a]±7.4
	Laborie '12	Norway, 841 M, 1,170 F, 19 years, R	30.4±6.3	29.1±6.3
FHEI (%)				
	Jacobsen'05 [32]	Denmark, 1,429 M, 2,430 F, 22–93 years, R	12.0[a]±8.7[c]	8.0[a]±7.8[c]
	Aly'11 [64]	Egypt, 134 M, 110 F, 18–60 years, R+L	86.6±4.7	84.0±4.0
	Laborie '12	Norway, 841 M, 1170 F, 19 years, R	86.0±6.3	85.6±6.6

[a] Median values

[b] Values based on right or left hip or both hips together

[c] Percentage of uncovered portion (lateral migration index), equals the inverse FHEI value

the site of maximum narrowing and reported a mean minimum JSW of 4.1 mm in 433 males and of 3.8 mm in 598 females (both mean age 64 years) [48]. In a Turkish study by Goker et al., 17 males and 14 females (age 20–29 years) demonstrated a mean value of 3.67±0.65 for the right hip, measured in the narrowest of three locations. They found that values were significantly lower in females compared to males, but no longer after adjusting for height [47]. However, the studies by Lanyon et al. and Goker et al. were performed with supine urograms and abdominal radiographs, respectively, whereas the weight-bearing AP position has been shown to be favorable in assessing hip dysplasia [66, 67]. Jacobsen et al. measured the JSW radially in three locations of the hip joint- at the lateral end of the sourcil, in the middle position corresponding to the vertical axis through the head center, and at the medial end of the sourcil [65]. They found right-sided minimal JSW values of 3.88 mm in males, and 3.91 in females. The minimal JSW represents the lowest value regardless of the three positions in the joint, and a value of ≤2 mm indicates OA [65]. The present study reports on values from three locations, since the aim of this study is to highlight reference values based on the two 2.5 % extremities, rather than prevalence of disease. A statistically significant difference for gender in each of the three locations was found, and a statistically significant difference for side in the middle and lateral location. Again, attention should be drawn to the clinical significance of these results, as a quite large intra- and inter-observer variation for the JSW has been previously shown [36].

To our knowledge, this is the largest population-based study addressing hip dysplasia at skeletal maturity based on all newborns delivered at the only hospital maternity unit of a well-defined area within a year. The large numbers strengthen the data. Analyses regarding non-responders show a statistically significant difference only between genders (Table 1). Contrary to other studies on hip dysplasia with wide age ranges, a well-defined age cohort additionally strengthens the study, as several of the radiographic markers are influenced by age [22, 68, 69]. The present study used a highly standardized radiographic protocol, and the radiographs were performed by one particularly trained radiographer who ensured correct posture in order to avoid pelvic tilting and rotation [70]. All radiographs were evaluated in regard to rotation. The use of a true pelvic AP radiograph also is important in the assessment of the dysplastic hip [44, 71, 72]. Several other retrospective studies are based on urograms or abdominal radiographs [73]. A weight-bearing AP view was used in the present study, given that this is the most physiological position when assessing acetabulum and related structures [19, 66, 67]. The digital measurement program was thoroughly tested and validated, and the measurements meticulously standardized before analyses [36]. Moreover, the fact that measurement results were automatically transferred to an Excel spreadsheet minimizes the risk of recording errors. Several limitations to this study are acknowledged. First, the attendance rate of 52 % is moderate. Since all participants were included in a randomized trial evaluating the DDH screening system at birth [31], a potential selection bias has been considered. However, analyses regarding the non-responders show no substantial differences among the responders and the non-responders except for the gender distribution. Second, the pelvic tilt was not assessed in a standardized manner, but all radiographs were subjectively evaluated by a senior musculoskeletal radiologist (KR). The standardization of the radiographic examination was emphasized in order to avoid excessive tilting. Third, the ethical considerations regarding radiation of healthy young adults must be properly addressed. By using fully digital equipment and a highly standardized protocol, the total mean radiation dose for both the AP and the frog-leg view together was 0.5 Gycm^2. The effective dose can then be calculated using an organ-specific transforming factor, which equals 0.29 mSV/Gycm^2 for the pelvis, yielding an effective dose of 0.5×0.29=0.15 msV for both radiographs together. The effective dose in the present study without gonadal shields equals around 2 weeks of daily background radiation in Norway, given that the daily background radiation in Norway is about 0.01 mSv. In addition, gonadal shields reduced the effective dose further, up to 50–80 %. Some authors advocate the use of CT rather than conventional radiographs [74]. We believe that a conventional AP view with a minimal radiation dose following a strictly standardized protocol allows images of very high quality, and in particular allows weight-bearing images, which are recommended in the DDH assessment [44, 67]. CT imaging can only be performed in the supine position. However, we recognize the need of CT and 3D reformatting tools when planning surgical interventions in dysplastic hips [75, 76]. Last, the digital measurements were performed by one of three investigators; however, large efforts were made to standardize the measurements prior to study start. Intra- and inter-observer variation for the measurements have been shown earlier to differ to some extent, with poorer results for the measurements with lower absolute values, namely the AA and the JSW [36]. Intra- and inter-observer variation and subsequent measurement errors related to a measurement performed in a study is likely to increase further during every day clinical practice, due to more observers, less standardization of both radiographs and measurements, and a tighter time schedule.

It is important to be aware of an ongoing discussion in the literature regarding the use of the lateral edge of the bony acetabular rim or the lateral point of the weight-bearing sourcil. Many authors advocate the use of the superolateral point of the sourcil rather than the lateral edge of the bony acetabular roof when performing measurements such as Sharp's angle, acetabular angle of Tönnis, and also the CE angle of Wiberg, which then corresponds to the refined CE angle of Ogata [28, 66, 77–79]. The present study population is young and without the formation of lateral osteophytes, but this

should be kept in mind when analyzing radiographs in older age groups [73]. The radiologist should clearly state which of the two lateral points are used in order to avoid confusion.

Accurate reference values and subsequent cut-off values when assessing DDH at skeletal maturity are obviously very important in the epidemiological aspect of determining prevalences of DDH, preferably based on a combination of several of the measurements [22, 80]. However, the radiographic findings must be carefully interpreted in light of the patient's history and clinical findings, before a diagnosis of DDH can be made. As mentioned above, values outside these 2.5 % percentile-based ranges represent the more extreme values in the population, without necessarily being pathological. Furthermore, the intra- and intervariability related to the measurements should be kept in mind.

DDH has been shown to vary according to sex and ethnicity [18, 81, 82]. Neonatal hip instability (NHI) in newborns is more often seen on the left than on the right side [83, 84]. The data of the present study show that for the CE angle, Ogata, ADR, and FHEI, higher rates of values indicating dysplasia at skeletal maturity were seen in the right compared to the left hip, for both sexes.

In conclusion, updated gender-specific reference ranges for common radiographic measurements used in assessing hip dysplasia at skeletal maturity are reported, similar to or slightly wider than earlier proposed values. Statistically significant gender differences are confirmed for most of the measurements, with a tendency of more dysplastic values in females.

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Radiology

Prevalence of Radiographic Findings Thought to Be Associated with Femoroacetabular Impingement in a Population-based Cohort of 2081 Healthy Young Adults[1]

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Purpose: To report the prevalence of qualitative radiographic findings for femoroacetabular impingement (FAI) and associations among them and to characterize the inter- and intraobserver variability of these interpretations.

Materials and Methods: This study is part of an institutional review board–approved population-based prospective follow-up of 2081 of 4006 (participation rate, 51.9%) young adults (874 [42.0%] male participants, 1207 [58.0%] female participants; mean age, 18.6 years) who took part in a randomized hip trial on developmental dysplasia of the hip. All participants gave informed consent. Two pelvic radiographs were obtained. Pistol-grip deformity, focal femoral neck prominence, and flattening of the lateral head, all suggestive of cam-type impingement, and the posterior wall sign, excessive acetabular coverage, and crossover sign, all suggestive of pincer-type impingement, were assessed subjectively by an experienced radiologist. To assess inter- and intraobserver agreement, images from 350 examinations were read independently twice by two observers.

Results: Cam-type deformities were seen in 868 male and 1192 female participants, respectively, as follows: pistol-grip deformity, 187 (21.5%) and 39 (3.3%); focal femoral neck prominence, 89 (10.3%) and 31 (2.6%); and flattening of the lateral femoral head, 125 (14.4%) and 74 (6.2%). Pincer-type deformities were seen in the same numbers of male and female participants, respectively, as follows: posterior wall sign, 203 (23.4%) and 131 (11.0%); and excessive acetabular coverage, 127 (14.6%) and 58 (4.9%) (all $P < .001$, according to sex distribution). The crossover sign was seen in 446 (51.4%) and 542 (45.5%) of the male and female participants, respectively ($P = .004$). There was a high degree of coexistence (odds ratio [OR] > 2) among most FAI findings. Interobserver agreement was good to very good ($\kappa = 0.74–0.84$) in rating cam- and pincer-type findings. Intraobserver agreement was moderate or good ($\kappa = 0.49–0.80$) for all findings for both observers.

Conclusion: Overall, radiographic FAI findings are quite common in a population of healthy young adults, especially in males, with a high degree of coexistence among most findings (OR > 2).

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Femoroacetabular impingement (FAI) has become a well-recognized clinical concept and is believed to increase the risk for early-onset osteoarthritis (1–3). The prevalence of FAI as a clinical diagnosis is estimated to be 10%–15% in a general adult population (4). The development of FAI results from femoral and acetabular abnormalities that cause abnormal contact between the proximal femur and the acetabular rim (2,5). It is classified as either cam or pincer type, on the basis of the underlying anatomic deformity (Fig 1) (6).

The diagnosis should be considered in patients with a history of long-standing hip pain; reduced hip motion, particularly internal rotation and flexion; and a positive test for anterior impingement (2,7,8). Initial radiographic examination includes assessment of the femoral head-neck junction, the shape of the femoral head and acetabular roof, and the contour of the acetabular rim (9). Assessment of acetabular depth, inclination, and version is important. Fibrocystic changes (FCCs) in the epiphyseal vicinity should also be noted, as there is growing evidence that these radiolucencies, first described in 1982 as herniation pits (11), may develop secondary to the impingement process (2,10).

During a long-term follow-up of a large randomized trial on developmental dysplasia of the hip, we noticed that qualitative radiographic features of FAI were quite frequent in a population-based cohort of 17–20-year-olds. We therefore set out to report on the prevalence of qualitative radiographic findings for FAI and the associations among them and to characterize the inter- and intraobserver variability of these interpretations.

Advances in Knowledge

- Radiographic features suggestive of femoroacetabular impingement (FAI) are quite common in a population of healthy young adults, especially in males.
- A high degree of coexistence is seen among most of these radiographic findings.
- The prevalence of fibrocystic changes (FCCs) in the epiphyseal vicinity was 5.8% (50 of 868) in male and 1.6% (19 of 1192) in female participants, and an association between FCCs and the presence of either a cam- or a pincer-type deformity was seen.

Implication for Patient Care

- Radiographic features suggestive of FAI may be seen in a large percentage of the general young population.

Materials and Methods

Study Population and Design

During February 2007 to March 2009, our cohort (n = 4006) was approached by letter and invited to participate in a long-term prospective clinical and radiographic follow-up of a randomized hip trial (12). The initial cohort comprised all 5068 newborns delivered at our institution (Maternity Unit, Haukeland Hospital, Bergen, Norway) in 1989, of which a total of 1062 were excluded from the follow-up because of death (n = 61), because of emigration abroad (n = 256), or because they did not live in the catchment area of our hospital at the time of birth (n = 745), leaving a total of 4006 subjects to be invited for participation. A total of 2081 of 4006 (51.9%, after one reminder) were enrolled (874 [42.0%] male participants, 1207 [58.0%] female participants; mean age, 18.6 years; range, 17.2–20.1 years for both sexes). Of 2081 of the subjects, 68 (3.3%) had developmental dysplasia of the hip as newborns (14 of 874 [1.6%] of the male participants and 54 of 1207 [4.5%] of the female participants). Exclusion criteria were radiographs of suboptimal technical quality (excessive pelvic rotation as assessed by an obturator foramen index outside 0.6–1.8 [13]) or uncertain pregnancy status. All participants gave written informed consent according to the Helsinki declaration. The research protocol was approved by the Medical Research Ethics Committee of the Western Region of Norway, and this committee also approved further analyses in regard to the nonresponders. Data on sex, age, birth weight, and weight and height (body mass index) at age 7 years were collected from the community health care centers in Bergen, Norway, and suburbs for all those born during the study period, including the nonresponders.

Radiographic Examination

This examination was performed at the Department of Radiology, Section of Paediatrics, Haukeland University Hospital, University of Bergen, Bergen, Norway, by one radiographer using a low-dose digital radiographic technique (DigitalDiagnost System, version 1.5; Philips Medical Systems, Hamburg, Germany). Gonadal shields were applied for both sexes. Two standardized views were obtained, one weight-bearing anteroposterior (AP) view and one supine frog-leg view. For the AP view, hips were kept in a neutral abduction-adduction position, with toes directed forward. The radiographer, who had undergone specific training for the examination, ensured correct posture during the exposures. We used a film-focus distance of 1.2 m with the beam centered at 2 cm proximal to the symphysis for the AP view and at the symphysis for the frog-leg view.

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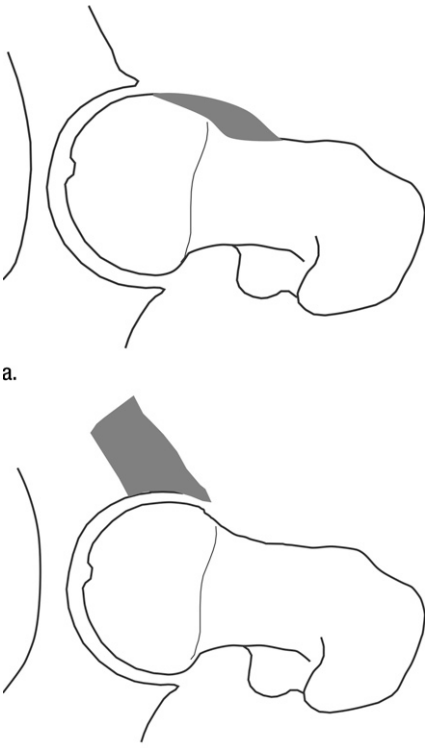
Abbreviations:
AP = anteroposterior
COS = crossover sign
FAI = femoroacetabular impingement
FCC = fibrocystic change
OR = odds ratio

Author contributions:
Guarantors of integrity of entire study, L.B.L., L.B.E., K.R.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, L.B.L., T.G.L., D.M.E., K.R.; clinical studies, L.B.L., T.G.L., L.B.E., K.R.; experimental studies, K.R.; statistical analysis, L.B.L., T.G.L., L.B.E., K.R.; and manuscript editing, all authors

Potential conflicts of interest are listed at the end of this article.

Figure 1

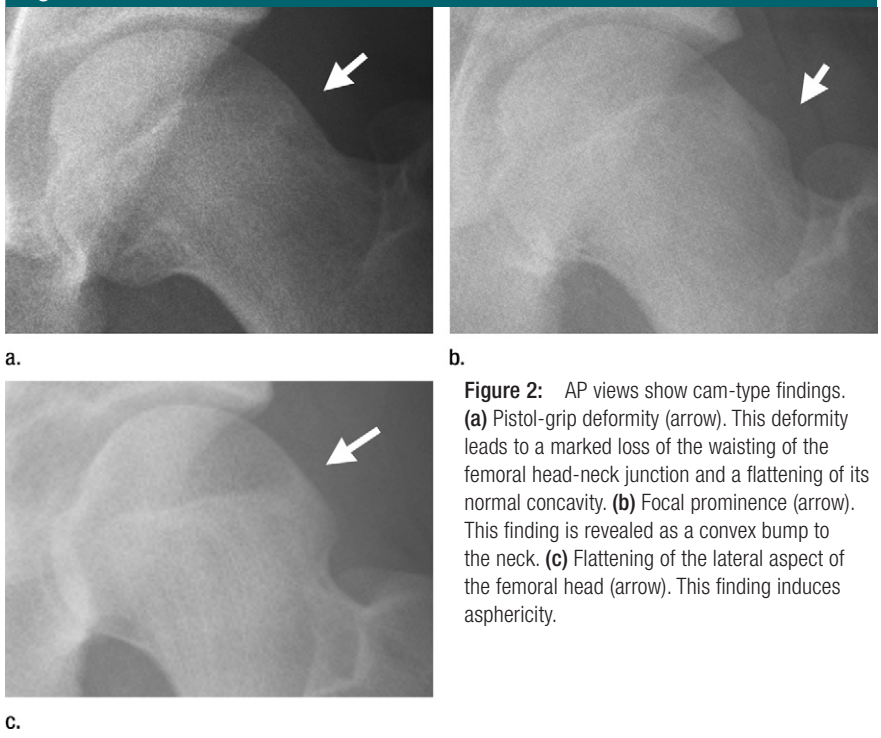


a.

b.

Figure 1: Normal anatomy of the hip joint allows sufficient space for the head to rotate properly into the acetabulum. In cam- and pincer-type impingement, abnormal contact between the proximal femur and the acetabular rim disturbs adequate movement. **(a)** Cam-type impingement. In this type of impingement, the prominence of bone and the reduced waist to the head-neck junction cause squeezing of the aspherical part of the head-neck junction underneath the acetabular rim, further damaging both the cartilage and the labrum. **(b)** Pincer-type impingement. Global or focal overcoverage of the femoral head by the acetabulum may lead to this type of impingement, disturbing adequate rotation of the head inside the acetabulum.

Figure 2



a. b. c.

Figure 2: AP views show cam-type findings. **(a)** Pistol-grip deformity (arrow). This deformity leads to a marked loss of the waisting of the femoral head-neck junction and a flattening of its normal concavity. **(b)** Focal prominence (arrow). This finding is revealed as a convex bump to the neck. **(c)** Flattening of the lateral aspect of the femoral head (arrow). This finding induces asphericity.

Image Evaluation

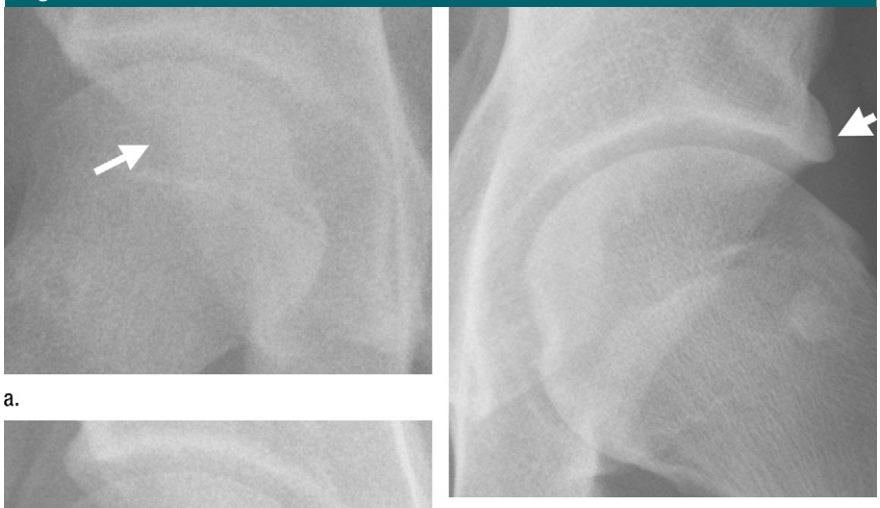
Patient identification was removed from all radiographs for patient confidentiality, and radiographs were analyzed on a high-resolution screen by one pediatric musculoskeletal radiologist (K.R., with 25 years of experience in reading them). The presence of the following features suggestive of impingement were assessed by means of gross visual inspection: *(a)* cam-type findings (Fig 2)—pistol-grip deformity, focal prominence of the femoral neck, and flattening of the lateral aspect of the femoral head (14–16); and *(b)* pincer-type findings (Fig 3)—COS, posterior wall sign, and excessive acetabular coverage (2,17–19). The presence of FCCs (Fig 4) was also noted (10). The pistol-grip deformity and the focal prominence, as well as the FCCs, were subjectively assessed from both the AP and the frog-leg views and were scored as positive if present in one or both views. The other four features were subjectively assessed from the AP view. Definitions were derived from the literature or in consensus (2,10,14–19). According to Bardakos and Villar (1), we classified the COS as mild, moderate, or severe, corresponding to the level of intersection between the anterior and the posterior rim, namely the superior third, the middle third, and the lower third, respectively. For the purpose of this study, all of them were noted as a positive COS. Images in a subset of 350 examinations were reread by the first observer (K.R.) after an interval of at least 3 months, and they were also read twice independently and with blinding by a second observer (L.B.L., with 1 year of experience). Prior to study initiation, these readers evaluated a sample set of 20 images not included in the study cohort and held several face-to-face meetings to review them and refine the standardized definitions.

Cadaveric Study

A cadaveric study that included 10 pairs of intact femora of unknown sex was performed to examine the effect of hip rotation on the contour of the femoral head and neck (ie, whether an excessive inward rotation would produce a false-positive cam deformity). Each femur was placed on the x-ray table with the distal femoral condyles abutting the table. AP radiographs were obtained in a neutral position and with internal and external rotation with 10° increments for both hips separately, by using a film-focus distance of 1.2 m and with the beam centered at 2 cm proximal to an imagined symphysis.

All images were read subjectively, in a blinded fashion, by one of the authors (K.R.), and the presence of a pistol-grip deformity, focal prominence of the femoral neck, or flattening of the lateral aspect of the femoral head was noted.

Figure 3



a.

b.

c.

Figure 3: AP views show pincer-type findings. **(a)** Crossover sign (COS) (arrow). This sign is positive when the anterior wall of the acetabulum crosses the posterior border of the acetabulum medial to the lateral rim of the weight-bearing sourcil area. **(b)** Posterior wall sign (arrow). This sign is positive when the posterior wall lies medial to the center of the femoral head. **(c)** Excessive acetabular coverage (arrow). This finding is seen as an extension of the lateral acetabular rim in the inferior and/or lateral direction.

Figure 4

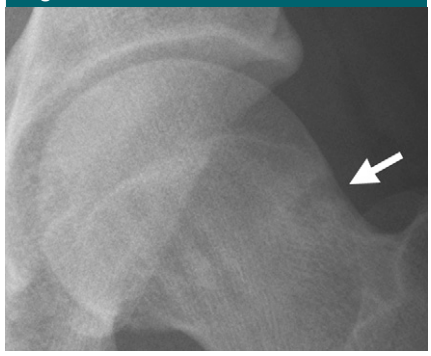


Figure 4: AP view shows FCC (arrow). FCC in the epiphyseal vicinity may develop secondary to the impingement process and is seen as a small area of cystic radiolucency surrounded by a thinner sclerotic margin.

Statistical Analysis

Differences in the distribution of the radiographic findings according to sex were investigated by using the χ^2 test (Fisher exact test). Associations among the radiographic findings were analyzed by calculating the odds ratio (OR) between each of the features separately, and an OR greater than 2 was considered to indicate an association. The probability of false-positive findings owing to chance is nonnegligible because of multiple statistical tests performed on the same data. The relationship between the presence of FCCs and the radiographic findings was investigated by using the χ^2 statistic (Fisher exact test) and a model of binary logistic regression for male and female participants, right and left sides, separately. Inter- and intraobserver agreement for the categorical variables for the experienced and nonexperienced radiologists were examined by using the κ value for measurement of agreement. Guidelines were slightly adapted from those in the report of Landis and Koch in 1977 (20), as follows: κ less than 0.20, poor agreement; κ of 0.21–0.40, fair agreement; κ of 0.41–0.60, moderate agreement; κ of 0.61–0.80, good agreement; and κ of 0.81–1.00, very good agreement. All calculations were performed by using statistical software (SPSS, version 17.0, release 2008; SPSS, Chicago, Ill). A significance level of .05 was decided a priori, and all the reported *P* values are two tailed.

Results

Of 2081 subjects who accepted the invitation to participate in this study, 2060 were included for further analysis; of 2060, 868 (42.1%) were male participants and 1192 (57.9%) were female participants. Twenty-one of 2081 subjects were excluded because of suboptimal radiographs or because of an uncertain pregnancy status. Baseline characteristics for participants and nonparticipants are given in Table 1. Fifteen subjects with uncertain or severe clinical and/or radiographic pathologic findings were immediately scheduled for a radiographic follow-up consultation or for a consultation as appropriate. Prevalence of radiographic findings for cam- and pincer-type impingement on the basis of the worse hip and also for bilateral findings are shown in Table 2. No major differences were seen between left and right hips. As for the COS, 31 of 446 male participants and 48 of 542 female participants had a positive score for COS in the middle third, and one of 446 male participants had a positive score for COS in the lower third. All the other subjects had a positive score for COS in the upper third.

Investigation of Associations among the Radiographic Features for FAI

There was a high degree of coexistence among most FAI findings (OR > 2), in particular for the coexistence between the COS and the posterior wall sign (OR, 7.45 and 13.49 in male and female participants, respectively). Results are shown in Table 3.

Association of FCCs and the Radiographic Features for FAI

When grouping the three cam-type findings in one single cam-type finding and

the three pincer-type findings in one single pincer-type finding, the χ^2 statistic (Fisher exact test) showed associations between FCCs in the epiphyseal vicinity and the presence of either a cam-type finding (male participants, $P = .001$ for the right hip and $P = .013$ for the left hip; female participants, $P = .003$ for the right hip and $P = .033$ for the left hip) or a pincer-type finding (male participants, $P > .99$ for the right hip and $P = .017$ for the left hip; female participants, $P = .125$ for the right hip and $P = .030$ for the left hip). An adjusted model of binary logistic regression with FCC as the outcome and the six radiographic FAI findings as predictors showed significant associations in male participants for right-sided femoral neck prominence ($P = .001$) and also left-sided acetabular coverage ($P = .002$), and in females for right-sided femoral neck prominence ($P = .029$) and right-sided laterally flattened head ($P = .009$), and also left-sided femoral neck prominence ($P = .002$). For all other findings, the binary logistic regression model yielded high P values of greater than .05.

Table 1

Characteristics for 4006 Subjects Invited to Participate in a Long-term Clinical and Radiographic Follow-up

Characteristics	Participants ($n = 2081$)	Nonparticipants ($n = 1925$)	*P* Value*
Sex			<.001
No. male	874	1194	
No. female	1207	731	
Age (y)†	18.6 (0.6)	18.7 (0.5)	<.001
Body mass index (kg/m^2)‡	23.2 (3.9)	NA	...
No. with birth weight data available§	1691 (81.3)	1289 (67.0)	<.001
No. male	724	814	
No. female	967	475	
Birth weight (g)‖	3529 (0.54)	3521 (0.55)	.684
No. with growth data available§	827 (39.7)	619 (32.2)	<.001
No. male	362	383	
No. female	465	236	
Weight at 7 y (kg)#	26.4 (4.6)	26.5 (4.8)	.62
Body mass index at 7 y (kg/m^2)#	16.3 (2.0)	16.4 (2.0)	.404

* *P* values were determined with the χ^2 test for sex and with the two-sided independent-samples *t* test for all other characteristics.

† Data are the means, and numbers in parentheses are the standard deviations except where otherwise indicated.

‡ Datum is the mean, and number in parentheses is the standard deviation. NA = not available.

§ Numbers in parentheses are percentages except where otherwise indicated.

‖ Data are the means, and numbers in parentheses are the standard deviations except where otherwise indicated. Data were available for 2980 of 4006 of those invited to participate (1691 participants and 1289 nonparticipants).

Data are the means, and numbers in parentheses are the standard deviations except where otherwise indicated. Data were available for 1446 of 4006 of those invited to participate (827 participants and 619 nonparticipants).

Inter- and Intraobserver Agreement

Interobserver agreement was good to very good ($\kappa = 0.74–0.84$) in rating cam-type and pincer-type findings. Intraobserver agreement was moderate or good ($\kappa = 0.49–0.80$) for all findings for both observers. The results are shown in Table 4.

Cadaveric Study Results

We did not detect any visual changes of the femoral head-neck contour that might indicate that excessive internal or external rotation would produce a false-positive cam deformity.

Discussion

Clinicians are increasingly aware of the diagnosis of FAI: The cam type is characterized by anatomic femoral abnormalities, seen as a decreased femoral head-neck offset and/or an asphericity of the lateral femoral head (2,14–16). Cam-type radiographic features include a pistol-grip deformity or a focal prominence or bump to the anterolateral aspect of the femoral neck (14–16). Also, an aspherical part of the head-neck junction can extend proximally, causing asphericity of the lateral femoral head (2). The pincer-type is characterized by acetabular abnormalities, and imaging typically demonstrates global or focal overcoverage of the femoral head (2). The global type often is associated with protrusio acetabuli or coxa profunda, while the focal type is seen in acetabular retroversion (19,21,22). Radiographic features suggestive of a pincer-type impingement include the COS, the posterior wall sign, and excessive coverage of the femoral head by the lateral acetabulum (2,17–19).

We showed that, overall, radiographic features suggestive of FAI, both cam and pincer types, are quite common in a population of healthy young adults, especially in males, with a high degree of coexistence among most findings.

With respect to the findings suggestive of a cam deformity, our results are similar to those of others (23,24). In a recently published study of 244 unselected, asymptomatic young male subjects, cam-type deformities, as assessed with magnetic resonance (MR) imaging, were seen in nearly one-fourth of all subjects (24). Similarly, in a cross-sectional population-based study of 3620 subjects (mean age, 60 years) (23), a pistol-grip deformity was found in one-fifth of male and in 5% of female subjects. If biased, this would be toward underestimation because only one AP view was used for the assessment, with the possibility of missing anterolateral deformities. The frequent findings among healthy adolescents, with male adolescents being three- to fourfold more likely to have findings suggestive of a cam deformity than are female adolescents, are intriguing, and we speculate that these findings may reflect anatomic variation rather than true pathologic abnormalities.

According to the literature, cam deformities are predominantly seen in young athletic male subjects, whereas pincer deformities are more often seen in

Table 2

Radiographic Findings for FAI in 868 Male and 1192 Female Healthy Participants at Skeletal Maturity on Basis of Worse Hip and Bilateral Findings

	Worse Hip			Bilateral Findings	
Radiographic Feature	Male Participants	Female Participants	*P* Value*	Male Participants	Female Participants
Cam					
Pistol-grip deformity	187 (21.5)	39 (3.3)	<.001	135 (15.6)	23 (1.9)
Focal prominence	89 (10.3)	31 (2.6)	<.001	47 (5.4)	17 (1.4)
Flattening of lateral head	125 (14.4)	74 (6.2)	<.001	85 (9.8)	41 (3.4)
Cam type (one or more findings)	304 (35.0)	121 (10.2)	<.001	214 (24.7)	75 (6.3)
Pincer					
Posterior wall sign	203 (23.4)	131 (11.0)	<.001	104 (12.0)	63 (5.3)
Excessive acetabular overage	127 (14.6)	58 (4.9)	<.001	99 (11.4)	43 (3.6)
COS	446 (51.4)	542 (45.5)	.004	307 (35.4)	367 (30.8)
Pincer type (one or more findings)	298 (34.3)	198 (16.6)	<.001	188 (21.7)	116 (9.7)
FCC	50 (5.8)	19 (1.6)	<.001	18 (2.1)	5 (0.4)

Note.—Data are numbers of findings, and numbers in parentheses are percentages except where otherwise indicated.

* The *P* value refers to significant differences according to sex.

Table 3

Associations among Radiographic Features for FAI

Radiographic Feature and Participants	Focal Prominence	Flattening of Lateral Head	Posterior Wall Sign	Excessive Acetabular Coverage	COS
Pistol-grip deformity					
Male	2.84 (1.66, 4.89)*	3.00 (1.89, 4.75)*	1.54 (1.01, 2.35)	1.31 (0.78, 2.16)	1.02 (0.71, 1.46)
Female	10.42 (3.29, 33.02)*	5.30 (1.93, 14.67)*	2.56 (0.95, 6.95)*	6.22 (2.24, 17.27)*	1.17 (0.53, 2.57)
Focal prominence					
Male	. . .	2.81 (1.53, 5.16)*	1.20 (0.65, 2.23)	4.40 (2.53, 7.64)*	1.44 (0.86, 2.39)
Female	. . .	4.38 (1.44, 13.29)*	2.13 (0.72, 6.37)*	2.22 (0.51, 9.71)*	1.90 (0.84, 4.28)
Flattening of lateral head					
Male	. . .	. . .	1.81 (1.12, 2.93)	5.15 (3.20, 8.30)*	1.40 (0.90, 2.15)
Female	. . .	. . .	1.56 (0.69, 3.55)	3.19 (1.30, 7.87)*	0.93 (0.53, 1.64)
Posterior wall sign					
Male	. . .	. . .	. . .	0.92 (0.54, 1.56)	7.45 (4.83, 11.48)*
Female	. . .	. . .	. . .	1.52 (0.63, 3.67)	13.49 (7.44, 24.45)*
Excessive acetabular coverage					
Male	. . .	. . .	. . .	. . .	1.19 (0.79, 1.79)
Female	. . .	. . .	. . .	. . .	1.69 (0.94, 3.04)

Note.—Data are ORs, and numbers in parentheses are 95% confidence intervals. Data for the right hip are shown. The findings were similar for the left hip in both male and female participants.

* OR greater than two.

middle-aged, athletic women (2,3,14). In contrast, we found that pincer deformities were quite frequent in subjects of both sexes, and more so in male subjects. It is outside the scope of this article to examine possible explanations for this finding.

The high degree of coexistence (OR > 2) was true in particular for the coexistence of the COS and the posterior wall sign. This multicolinearity has already been described in the literature (1,19). Approximately one-half of the subjects, both male and female subjects, had a positive COS, indicating acetabular retroversion in the weight-bearing position, as the upper part of the anterior acetabular wall lies more laterally than usual, and crosses over the posterior wall. A positive posterior wall sign indicates a deficient posterior wall (19). According to Clohisy et al (25), the combination of these two signs indicates a true acetabular retroversion, while a positive COS alone indicates anterior overcoverage. Our prevalence numbers for both the COS and the posterior wall sign are high as compared with those of others (26), in part reflecting differences in pelvic positioning and definitions

Table 4

Intra- and Interobserver Measurements: Radiographic Features of FAI

Measurements	Intraobserver κ Value		Interobserver κ Value
	Observer 1	Observer 2	
Pistol-grip deformity	0.65	0.78	0.74
Focal prominence	0.65	0.77	0.84
Flattening of lateral head	0.55	0.77	0.76
Posterior wall sign	0.55	0.73	0.83
Excessive acetabular coverage	0.49	0.71	0.75
COS	0.59	0.80	0.82

used for a positive COS. Obviously, pelvic positioning (ie, the pelvic tilt) influences the two-dimensional projection of the acetabulum and, hence, the prevalence of both the COS and the posterior wall sign. Several techniques have been suggested to control for pelvic tilt on an AP pelvic view (17,21,27,28). We considered using the distance between the coccyx and the symphysis (2,27) but found it difficult to assess in a high proportion of images owing to overlying bowel content. In another article, Kalberer et al (29) found a high correlation between the projection of the ischial spine into the pelvis and the COS. Although others have observed this ischial spine sign to be a valid marker for acetabular retroversion regardless of pelvic tilt and rotation (30), we were not able to reproduce their findings in a subset of 146 cases and, as such, did not include the ischial spine sign in our analysis.

Hips with impingement are often thought to represent hips with a mixed type of both cam and pincer features (2,3,22). Our findings show little overlap between cam and pincer findings (Table 2) and lend support to findings in a recent article by Cobb et al (31) in which the authors conclude that hips with cam and pincer deformities are distinct pathoanatomic entities.

The prevalence of FCCs in the epiphyseal vicinity was 5.8% in male participants and 1.6% in female participants. An association between FCCs and the presence of either a cam-type or a pincer-type deformity was seen, especially the femoral neck prominence, indicating that FCC may be a radiographic indicator of FAI. This confirms findings described by Leunig and colleagues in 2005 (10), although it has also been shown that herniation pits are not necessarily correlated with FAI findings (32).

We found high agreement both within and between observers for the reliability for most of the findings, which is in accordance with data in studies by others (17,33). Jamali and colleagues (17) report on κ values between 0.6 and 0.7 for both intra- and interobserver studies for the COS. Kappe and colleagues (33) report on the reliability of radiographic signs for acetabular retroversion, with κ results for the COS (r = 0.53) and the posterior wall sign (r = 0.74). Clohisy and colleagues (34) reviewed the reliability of the head-neck offset and the head sphericity on both AP and frog-leg views and found κ values below 0.6 for both intra- and interobserver reliability.

The prospective, population-based design and the large numbers strengthen the findings in our study. So does the standardized imaging protocol used. We, however, acknowledge several limitations to our study. First, only two radiographic views were available, namely an AP and a frog-leg view. For the purpose of the main study focusing on hip dysplasia and secondary osteoarthritis, the AP view was obtained with the subject in a weight-bearing, anatomic, and physiologic position, as a supine position tends to give different findings of acetabular version (35).

We are aware that several protocols have been suggested for the radiographic assessment of impingement, of which a supine AP and a cross-table lateral view seem to be preferred over others (9,36). The supine AP view has traditionally been obtained with internally rotated hips, as the femoral necks project better in this position; thus, fractures are more easily detected. For the assessment of the acetabulum, however, a weight-bearing view in the anatomic position appears to be more appropriate as acetabular version is more correctly visualized. Further, weight-bearing images are preferred for the measurements of joint space width (17,21,28,35). It is reasonable to believe that two-dimensional imaging, as performed in our study, yields an underestimation of the prevalence of features suggestive of FAI. However, in a recent MR imaging study by Reichenbach and colleagues (24), most of the cam deformities were located in a superoanterior position and, as such, should be possible to detect on a lateral view. As for the pistol-grip deformity, Clohisy and colleagues (37) found that the femoral head-neck offset in patients with FAI is accurately visualized on a frog-leg lateral radiograph. Others (36) believe that the femoral head-neck asphericity is best visualized on the Dunn view in 45° or 90° flexion or on a cross-table projection in internal rotation.

Another limitation to our study was the subjective assessments; thus, measurements for acetabular shape were not included. However, the radiographs were evaluated by an experienced radiologist with a special interest in developmental dysplasia of the hip. Radiographic criteria for anterior impingement are not yet well established. The alpha angle, which was initially based on MR images (15), is a commonly used measurement to quantify the head-neck offset in cam impingement. However, the accuracy of this measurement has been questioned in a recent article (38). Gosvig and colleagues (39) suggested another measurement, the triangular index, for the same purpose; however, to our knowledge its accuracy has not been validated in later studies.

Other limitations include that of a quite small catchment area of our cohort, which could possibly have resulted in stronger relationships among our data, most likely caused by genetic or environmental factors. As for the high degree of coexistence among most FAI

findings, the probability of false-positive findings owing to chance is nonnegligible because multiple statistical tests were performed on the same data. It is also important to acknowledge the possibility of an induced correlation between the radiologists' readings, affecting the interrater variability, as a result of the standardization of 20 images prior to interobserver readings.

Our study emphasizes the need for further work on this topic, as the radiographic FAI findings in the general population seem to be relatively common. These features should be interpreted carefully and related closely to the clinical findings.

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Is a Positive Femoroacetabular Impingement Test a Common Finding in Healthy Young Adults?

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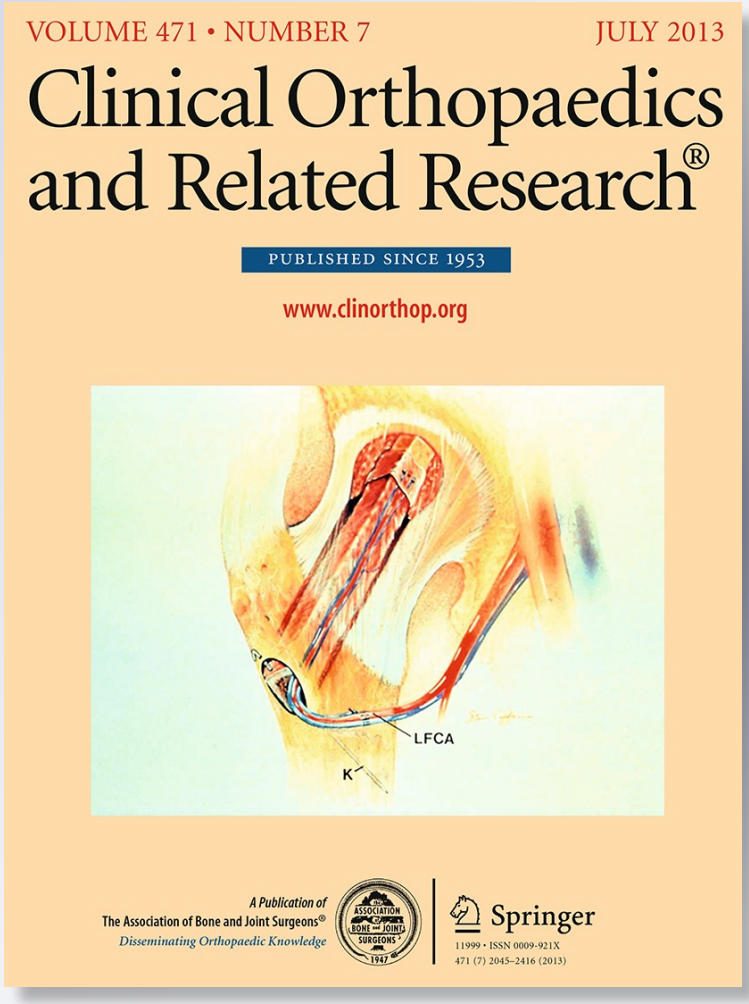

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CLINICAL RESEARCH

Is a Positive Femoroacetabular Impingement Test a Common Finding in Healthy Young Adults?

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Abstract

Background Femoroacetabular impingement (FAI) is an incompletely understood clinical concept that implies pathomechanical changes in the hip as a cause for hip-related pain in young adults. While a positive anterior impingement test is suggestive of FAI, its association with clinical and radiographic findings remain unconfirmed in healthy young adults.

Questions/purposes We determined the prevalence of a positive test in 1170 young adults and examined its possible associations with (1) self-reported hip discomfort for the past 3 months; (2) weekly physical exercise; (3) hip ROM; and (4) radiographic findings associated with femoroacetabular impingement.

Methods We invited 2344 healthy 19-year-olds to a population-based hip study between 2008 and 2009; 1170 patients (50%) consented. The study included questionnaires on medical and functional status, a clinical hip examination including the impingement test and hip ROM, and two pelvic radiographs (AP and frog-leg views).

Results Based on at least one affected hip, 35 of 480 (7.3%) men and 32 of 672 (4.8%) women had positive impingement tests. Eighteen of the 1170 patients were excluded owing to suboptimal or missing radiographs. Self-reported hip discomfort in the women and increased physical exercise in the men were strongly associated with the positive impingement tests. Decreased abduction and internal rotation in the men, decreased flexion in both genders, and radiographic cam type findings in the men also were associated with positive tests.

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All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request.
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Each author certifies that his or her institution approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
This work was performed at the Haukeland University Hospital, Bergen, Norway.

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Conclusion A positive test for anterior impingement is not uncommon in healthy young adults, especially in males. We believe it always should be performed along with pelvic radiographs in young, active patients presenting with hip pain.

Level of Evidence Level II, diagnostic study. See the Guidelines for Authors for a complete description of level of evidence.

Introduction

Femoroacetabular impingement (FAI) has gained increasing interest as a clinical concept during the last decade and is now recognized as a risk factor for early hip osteoarthritis [1, 11, 12]. The diagnosis of FAI should be suspected when there is a history of hip and/or groin discomfort or pain and reduced hip motion on clinical examination; specifically, decreased hip flexion and internal rotation [12, 20, 53]. The pain in FAI can be reproduced by a positive clinical test for anterior impingement [23, 29] (Fig. 1). However, the test alone is not specific [30, 35] and radiographic findings associated with FAI are needed to confirm the diagnosis [49].

FAI can be divided pathomechanically into a cam-type or a pincer-type impingement, based on the underlying anatomic deformity [10] (Fig. 2). The cam-type is characterized by a flattened or convex femoral head-neck junction, commonly seen at the anterosuperior aspect [13, 20, 36, 46, 48]. For the pincer-type, the underlying mechanism lies on the acetabular side, resulting in global or focal overcoverage [3, 12, 19, 21, 37, 42, 45]. In a recent population-based study on 2081 young adults (58% women), also including the 1170 subjects of this study, we reported prevalences of radiographic findings thought to be associated with cam- and pincer-type FAI on plain radiographs [24]. One or more findings indicating cam-type or pincer-type FAI were seen in 35 and 34% of the men and 10 and 17% of the women, respectively. Many of the radiographic findings coexisted. Clinically, the cam-type FAI is predominant in young, athletic boys and men, whereas the pincer-type FAI is seen more often in middle-aged women [11, 12, 20]. Often, a mixed type is present [3]. FAI can occur as a result of abnormal morphologic change or excessive ROM in the hip [8]. Increased physical exercise has been associated with FAI [11, 35]. Additional knowledge regarding the prevalence of a positive clinical test and its associations with clinical and radiographic findings would help to further understand FAI as a clinical concept and to integrate it in daily clinical practice, but remain to be confirmed in large population-based cohorts.

We, therefore, determined the prevalence of a positive femoroacetabular impingement test in a cohort of healthy young men and women, and examined associations of a positive test with (1) self-reported hip discomfort the past 3 months; (2) physical exercise; (3) clinically assessed hip ROM; and (4) radiographic findings associated with FAI.

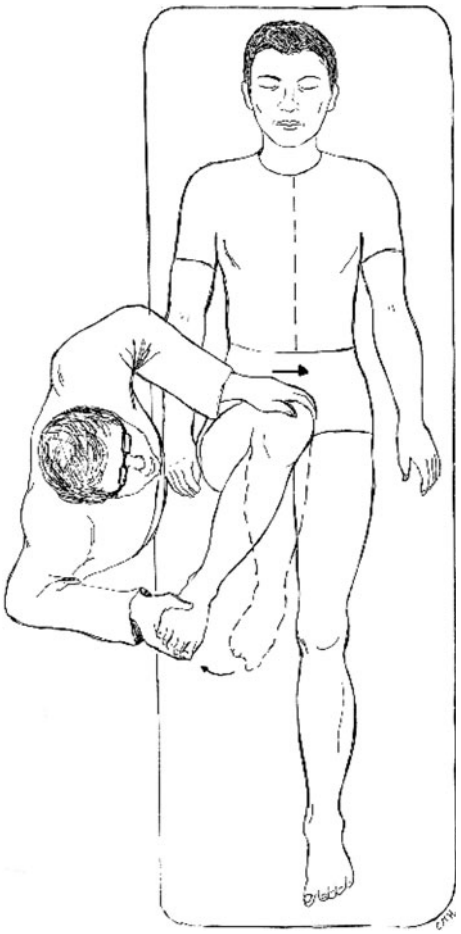

Fig. 1 A pain-provocation test for anterior impingement was performed with the patient supine and scored as 0 (no pain provoked) or 1 (definite pain provoked when asked). A combined maneuver, consisting of 90° passive flexion of the hip, followed by forced adduction and internal rotation, was used.

Patients and Methods

This study was performed on healthy young adults 18 to 20 years old as part of the followups of the population-based '1989 Bergen Birth Cohort' which comprised all babies born at Haukeland University Hospital during 1989 (n = 4703). They were part of a large randomized trial at birth, designed to assess different screening strategies for developmental dysplasia of the hip in 11,925 newborns born from 1988 to 1990 [43]. Between 2007 and 2009, 3935 of the 4703 subjects from the 1989 cohort were invited for long-term followups when they were 18 to 20 years old (Fig. 3). For this paper, we included only the

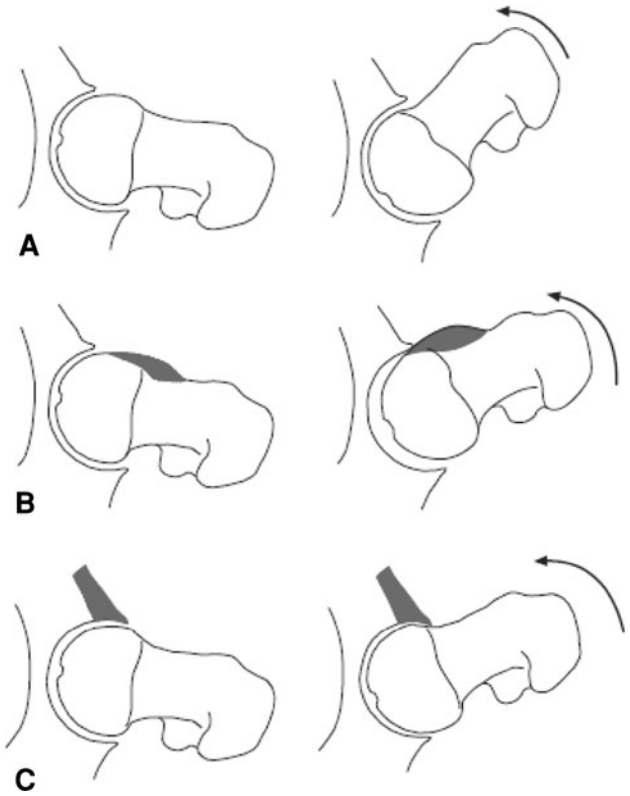

Fig. 2A–C (**A**) Normal anatomy of the hip (left) allows sufficient space for the caput to rotate properly in the acetabulum (right). In cam-type and pincer-type impingements, abnormal contact between the proximal femur and the acetabular rim disturbs adequate movement. (**B**) In cam-type impingement, during forceful motion, the aspheric portion of the head abuts and subsequently damages the acetabular rim, further damaging the cartilage and labrum. (**C**) In pincer-type impingement, an increase in either the coverage of the femoral head or the relative depth of the acetabulum causes an injured acetabular rim, followed by hypertrophy and degenerative changes in the labrum.

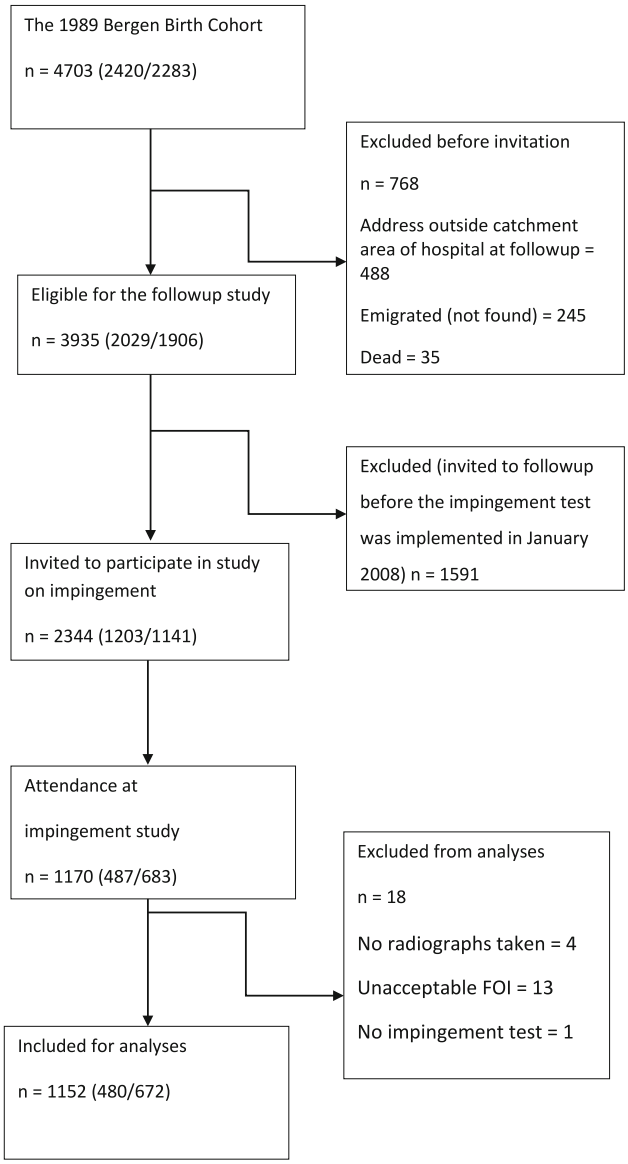

Fig. 3 The flow chart shows the inclusion and exclusion criteria for our study (n = 1170) at followups. Babies with birth weight less than 1500 g, who died within the first month, or whose mother resided outside the catchment area of the hospital were not included in the 1989 Bergen Birth Cohort. FOI = obturator foramen index.

2344 who were invited after the impingement test was added to the clinical assessment. Of 2344 invited, 1170 (50%) attended the followups. These 1170 patients also were reported in our earlier report on radiographic FAI findings [24]. Patients with excessive pelvic rotation as assessed by an obturator foramen index outside 0.6 to 1.8 [51] or without radiographs owing to possible early pregnancy were excluded. Thus, 1152 patients, 480 men (42%; mean age, 19 years [SD, 0.4]) and 672 women (58%; mean age, 19 years [SD, 0.4]), were included for further analyses. Fifteen men and 46 women had been treated for developmental dysplasia of the hip as newborns. A sensitivity analysis was performed while considering an inverse probability weighted (IPW) approach to take into account a possible no response bias [44]. The results of the observed data were reported, as they gave similar results. The research protocol was approved by the Medical Research Ethics Committee of the Western Region of Norway and the Norwegian Data Inspectorate (No 3.2006.144). All participants gave written, informed consent, according to the Helsinki declaration.

The followups consisted of questionnaires, clinical examinations, and two pelvic radiographs (one weightbearing AP view and one supine frog-leg view). The first questionnaire comprised questions on medical history, including hip-related problems in childhood, and the second questionnaire included computer-based standardized questionnaires on quality of life (EQ-5D) [50] and on hip problems (WOMAC^{TM} osteoarthritis index) [4], and specific questions related to hip discomfort and to physical activity.

The participants were asked the following questions regarding each hip separately: "Have you experienced hip discomfort from the hip the past 3 months?", and "Outside school hours, how many hours do you usually exercise in your free time—so much that you get out of breath or sweat?" This last question originates from the WHO Health Behaviour in School Children (HBSC) physical activity questionnaire and had six response alternatives: none, about half an hour a week, about one hour a week, about 2 to 3 hours a week, about 4 to 6 hours a week, or 7 hours per week or more [5, 28, 40]. One experienced senior orthopaedic surgeon (LBE) standardized the clinical examination and trained the four less-experienced physicians (LBL, IØE, TGL, AMH). They were blinded to the results of the questions and the radiographs. A standardized protocol was obtained, including hip ROM and impingement test assessments. Flexion, abduction, and adduction were measured with the patient supine, whereas extension and internal and external rotations were measured with the patient prone and the knee flexed 90°. Extension was not measured in one man and six women.

The standardized radiographic examination was performed by a specially trained radiographer (ST) using a low-dose, digital radiography technique (Digital Diagnost X-ray System, release 1.5, Philips Medical Systems DMC GmbH, Hamburg, Germany). The mean total effective dose was 0.15 mSv for both radiographs together. Men were offered gonadal shields. In women, however, shields were not offered as they risk obscuring important anatomy. In addition, the effect of shielding on dose reduction in females has been questioned [2]. Hips were kept in a neutral abduction-adduction position with the toes directed forward for the AP view. The radiographer ensured correct posture to avoid excessive tilt or rotation of the pelvis [47]. We used a film and focus distance of 1.2 m and centered 2 cm proximal to the pubic symphysis for the AP view and at the pubis symphysis for the frog-leg view. All radiographs were blocked for patient confidentiality, and assessed by gross visual inspection on a high-resolution screen by one experienced pediatric musculoskeletal radiologist (KR). Positioning of the pelvis on the AP view and presence or absence of any of the qualitative cam-type and pincer-type radiographic findings on the two views were noted. In addition, all the AP views were assessed in a validated digital measurement program by three of the authors (LBL, IØE, TGL) (Adult DDH, University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA) [9, 38]. The digital program initially included the center edge (CE) angle [52], and later was extended to include the alpha angle and the triangular index [13, 36] (Appendix 1). To assess a cam-type deformity one of the physicians (LBL) measured the alpha angle measurement and the triangular index (Fig. 4), while the radiologist (KR) by gross visual

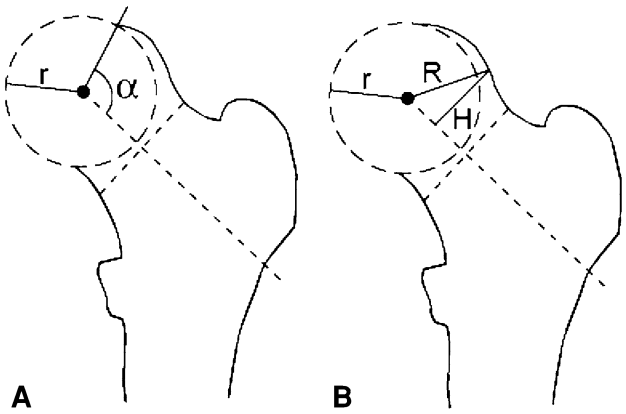

Fig. 4A–B (**A**) The alpha angle is the angle between a line running through the head center and the long axis of the femoral neck, and a line originating from the head center and to the point where the bone of the head neck junction crosses outside the radius curvature of the head. The higher the alpha angle, the greater the cam defect will be. (**B**) The triangular index is based on the equation $R \geq r + 2$, where "r" is the head radius, and "R" is the pathologically increased radius. Half of the head radius distance measured along the neck axis is found, and a perpendicular line H is drawn up to the crossing point of the bony cam curvature. "R" then is found. If $R \geq r + 2$, a head-neck asphericity indicating a cam type is confirmed.

inspection determined the presence of a pistol grip deformity, focal prominence of the femoral neck, and lateral flattening of the femoral head [12, 20, 46] (Fig. 5). The presence of a pincer-type FAI was determined by measuring increased CE angles (LBL, IØE, TGL), indicating lateral overcoverage, and by gross visual inspection (KR) by the posterior wall sign and the crossover sign [12, 21, 37, 42, 52] (Fig. 6). The pistol grip deformity and the focal prominence were scored as positive if present in the AP and/or the frog-leg view. All other measurements were performed on the AP view. The alpha angle, crossover sign, and lateral flattening of the femoral head were not measured on three, 33, and five radiographs respectively.

Interobserver reliabilities for flexion, extension, abduction, adduction, and external and internal rotations presented as intraclass correlation coefficients (ICC), have been reported as 0.87, 0.44, 0.34, 0.54, 0.18, and 0.79, respectively [39]. The κ value for interobserver variability for the anterior impingement test is reportedly 0.58 (95% CI, 0.29–0.87) [31], and the interobserver agreement for the impingement test is reportedly 96% [39]. A small interobserver study (30 right hips, 30 left hips) (LBE, TGL) showed the interrater agreement for the impingement test to be 95%. Two of the authors (blinded to the patients' identification), measured and remeasured the images (after an interval of at least 8 weeks), and found intraobserver and interobserver agreements of $\kappa = 0.85$ and $\kappa = 0.69$, respectively for the triangular index, and 95% limits of agreement of intraobserver and interobserver variabilities

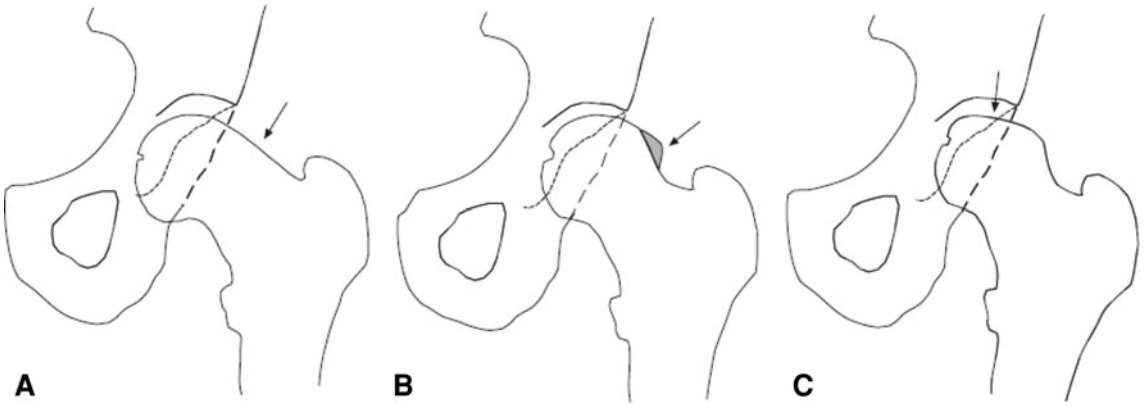

Fig. 5A–C (**A**) A pistol-grip deformity is flattening of the normal concavity of the femoral head-neck junction. (**B**) A focal prominence is a prominence or bump to the femoral neck. (**C**) Flattening of the lateral aspect of the femoral head is shown in this drawing.

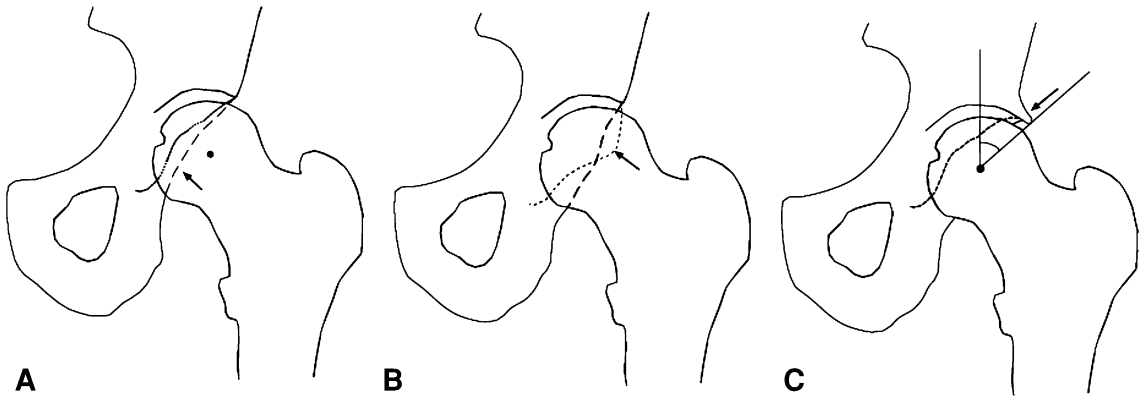

Fig. 6A–C (**A**) The posterior wall sign is scored positive when the posterior wall lies medial to the center of the femoral head. (**B**) The crossover-sign is scored positive when the upper part of the anterior acetabular wall lies more laterally than the posterior wall and crosses medially. (**C**) Excessive acetabular coverage leading to a deep acetabular socket is seen as a bony extension of the upper acetabular roof, quantified by an increased center-edge angle.

for the alpha angle; −5.95°; 6.71° and −7.76°; 12.78°, respectively. Interobserver agreements for assessments of findings for the cam-type and pincer-type impingements were reported earlier ($\kappa = 0.74$–0.84) [24]. For the CE angle, the 95% limits of agreement of intraobserver and interobserver statistics have been reported at −4.18; 4.20 and −3.61; 3.32 [9].

The prevalences of a positive impingement test are presented as numbers (percentages) with corresponding 95% CIs. Differences in the prevalence of a positive impingement test according to sex and side were examined using Pearson chi-square test. Descriptive statistics for the variables considered as possible predictors of a positive impingement test were summarized by sex and side and were reported as numbers (percentages) or means (SD) as appropriate (Table 1). We used generalized estimating equations (GEE) models to study possible associations between the predictor variables and a positive impingement test. P values and prevalence rate ratios (PRR) with corresponding 95% CIs were estimated with GEE models [18], adjusted by side (left or right), to take into account the correlation between bilateral hips. The p value was used to evaluate the effect of the variables on a positive test. All the reported p values were two-tailed. A PRR value describes how the presence of a given variable alters the prevalence of a positive test; ie, a PRR of 3.1 means an increase of 210%. For continuous variables (hip ROM and CE angle) the PRR represents the increase of the prevalence for a unit (5°) change of the continuous variable.

Weekly physical activity was treated as a continuous variable with 1-hour increments; ie, a linear effect was assumed. The hip ROM values were continuous variables with 5° decrements. All the cam-type and pincer-type variables assessed by gross visual inspection were categorical variables. The alpha angle was categorized into normal (men (M) ≤ 68, women (W) ≤ 50), borderline (M = 69–82; W = 51–56), or pathologic (M ≥ 83; W ≥ 57) groups [13]. A CE angle greater than 45° was

Table 1. Descriptive statistics for variables considered possible predictors of a positive impingement test

Variable	Men, number (%) or mean (SD)		Women, number (%) or mean (SD)	
Physical activity (hours/week), n (%)				
None	41 (9)		74 (11)	
0.5	37 (8)		57 (9)	
1	55 (12)		109 (17)	
2–3	113 (24)		196 (30)	
4–6	122 (26)		142 (22)	
≥ 7	104 (22)		82 (12)	
	Right	Left	Right	Left
Hip discomfort, n (%)	7 (1.5)	15 (3.1)	47 (7)	55 (8)
Hip ROM (°), mean (SD)				
Flexion	118 (10)	118 (10)	122 (11)	122 (11)
Abduction	59 (6.0)	59 (5.9)	62 (6.5)	62 (6.5)
Adduction	38 (4.7)	38 (4.6)	39 (4.3)	39 (4.4)
Extension	26 (6.1)	26 (6.1)	28 (6.0)	28 (6.0)
Internal rotation	38 (12)	38 (12)	51 (12)	52 (12)
External rotation	58 (13)	57 (13)	47 (11)	46 (11)
Radiographic cam-type findings				
Alpha borderline*, n (%)	114 (24)	99 (21)	101 (15)	111 (16)
Alpha pathologic**, n (%)	39 (8.2)	18 (3.8)	124 (19)	103 (15)
Triangular index, n (%)	166 (35)	163 (34)	64 (10)	45 (6.7)
Pistol grip, n (%)	78 (16)	93 (19)	13 (1.9)	19 (2.8)
Focal prominence, n (%)	46 (10)	50 (10)	15 (2.2)	17 (2.5)
Flattened lateral head, n (%)	63 (13)	71 (15)	28 (4.2)	34 (5.1)
1 cam marker, n (%)	70 (15)	78 (17)	180 (27)	185 (28)
2 cam markers, n (%)	80 (17)	77 (16)	61 (9)	46 (7)
≥ 3 cam markers, n (%)	78 (16)	71 (15)	12 (1.8)	14 (2.1)
Radiographic pincer-type findings				
Acetabular overcoverage:				
CE angle (°), mean, (SD)	32 (6)	33 (6)	31 (6)	31 (6)
CE angle > 45°, n, (%)	9 (1.9)	10 (2.1)	9 (1.3)	8 (1.2)
Posterior wall sign, n, (%)	100 (21)	86 (18)	70 (10)	55 (8)
Crossover sign, n, (%)	213 (46)	228 (49)	271 (41)	273 (41)
1 pincer marker, n, (%)	158 (34)	202 (43)	217 (33)	235 (35)
≥ 2 pincer markers, n, (%)	79 (17)	59 (13)	64 (10)	49 (7)

* Men, 69°–82°, women, 51°–56°, ** men ≥ 83°, women ≥ 57°.

considered to indicate acetabular overcoverage [15]. The CE angle also was considered as a continuous variable with 5° increments. We created a radiographic composite score of 1, 2, or cam-type three or greater and of 1 or 2 or greater pincer-type findings, respectively. All 1152 patients included in the analyses had the clinical examinations, impingement tests, and radiographs taken. For the analyses only patients without missing data were analyzed for each variable. Statistics were performed in Stata® Statistical Software: Release 11 (StataCorp LP®, College Station, TX, USA) and in IBM® SPSS® Statistics, version 20.0 (Armonk, New York, USA).

Results

Based on the worst affected (ie, at least one) hip, 35 of 480 men (7.3%) and 32 of 672 women (4.8%) had positive tests for anterior impingement (Table 2). Fourteen of 480 (2.9%) men and eight of 672 (1.2%) women tested positive bilaterally. The differences in the prevalences of a positive test for males compared with females were 21 of 480 versus 24 of 672 unilaterally ($p = 0.451$), 14 of 480 versus eight of 672 bilaterally ($p = 0.039$), and 35 of 480 versus 32 of 672 when based on at least one hip ($p = 0.073$).

Table 2. Positive tests for anterior impingement in 480 men and 672 women

Positive test for anterior impingement	Men, number (%)	95% CI	Women, number (%)	95% CI
Right hip	25 (5.2)	3.2–7.2	18 (2.7)	1.5–3.9
Left hip	24 (5.0)	3.0–7.0	22 (3.3)	1.9–4.6
Unilateral	21 (4.4)	2.5–6.2	24 (3.6)	2.2–5.0
Bilateral	14 (2.9)	1.4–4.4	8 (1.2)	0.4–2.0
At least one hip (worst)	35 (7.3)	5.0–9.6	32 (4.8)	3.1–6.4

The 95% CIs were calculated using binomial CIs.

Table 3. Analysis of associations of positive impingement tests

Variable	Men			Women		
	p value	PRR*	95% CI**	p value	PRR*	95% CI**
Physical exercise (hours/week)	0.001	1.23	1.08–1.40	0.967	1.00	0.86–1.15
Hip discomfort past 3 months	0.437	1.67	0.46–6.15	< 0.001	3.88	1.90; 7.92
Hip ROM (5° decrement)						
Flexion	0.062	1.16	0.99–1.35	0.003	1.24	1.08–1.44
Abduction	0.018	1.32	1.05–1.67	0.271	1.15	0.90–1.46
Adduction	0.675	1.08	0.76–1.53	0.271	0.78	0.51–1.21
Extension	0.119	1.22	0.95–1.57	0.133	1.26	0.93–1.71
Internal rotation	0.001	1.31	1.12–1.54	0.366	0.93	0.80–1.08
External rotation	0.212	0.92	0.81–1.05	0.243	1.10	0.94–1.28
Radiographic cam findings						
Alpha angle borderline[†]	0.518	1.23	0.66–2.28	0.724	0.85	0.35–2.06
Alpha pathological[‡]	0.249	1.68	0.69–4.08	0.647	1.20	0.55–2.60
Triangular index	0.288	1.33	0.78–2.27	0.372	0.51	0.11–2.25
Pistol grip deformity	0.548	1.26	0.59–2.67	0.945	1.08	0.13–8.63
Focal prominence	0.181	1.70	0.78–3.68	0.930	1.10	0.14–8.77
Flattened lateral head	0.165	1.71	0.80–3.65	–	–	–
Composite cam score						
1	0.043	2.04	1.02–4.09	0.980	1.01	0.52–1.97
2	0.050	2.04	1.00–4.18	0.224	0.31	0.05–2.06
≥ 3	0.309	1.58	0.65–3.83	0.878	1.18	0.14–9.66
Radiographic pincer findings						
Acetabular overcoverage[§]	0.367	0.89	0.70–1.14	0.508	0.91	0.69–1.20
Posterior wall sign	0.921	0.96	0.47–1.97	0.199	0.25	0.03–2.10
Crossover sign	0.804	0.93	0.51–1.68	0.189	0.62	0.30–1.27
Composite pincer score						
1	0.780	1.09	0.60–1.99	0.281	0.67	0.32–1.39
≥ 2	0.598	0.78	0.30–1.99	0.175	0.21	0.02–2.00

* PRR = prevalence rate ratio describes how the presence of a given variable alters the prevalence of a positive test; ** 95% CI, PRR values are presented with corresponding 95% CI; [†]men, 69°–82°, women, 51°–56°; [‡]men ≥ 83°, women ≥ 57°; [§]based on a continuous center-edge angle with 5° increment; [¶]none of the women with a flattened lateral head had a positive impingement test and therefore the statistical model is not valid in this case.

Self-reported hip discomfort during the past 3 months was associated with positive impingement tests by women ($p < 0.001$), but not by men ($p = 0.437$) (Table 3).

Increased physical exercise was found to be associated by men ($p = 0.001$) but not by women ($p = 0.967$) (Table 3).

As for the ROM, decreased hip flexion in women and men ($p = 0.003$ and $p = 0.062$), and abduction ($p = 0.018$) and internal rotation ($p = 0.001$) for men were associated with positive impingement tests (Table 3).

A cam-type finding was associated with positive impingement tests in men for a composite score value of

one or two ($p = 0.043$ and $p = 0.050$, respectively) positive findings, respectively. In men with three or more positive findings, no association was seen with a positive test ($p = 0.309$) (Table 3). Radiographic pincer-type findings were not associated with positive tests in either gender.

Discussion

The prevalence of a positive anterior impingement test and its association with clinical and radiographic findings thought to be related to FAI remain unconfirmed in healthy young adults. We, therefore, determined the prevalence of a positive impingement test in a population-based cohort of 1170 young adults and examined possible associations of a positive test with (1) self-reported hip discomfort; (2) physical exercise; (3) clinically assessed hip ROM; and (4) radiographic findings associated with FAI.

We acknowledge some limitations that require consideration. First we had a moderate attendance rate of 50%. A selection bias could exist, as the cohort was drawn from a previous population-based hip trial designed to evaluate the effect of ultrasound screening in the diagnosis of hip dysplasia in newborns. Those who received a hip ultrasound as newborns or experienced hip-related problems in infancy possibly could be more prone to participate, along with participants with hip-related problems at the time of followups. A sensitivity analysis with an inverse probability weighted approach, however, did not reveal any no-response bias. Furthermore, no noteworthy differences in growth data characteristics for attendees and nonattendees were seen at birth or at 7 years of age, except for sex distribution, as reported previously [24]. Second, our cohort was homogenous and young, and there are likely to be at-risk patients who have not had the anterior acetabular labral disorder fully developed that will make the impingement test positive, even though they have typical radiographic cam-type findings. The prevalences presented here therefore are likely to be age-dependent. Further followup of the cohort may provide more answers. Third, there is the possibility of a false positive or false negative impingement test. According to the literature, the sensitivity and specificity of the test for anterior impingement are 70% and 44%, when the test represents the most painful provocative movement [35]. In addition, patients with acetabular dysplasia could test positive [25, 27]. A high positive predictive value of the anterior impingement test was recently reported [17]. Fourth, the question regarding hip discomfort during the past 3 months for each of the hips was not validated. However, it appeared to be appropriate and without risk for confusion. Fifth, our digital software program allowed measurements of the alpha angle on the AP view only, which is believed adequate by some authors [13, 22, 34]. Others advocate the modified Dunn or the frog-leg view shows the cam deformity better [7, 32]. We therefore included scoring of the cam-type findings from the frog-leg view into the composite cam score. The strengths of our study included the population-based cohort design with a homogenous age group, the standardized protocols for radiographic and clinical examination, and GEE models to account for the correlation between bilateral hips when evaluating the associations with the different variables.

The prevalence of clinically assessed FAI has been estimated at 10% to 15% in a general adult population [26], as compared with our figures of 7.3% in men and 4.8% in women at age 19 years. The difference may in part be age-related, as the impingement test turns positive after labral damage has occurred; ie, with time. A study presenting the prevalence of cam type FAI morphology in 200 asymptomatic volunteers (89 men, 111 women; mean age 29.4 years) reported three of 200 patients (1.5%) had tested positive for anterior impingement [16]. Patients with ongoing hip or groin problems and/or earlier childhood hip problems were not included, which may explain the lower prevalence of positive tests compared with our results. Numerous studies reported the prevalence of radiographic cam type FAI (Table 4). Overall, the radiographic prevalence in young men was higher than the prevalence of the positive impingement test. Followup studies are needed to understand if these radiographic cam-type findings actually represent a potentially large amount of at-risk patients in a presumed presymptomatic FAI stage.

We found that radiographic cam-type findings were associated with a positive impingement test in men for a composite score value of one or two findings. No such association was seen in women. Interestingly, we found no association between the alpha angle measurement and a positive impingement test, in accordance with earlier findings [16]. The radiographic cam-type findings might be associated with lower-limb dominance in sporting activities, particularly those involving hip flexion, for instance, soccer. We found a higher level of weekly physical activity was associated with positive tests in men. Others have found that 70% of patients with FAI participated in sporting activities, 30% of them on a high-level basis [35]. Our results support these findings. We have confirmed a positive test also is associated with decreased hip ROM in both genders for flexion, and for internal rotation and abduction in men. In a prospective study [6] of 51 patients with FAI (29 men, 22 women; mean age, 35 years), 88% had positive tests for anterior impingement, and internal rotation and hip flexion were confirmed to be reduced in symptomatic patients with FAI.

Overall, a positive test for anterior impingement in a cohort of healthy young adults is not uncommon, with a

Table 4. Prevalence of femoroacetabular impingement reported in the literature

Study	Year	Country	Study population	Prevalence of FAI, based on:		Radiographic modality and FAI findings
				Positive impingement test	Radiographic cam findings	
Gosvig et al. [14]	2008	Denmark	3202 (M = 1184, F = 2018)		M = 17%, F = 4%, age range, 22–93 years	Standardized AP pelvic radiographs, alpha angle, and triangular index
Hack et al. [16]	2010	Canada	200 (M = 89, F = 111); mean age, 29 years (range, 21–51 years)	At least one hip, 1.5% (M + F)	14% (M + F) (10.5% unilateral, 3.5% bilateral) M = 25%, F = 5%	MRI, alpha angle
Reichenbach et al. [41]	2010	Switzerland	M = 244; mean age, 20 years		M = 24%	MRI, scoring system for grading the maximum offset of the head-neck junction
Jung et al. [22]	2011	USA	380 (M = 108, F = 272); M = mean age, 63 years (range, 27–93 years), F = 60 years (range, 26–91 years)		M: pathological (≥ 83°): 14%, borderline (6–82°): 15%; F: pathological (≥ 57°): 6%; borderline (51–56°): 6%	AP pelvic CT scout, alpha angle
Laborie et al. [24]	2011	Norway	2060 (M = 868, F = 1192); mean age, 19 years (range, 17–20 years)		At least one hip, M = 35%, F = 10%; M = 25%, F = 6%	Standardized AP and frog-leg pelvic radiograph, subjective evaluation of cam type
Current study	2012	Norway	1152* (M = 480, F = 672); mean age, 19 years (SD 0.4).	At least one hip: M = 7.3%, F = 4.8% Bilaterally: M = 2.9%, F = 1.2%		

FAI = femoroacetabular impingement; * these 1152 were included in the study by Laborie et al. [24].

higher prevalence in men (7.3%) than in women (4.8%). A positive impingement test is associated with radiographic cam-type FAI and increasing physical activity in men, confirming the cam-type impingement is more common in young, active men. Self-reported hip discomfort was associated with positive tests in women. Our results also confirm the decrease in ROM in patients with positive impingement tests, particularly for flexion and internal rotation, and also in abduction. It is important that the anterior impingement test along with hip ROM tests are used in a standardized fashion. FAI can be difficult, clinically and radiographically, to diagnose, and a consensus regarding the radiographic criteria is needed.

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Appendix 1: The Digital Measurement Program Adult DDH

The digital measurement program (Adult DDH, University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA) [9, 38], was expanded to include the measurements of the alpha angle and triangular index on the AP view.

First, four points outline the femoral head circle, identical to the circle otherwise applied in the manner described by Mose [33], using a hard transparent plastic sheet containing concentric circles. The four points are placed in the

medial and superior part of the head circumference, the most lateral corresponding approximately to the point facing the lateral acetabular edge. None of the four points are placed directly in the cam region. The program automatically generates the best-fit circle based on these four points. Afterward, two more points depict the narrowest collum width, and the program automatically adds the midaxis of the collum, connecting the middistance of the narrowest collum width to the head center. Then the alpha angle is determined by adding a point where the bony head femoral junction crosses outside the femoral head circle. Last, the program automatically draws a line perpendicular to the midaxis of the collum, at the distance of half the radius from the circle center. The last point, determining the triangular index, is set where this line intersects with the bony curvature of the head-neck junction (H). The program then calculates the distance from this point until the head center (R).

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The alpha angle in cam-type femoroacetabular impingement – new reference intervals based on 2038 healthy young adults

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Abstract:

The cam deformity of femoroacetabular impingement can cause hip pain and degenerative hip disease. Based on a population-based cohort of 2038 19-year-olds (58% females), gender-specific reference intervals of the alpha angle and its association with other qualitative cam-type findings are reported. The alpha angle was measured on standardised frog-leg lateral and anteroposterior (AP) views in a digital measurement program, and qualitative cam-type findings (pistol grip deformity, focal femoral hump, lateral flattening of femoral head) were assessed subjectively on both views. 2005 (837 males, 1168 females, mean age 18.6 (range 17.2 to 20.1) years) participants were included for analyses. For the frog-leg view, mean alpha angle (right hip) was 47° (range 26°-79°) in males and 42° (range 29°-76°) in females, with 97.5 percentiles of 68° and 56°, respectively. For the AP view, mean (range) values were 62° (40°-105°) and 52° (36°-103°) for males and females respectively, with 97.5 percentiles of 93° and 94°. Associations between higher alpha angles and all qualitative cam-type findings were seen for both genders on both views. The reference intervals presented for the alpha angle in this cross-sectional study are wide, especially for the AP view, with higher mean values for males than females on both views.

INTRODUCTION

The cam-type femoroacetabular impingement (FAI) is a recognised cause of hip pain in young adults, and can contribute to osteoarthritis.[1] Clinical assessment is accompanied by radiological work-up, ranging from plain radiographs to CT and MRI. On plain radiographs, both quantitative and qualitative measurements depicting the anatomy of the femoral head-neck junction are used to describe cam pathology, usually located on the anterosuperior aspect of the femoral head.[2] Different views are advocated, mostly lateral views including frog-leg, cross-lateral or Dunn views, and by some authors, also the anteroposterior (AP) view.[3-6] The most commonly used quantitative measurement is the alpha angle (Fig. 1).[7] A qualitative assessment can also be made, and findings readily assessed by gross vision such as the pistol grip deformity, a focal femoral hump and a flattening of the lateral aspect of the femoral head are all thought to be associated with cam-type pathology.[1, 2, 8] Recent studies have confirmed that several of these radiological findings appear to be more common than first thought.[9-11] We have previously shown that these subjectively assessed qualitative measurements are quite common in this unselected population of young adults, particularly in males, with a high degree of co-existence between findings.[10] In a sub-set of the same study, a positive anterior impingement test was reported in 7.3% of the males and in 4.8% of the females.[12] Taken together as a group, quantitative and qualitative radiographic cam-type findings were associated with positive tests in males. The alpha angle was available only for the AP views for these analyses. Based on already existing cut-off values in the literature of ≥83° and ≥57° for males and females respectively,[13] high alpha angles were not associated with positive impingement tests.

The alpha angle was first proposed by Nötzli et al on MRI scans in 2002 with a pathological cut-off value of 50°.[7] The alpha angle was thereafter adapted to first lateral and later AP view.[3, 13] Increased knowledge of the distribution of the alpha angle based on standardised pelvic radiographs in a large healthy population might help clarify the diagnostic criteria for cam-type FAI. We therefore aimed to present gender-specific reference intervals for the alpha angle on the frog-leg and the AP view in a population-based cohort of 2038 young adults, using a digital measurement program, and to compare the quantitative alpha angle measurement with the qualitative assessment of the cam-deformity for both views.

PATIENTS AND METHODS

Study population and design

This population-based cross-sectional study was carried out from February 2007 until March 2009 as a follow-up of the 1989 Bergen Birth Cohort (n=4703). This cohort comprises all babies born at the maternity unit of Haukeland University hospital in Bergen, Norway, during 1989, who took part in a large randomised controlled trial, designed to evaluate the effect of different screening strategies for developmental dysplasia of the hip (DDH) (Fig. 2).[14] A total of 3935 from the 1989 cohort were invited to the follow-up study, of which 2038 (51.8%) attended (58.2% females), predominantly ethnic Norwegians. Exclusion criteria after attendance were missing radiographs (due to uncertain pregnancy status or radiographs not taken) or radiographs of suboptimal quality (excessive pelvic rotation as assessed by a foramen obturator index beyond range of 0.6-1.8)[15] (fig 2). The study consultation has previously been described in detail [12]. Fifteen subjects were immediately scheduled for a radiological and/or orthopaedic consultation, due to uncertain or severe radiological and/or clinical findings related to the back, pelvis or hips. All participants gave written informed consent according to the Declaration of Helsinki. The study research protocol, including analyses of the non-responders, was approved by the Medical Research Ethics Committee of the Western region of Norway (No. 018.06). Information regarding sex, age, birth weight, weight and height at 7 years (±3 months) was collected from the community health care centres in Bergen and suburbs, for those born in 1989 and whose information was available, including the non-responders. Analysis of these baseline characteristics showed similar values for birth-weight and for weight and height at age seven years for those who attended vs. those who did not.[16] Only the sex-distribution differed significantly between the two groups, as more girls than boys attended the follow-up study.

Radiographic protocol

All radiographs were performed by one particularly trained radiographer, in the paediatric unit of the Radiology department. A low-dose digital radiography technique (Direct Digital Radiography, Digital Diagnost System, version 1.5, Philips Medical Systems, Best, the Netherlands) was used. Supine frog-leg and weight-bearing AP views were obtained according to a standardised protocol. The film/focus distance was 1.2 meters and centered 2 cm proximal to the symphysis for the AP view, and at the symphysis for the frog-leg view. Hips were kept in a neutral abduction-adduction position with toes pointing forwards for the

AP view, and the radiographer took particular care of the posture during exposure in order to avoid excessive tilt or rotation. Gonadal shields were offered to males. The total mean radiation dose was 0.5 $Gycm^2$ for the two radiographs together.

Digital radiographic measurement program

The radiographs were stored in the PACS (Picture Archiving and Communications System) of the hospital, and also retrieved as DICOM (Digital Imaging and Communications in Medicine) files. A validated digital measurement program used for measurements related to hip dysplasia at skeletal maturity, 'Adult DDH' (University of Iowa Hospitals and Clinics, Iowa City, USA)[17] was extended to include the alpha angle on both the AP view,[12] and the frog-leg view. All alpha angles on both views were measured by the same observer (LBL) (Fig 3). In the digital program, each hip is magnified one at the time to allow for more precise measurements. A curser was used to manually place four points corresponding to the circle of the femoral head, the most lateral point corresponding approximately to the point facing the lateral acetabular edge. None of the points are placed directly in the cam-region. The four points allow the program to determine and draw a circle of best fit, corresponding to the circle found by using Mose's templates, i.e. a transparent hard plastic sheet with concentric circles. The mid-axis of the femoral neck was found by placing one point on each side of the neck at its most narrow part, and the program automatically drew the mid-axis passing through the circle centre. The alpha-point was placed where the anatomical bony curvature crosses outside the circle. The program calculated the angle between the mid-axis of the femoral neck and the alpha-point, and automatically transferred the result to an excel spreadsheet.

Qualitative image evaluation

All radiographs were also assessed subjectively by a blinded paediatric musculoskeletal radiologist with 25 years of experience (KR). Findings thought to be associated with cam-type FAI (pistol neck deformity, focal femoral hump, flattening of lateral femoral head) were noted on both views. A detailed description of these findings together with their prevalences in this study population and inter- and intraobserver agreements are presented previously.[10]

Reproducibility of measurements

A balanced set of 100 radiographs were used to assess intra- and inter-observer and inter-method reproducibility. Ten frog-leg and AP radiographs were assessed for standardisation prior to and not included in the reproducibility analyses. One observer (LBL) measured all radiographs (both views) in the digital measurement program and manually in the IMPAX (Version 6.4, Agfa HealthCare System, Mortsel, Belgium), using Mose's templates to determine the circle of best fit around the femoral head and its circle centre. As in the digital measurement program, one point was placed at each side of the narrowest portion of the femoral neck. The mid-axis of the neck was drawn through the mid-point of the narrowest portion and running through the head centre. The alpha-point was placed following the same method as in the digital program. All digital and manual measurements were remeasured after an interval of two months by the first observer. In addition, one observer (KR) measured all radiographs (both views) once in the digital measurement program.

Statistical analysis

Mean values, standard deviation (SD), range, and empirical 97.5 percentiles with their corresponding 95% confidence intervals (CI) were calculated for both sex and sides separately for the alpha angle on the frog-leg and the AP view, respectively.[18] The binominal method was used to obtain the 95% CIs.[19] Repeated measure analysis of variance was used to account for potential non-independence of radiological findings on right and left hips. In order to evaluate the effects of sex and side on the alpha angle values, subjects were considered as random term, side as within subject and sex as between subject factors. Each of the three qualitative cam-type findings was dichotomised variables (yes/no), and each finding was scored separately on the two views. In order to examine the association of alpha angles with the presence of quantitative cam-type findings, random effect models were fitted with alpha angle as outcome and dichotomized qualitative cam-type as exposure, for each of the qualitative cam-type findings and for each view. Random effect models take into account a possible non independence of alpha measurements, considered as outcome, for right and left hip measurement within a subject, including a subject effect considered as random variable. The coefficient (°), adjusted by sex and side, resulting from each model indicates how many degrees higher the mean alpha angle is for the group with a positive subjective cam-type finding, compared to the group without subjective findings.

Intra- and inter-observer and inter-method reproducibility were assessed. The 95% limits of agreement (LoA) method was used for examining the mean difference between two sets of readings performed by same observer (intraobserver) between a set of readings performed by two observers (interobserver), and between a set of readings in the digital program and a set of manual readings (inter-method).[20, 21] For the inter-method reproducibility, we first calculated the mean for each method and on each subject and used these pairs of means to compare the two methods, as described in a previous paper presenting the 'Adult DDH' digital program.[17] The 95% LoA were estimated as mean difference between the two measurements ±1.96 standard deviations (SD). The intra-and interobserver reliability were also expressed by the intra-class correlation coefficient (ICC), using a one-way random effect ANOVA table [formula ICC (1)].[22] The inter-method reliability was expressed by ICC calculated using two-way random effect ANOVA table [formula ICC (A,1)].[22]

All reported p-values are two-tailed. A p-value of <0.05 was considered statistically significant. No corrections for multiple comparisons were performed. Statistics were performed in IBM® SPSS® Statistics, version 20.0 (Armonk, New York, USA), and in Stata® Statistical Software: Release 11 (StataCorp LP®, College Station, TX, USA).

RESULTS

A total 2005 (837 males, 1168 females, mean age 18.6 (SD 0.6) years, range 17.2-20.1, for both genders) participants had their two radiographs analysed (Fig. 2).

Reference values

The gender-specific reference intervals for the alpha angle are presented, for both the frog-leg view and the AP view (Table I). All p-values for differences between sex and between side were <0.001 for both views. Higher mean values with wider 95% reference intervals were seen for the AP view than the frog-leg view, for both genders.

Associations between the alpha angle and qualitative radiographic findings

The random effects models, adjusted by sex and side, demonstrated significantly higher mean alpha values for those with qualitative cam-type findings compared to those without, on both

views (all p values <0.0001). The mean alpha angle was 15.3° higher in those with a pistol grip deformity on the frog-leg view, compared to those without (table II).

Intra- and interobserver reproducibility

The intra- and interobserver reproducibility for the alpha angle on the frog-leg and the AP views, together with the inter-method reproducibility for digital vs. manual measurement techniques of the alpha angle on both views are reported, expressed as 95% LoA and ICC (Table III). The LoA were wider for all measurements on the AP view.

DISCUSSION

This population-based cross-sectional study presents gender-specific reference ranges for the alpha angle in the cam-type deformity. Higher mean values with wider 95% reference intervals were seen for the AP view than the frog-leg view, for both genders. Mean alpha angle for the right hip on the frog-leg view was 47° in males and 42° in females, with 97.5 percentiles of 68° and 56°, respectively. For the AP view, mean values were 62° and 52° for males and females respectively, with 97.5 percentiles of 93° and 94° and wider intervals than the frog-leg values. Associations between higher alpha angles and present qualitative cam-type findings were seen on both views.

We acknowledge several limitations to the present study. First, the attendance rate of 52% for this cross-sectional analysis is moderate. Second, subjects with previous or ongoing hip problems could possibly be more encouraged to attend the study. However, comparisons of baseline growth characteristics at birth and at age seven years did not reveal any differences between the attenders and the non-attenders, except for the sex distribution.[16] Third, the ethical aspects of a radiographic study in a population of healthy young adults need to be considered. The effective dose without gonadal shields was as low as 0.15 mSv for both radiographs together [16], and the use of gonadal shields in males reduces this number further. Fourth, the results of the present study might be age-dependent and are thus confirmed for young adults only. The strengths of this study include the large numbers and homogenous age group, a standardised radiographic protocol and only one radiographer. All alpha angle measurements were performed by the same observer. The intra- and inter-reproducibility

statistics for observers and for measurement technique when measuring the alpha angle were overall satisfying, and compared well with other studies.[3, 13, 23] The use of a digital measurement program with automatic storage of results was time-saving with respect to both measuring and recording, and avoided potential recording errors.

Consensus on the best way to define cam-type FAI is lacking. The alpha angle is often used as a quantitative measurement of the cam-deformity, although its accuracy and diagnostic value have been questioned.[24-26] Subjective assessment of alpha angles was judged suboptimal in one study unless the observer was confident of a bone abnormality.[27] The alpha angle was first proposed on MRI scans, together with a pathological threshold value of 50° for both genders.[7] This measurement has been transferred to CT,[28] and different lateral radiographs.[29] Threshold values for lateral views of all three modalities are commonly defined as 50° or 55°.[7, 30] Recent studies of the alpha angle based on healthy populations indicate that these threshold values are set too low (Table IV). Higher threshold values of 62° for both males and females were proposed based on the 97.5 percentile estimated from 83 individuals with normal hips.[23] Also, an increased cut-off value of 60° rather than 55° was recently proposed, in order to reduce false-positive results and still maintain an acceptable sensitivity.[26] The results of the present study support the thought that threshold values often used in the literature seem to have been set too low for the lateral view. The alpha angle is also reported on the AP view,[11, 13] although the validity on this view is debated. A Danish study suggested gender-specific threshold values of ≥83° and ≥57° for males and females, respectively.[13] The reference intervals for the AP view in the present study are wide, and suggest that the existing threshold values are set too low, especially in females. The anatomy of the femoral head-neck junction ranges from normal variants through borderline cases to pronounced pathology. An aspheric head-neck junction does not necessarily indicate a positive diagnosis of FAI, and a large part of subjects with radiographic cam-type FAI seems to be asymptomatic.[12]

In the present study, higher alpha angles were associated with the presence of qualitative cam-type findings on both views. We believe that it is beneficial to assess both quantitative and qualitative cam-type findings, as radiographic diagnostic criteria for cam-type FAI are not entirely agreed upon. The alpha angle is proposed for several radiographic views [29]. The frog-leg view is commonly preferred to the AP view,[3] although its accuracy in the diagnosis of the cam deformity has been questioned.[32] However, both views should be assessed if available as they visualise different parts of the femoral head-neck junction (Fig. 3). A standardised

radiographic protocol is necessary. Some authors believe that radiographs are not accurate enough for detecting the cam deformity compared to CT and MRI scans.[33] As emphasised by others, the establishment of diagnostic criteria for FAI and even new sets of measurements or methods are needed.[34, 35]

The intra- and inter-observer and inter-method variability results for the alpha angle show overall good values as demonstrated by the 95% limits of agreement and ICC values. The radiological assessment should always be interpreted in the light of the corresponding clinical information, including the presence of hip pain, restricted hip range of motion and a positive anterior impingement test.[12] In daily clinical practice, values close to threshold values must also be interpreted in the light of the variability of the alpha angle. Knowledge of how the different radiographic views visualise the cam deformity is equally important. This cross-sectional study presents wide reference intervals with higher mean alpha values in males than females on both views. The reference intervals are wider for the AP view. Higher alpha angles are associated with qualitative cam-type findings on both views.

Conflict of interest:

The authors have no conflicts of interest to declare. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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FIGURES

Fig. 1a

The alpha angle (α) quantifies the cam deformity on the frog-leg lateral view. The longitudinal axis of the femoral neck is defined, through its narrowest point and through the head centre. The alpha-point is placed where the radius (r) of the curvature of the femoral head first exits the circle of best fit corresponding to a circular head. A straight line is drawn from the alpha-point to the head centre, and this line, together with the longitudinal axis of the neck defines the alpha angle.

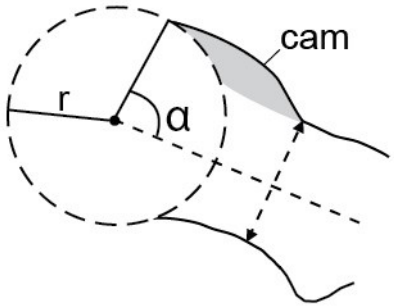

Fig. 1b

The alpha angle (α) on the AP view is measured using the same method as for the frog-leg view.

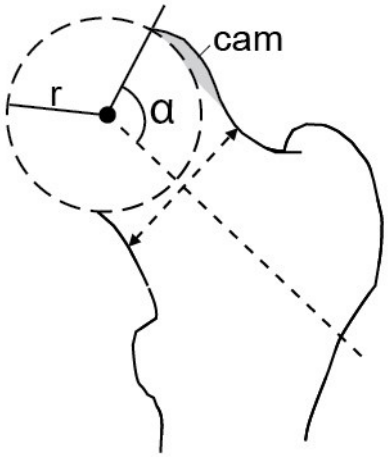

Fig. 2 Flow of participants in the study

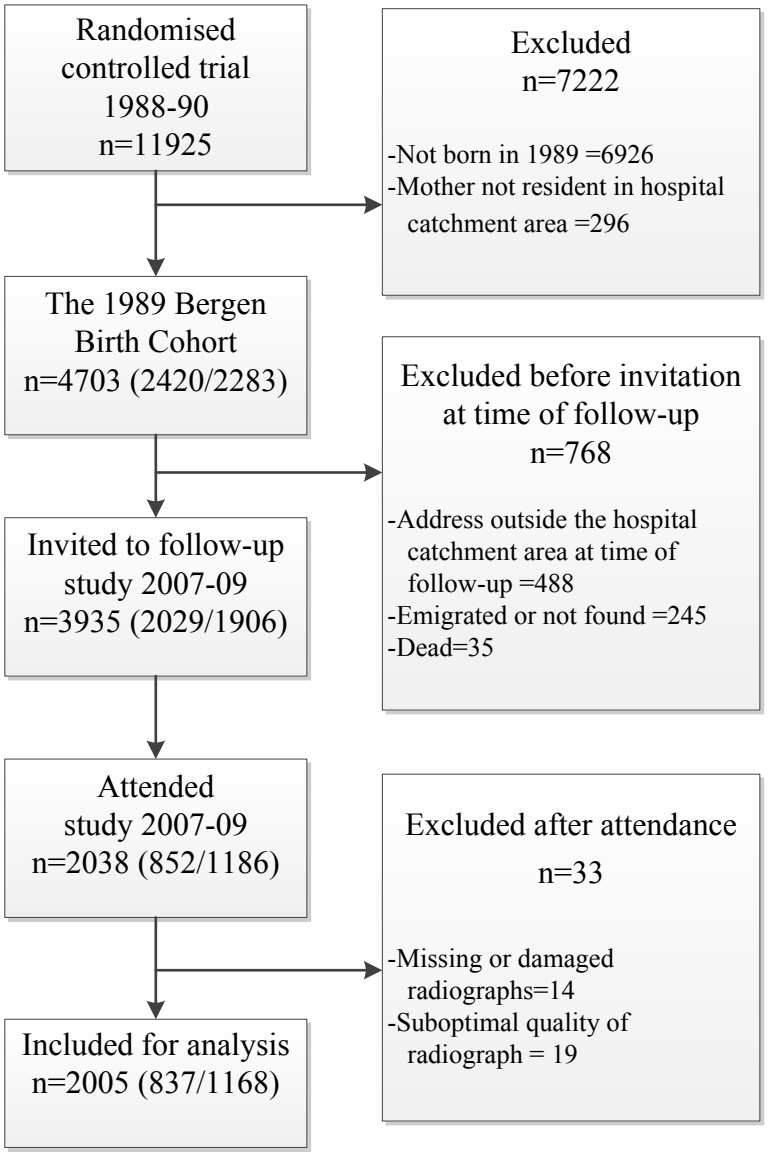

Fig. 3a
The cam-deformity is assessed by the alpha angle on the anterosuperior part of the head-neck junction on a frog-leg lateral view at 19 years of age. The measurement lines have been modified from the measurement program.

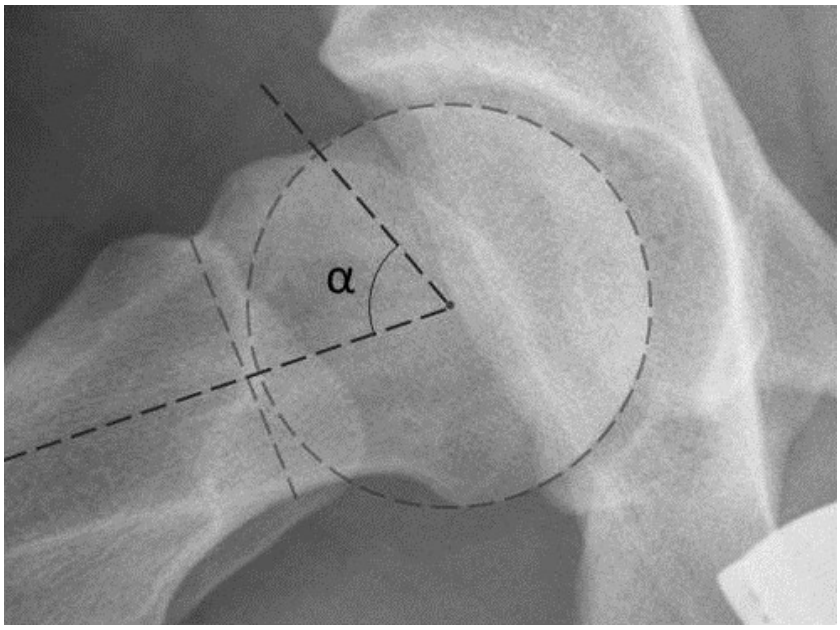

Fig. 3b
The cam-deformity is assessed by the alpha angle on the superior part of the head-neck junction on an anteroposterior (AP) view at 19 years of age. The measurement lines have been modified from the measurement program.

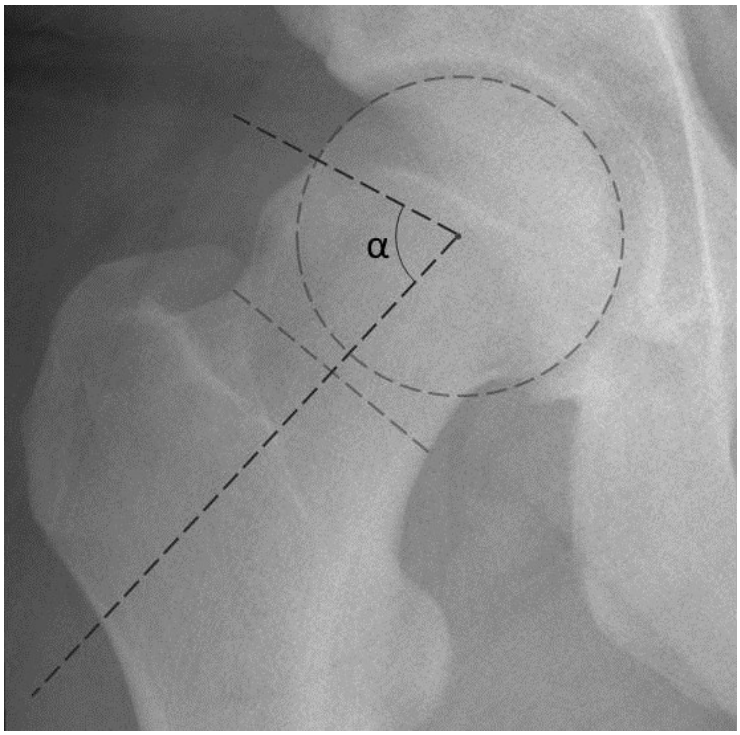

Table I: Gender-specific reference values (°) for the alpha angle measured on the frog-leg and the AP view, in 837 males and 1168 females aged 18-20 years, for right(R) and left (L) hip. Data are presented as mean, standard deviation (SD) and range, with corresponding reference intervals based on 2.5 and 97.5 percentiles with 95% confidence intervals (CI) for each of the percentiles.

	Side	n*	Mean (°)	SD (°)	Range (°)	2.5 percentile (95% CI)	97.5 percentile (95% CI)
Frog-leg view							
Males	R	831	46.9	8.4	26.2-78.9	35.1 (33.7-36.0)	68.4 (66.1-70.9))
	L	829	45.9	7.7	30.5-80.4	35.1 (34.5-35.7)	66.9 (64.5-69.2)
Females	R	1168	42.3	5.7	29.3-75.6	33.8 (33.4-34.2)	56.4 (54.7-58.7)
	L	1168	41.6	5.4	21.0-66.8	33.3 (32.8-33.7)	54.4 (53.1-56.5)
Anteroposterior view							
Males	R	834	61.6	14.2	39.7-105.2	43.2 (42.3-43.7)	92.7 (90.8-93.5)
	L	834	60.6	12.4	38.6-95.8	43.7 (43.0-44.4)	89.1 (85.7-91.5)
Females	R	1168	51.9	14.1	36.4-103.4	39.3 (38.9-39.6)	93.7 (92.0-95.6)
	L	1168	50.7	11.4	37.0-102.3	39.4 (39.7-40.4)	87.6 (84.2-90.9)

*In subjects where radiation shields covered important anatomical landmarks on one side, only the contralateral side was included for analyses.

Table II: Associations between the alpha angle (°) and the three qualitative radiographic cam-type findings on the frog-leg view and the AP view respectively. Results of random effects models, adjusted by sex and side, are shown for 2005 participants. The coefficient indicates how many degrees higher the mean alpha angle is for the group with a positive subjective cam-type finding, compared to the group without subjective findings.

	Alpha angle (°) on frog-leg view			Alpha angle (°) on AP view		
Subjective assessment	Coefficient	95% CI	p-value	Coefficient	95% CI	p-value
Pistol grip deformity	15.3	13.7-16.8	<0.0001	11.4	9.8-13.0	<0.0001
Focal femoral hump	6.5	5.5-7.6	<0.0001	10.0	6.2-13.7	<0.0001
Flattened lateral head	3.7	2.9-4.5	<0.0001	10.1	8.5-11.8	<0.0001

Table III Reproducibility studies for alpha angle measurements on the frog-leg and the AP view. Results are presented for the left hip.

	First mean	Second mean	Mean difference (SD)	95% limits of agreement	ICC
Frog-leg view					
Intra-observer (A) Digital 1- Digital 2	46.58	46.51	0.07 (2.68)	(-5.30;5.44)	0.95 (0.93; 0.97)
Inter-method (A) Digital 1 - Manual 1	46.54	47.33	-0.77 (2.35)	(-6.70;5.15)	0.94 (0.92; 0.96)
Intra-observer (A) Manual 1- Manual 2	47.16	47.50	-0.33 (1.90)	(-4.13;3.46)	0.97 (0.96; 0.98)
Inter-observer (A+B) Digital A 2 - Digital B 1	46.51	44.81	1.70 (2.73)	(-3.76;7.16)	0.92 (0.89; 0.95)
Anteroposterior view					
Intra-observer (A) Digital 1- Digital 2	58.03	57.60	0.43 (3.22)	(-6.01;6.86)	0.96 (0.95; 0.98)
Inter-method (A) Digital - Manual	57.81	57.73	0.08 (3.18)	(-8.53;7.76)	0.95 (0.93; 0.96)
Intra-observer (A) Manual 1- Manual 2	57.52	57.94	-0.42 (3.29)	(-6.99;6.16)	0.96 (0.94; 0.98)
Inter-observer (A+B) Digital A 2 - Digital B 1	57.60	55.52	2.08 (5.13)	(-8.16;12.34)	0.89 (0.85; 0.93)

Observer A (LBL), Observer B (KR), 1: first reading, 2: repeated reading, SD standard deviation

Table IV

Mean, standard deviation (SD) and/or range for the alpha angle on different radiographic views, as published in the literature

Author, year	Population	View	Mean (SD)	Range	P-value Gender difference
Pollard et al,[23] 2010	83 healthy adults with normal hip (43 males, 44 females, mean age 46 (22-69) years)	Cross-table lateral, 15° internal rotation	Males: 48° (±8°) Females: 47° (±8°)		NA
Toogood et al,[31] 2009	375 normal femora of adult skeletons (188 males, 187 females, mean age 44 (18-89) years)	Pelvic AP and a lateral view	AP (named gamma): 53.46° (±12.68°), Lateral (named alpha): 45.61° (±10.46°) Males lateral: 47.50° (±10.71°) Females lateral: 43.71° (±9.88°)	AP: 31.21°-111.50° Lateral: 16.87°-78.57°	<0.01 (lateral view)
Clohisy et al,[3] 2007	24 normal subjects (24 hips, mean age 35 (18-49) years), 46% females	Frog-leg lateral, cross-table lateral, and AP	Frog-leg: 43.7° (±12.1°), Cross-table lateral: 47.2° (±15.4°) AP:		NA

			51.2° (±15.7°),		
Gosvig et al,[13] 2007	2803 healthy adults (1055 males, mean age 62 (23-93) years, 1748 females, mean age 65 (22-92) years)	Pelvic weight-bearing AP radiographs (left hips)	Males AP: 53.1° (±13.9°) Females AP: 45.5° (±5.1°)	Males AP: 30.0-94.0 Females AP: 32.0-108.0	<0.0001
Laborie et al, 2013*	2005 healthy young adults (837 males, 1168 females, mean age 18.6 (17.2-20.1) years	Pelvic frog-leg lateral and weight-bearing AP (right hips)	Males frog-leg: 46.9° (±8.4°) Females frog-leg: 42.3° (±5.7°) Males AP: 61.6° (±14.2°) Females AP: 51.9° (±14.1°)	Males frog-leg: 26.2°-78.9° Females frog-leg: 29.3-75.6 Males AP: 39.7-105.2 Females AP: 36.4-103.4	<0.0001 (frog-leg) <0.0001 (AP)

*Present study. AP anteroposterior, OA Osteoarthritis, NA not available.

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