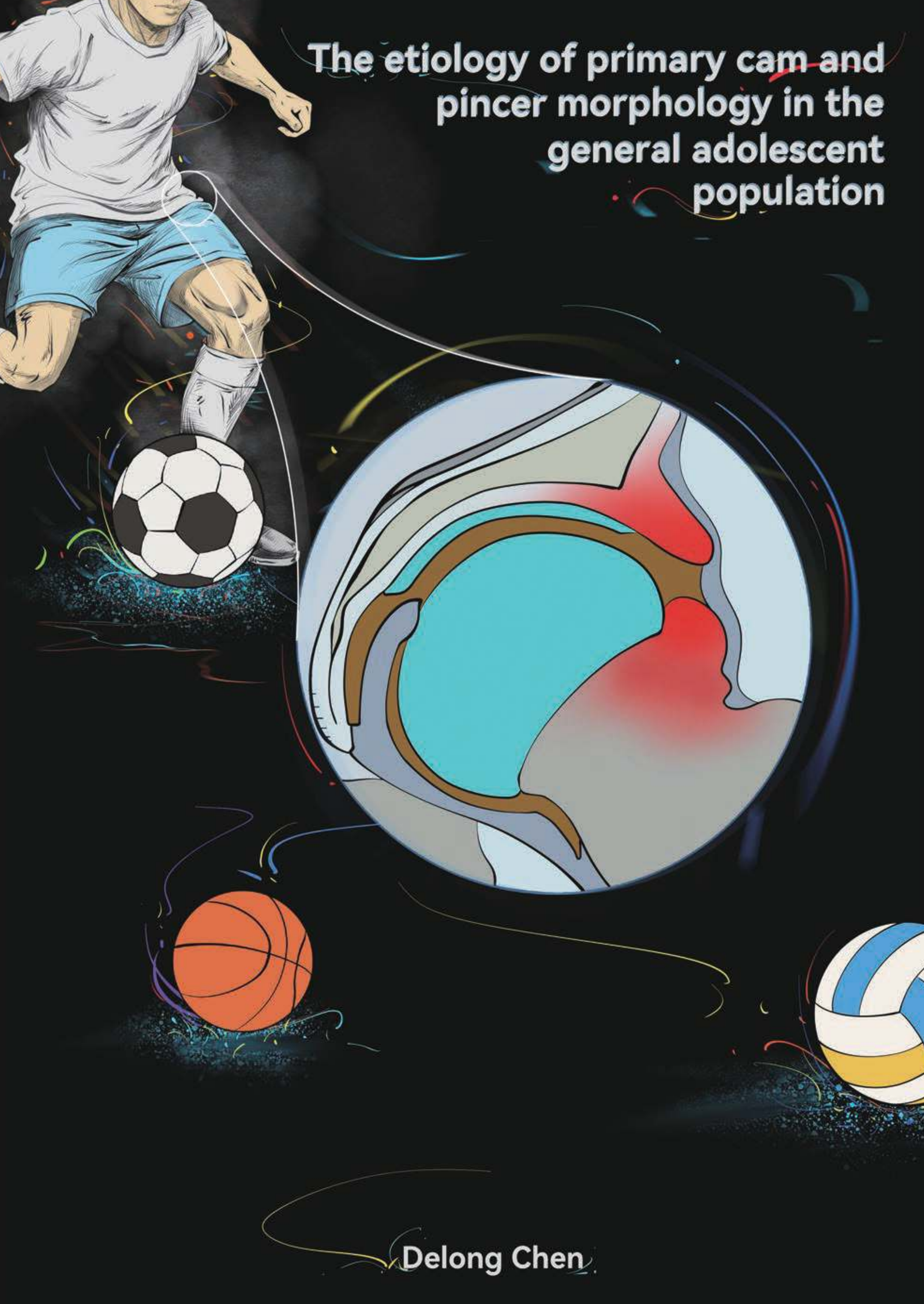
The etiology of primary cam and pincer morphology in the general adolescent population

Publication status and date:
Published: 16/04/2026

Document Version
Publisher's PDF, also known as Version of record

Citation for the published version (APA):
Chen, D. (2026). *The etiology of primary cam and pincer morphology in the general adolescent population*. [Doctoral Thesis, Erasmus University Rotterdam].

The etiology of primary cam and pincer morphology in the general adolescent population



Delong Chen

The Etiology of Primary Cam and Pincer Morphology in the General Adolescent Population

Delong Chen

Cover design: Delong Chen
Layout: Optima
Printing: Optima

Delong Chen was supported by a Chinese Scholarship Council (CSC) PhD Fellowship for his PhD study in Erasmus MC, University Medical Center Rotterdam, the Netherlands, grant number 202108430032.

The printing of this thesis was kindly supported by the Department of Orthopaedic Surgery and Sports Medicine at Erasmus MC, University Medical Center Rotterdam, The Netherlands; and Erasmus University Rotterdam.

The Etiology of Primary Cam and Pincer Morphology in the General Adolescent Population

De etiologie van primaire cam- en pincermorfologie in
de algemene adolescentenpopulatie

Thesis

to obtain the degree of Doctor from
Erasmus University Rotterdam
by command of the
rector magnificus

Prof.dr.ir. A.J. Schuit

and in accordance with the decision of the Doctorate Board.
The public defence shall be held on

Thursday 16 April 2026 at 10.30 hrs
by

Delong Chen
born in Guangdong, People's Republic of China.

Erasmus University Rotterdam

Doctoral Committee:

Promoter:	Prof.dr. S.M.A. Bierma-Zeinstra
Co-promoter:	Dr. R. Agricola
	Dr. F.D.E.M. Boel
Assessment committee:	Prof.dr. J. Harlaar
	Prof.dr. J.B.J. Van Meurs
	Prof.dr. J.L. Tol

Table of Contents

Chapter 1	General Introduction	7
Chapter 2	The prevalence of primary cam morphology in early adolescents from the general population: a population-based study (Generation R)	29
Chapter 3	The prevalence of pincer morphology in early adolescents from the general population: a population-based study (Generation R)	43
Chapter 4	Associated factors of primary cam morphology in 4,477 early adolescents: a multi-ethnic, population-based, cross-sectional study (Generation R)	57
Chapter 5	Associated factors of pincer morphology in 3,986 early adolescents: a multi-ethnic population-based study in the Netherlands (Generation R)	81
Chapter 6	Development of primary cam morphology and associated factors: a longitudinal population-based study (Generation R)	103
Chapter 7	General Discussion	127
Chapter 8	Summary/Samenvatting	147
Appendics	PhD portfolio	156
	Acknowledgments	157
	About the author	159
	List of publications	160

Chapter 1

General Introduction

1. THE HIP

The hip joint (**Figure 1**) is a ball-and-socket synovial joint, one of the most stable and deepest joints in the human body. It connects the femoral head (the "ball") to the acetabulum (the "socket") of the pelvis. This joint is critical for weight-bearing and movement, transferring the weight of the upper body to the lower limbs. The acetabulum is a cup-shaped structure formed by three bones: ilium, ischium and pubis. The ilium forms the superior portion of the acetabulum, accounting for 2/5 of its structure; the ischium constitutes the posterior and inferior parts, also making up 2/5 of the acetabulum; the pubis forms the anterior portion, contributing 1/5 of the acetabulum. A fibrocartilage labrum surrounds the periphery of the acetabulum, deepening the socket and improving hip stability.

The proximal femur consists of the femoral head, femoral neck and greater and lesser trochanters. The femoral head is a spherical structure that articulates with the acetabulum of the pelvis to form the hip joint. Most of its surface is covered by hyaline cartilage, allowing smooth movement. A small depression, the fovea capitis, located medially on the femoral head, serves as the attachment site for the round ligament, which contributes to joint stability and vascular supply. Positioned superolaterally at the base of the femoral neck, the greater trochanter serves as an attachment site for several muscles. The gluteus medius inserts on its lateral surface, the gluteus minimus inserts on its anterior surface, and piriformis and obturator internus insert on its superior aspect. Located posteromedially on the proximal femur, the lesser trochanter serves as the insertion point for the iliopsoas muscle. The hip joint allows a wide range of motion, including flexion, extension, abduction, adduction, and internal and external rotation. This mobility is facilitated by surrounding muscles and stabilized by three primary fibrous ligaments. The iliofemoral ligament prevents hyperextension, the ischiofemoral ligament reinforces posterior stability, and the pubofemoral ligament limits excessive abduction and extension. These ligaments, along with the surrounding muscles, ensure both stability and flexibility of the hip joint during movement.

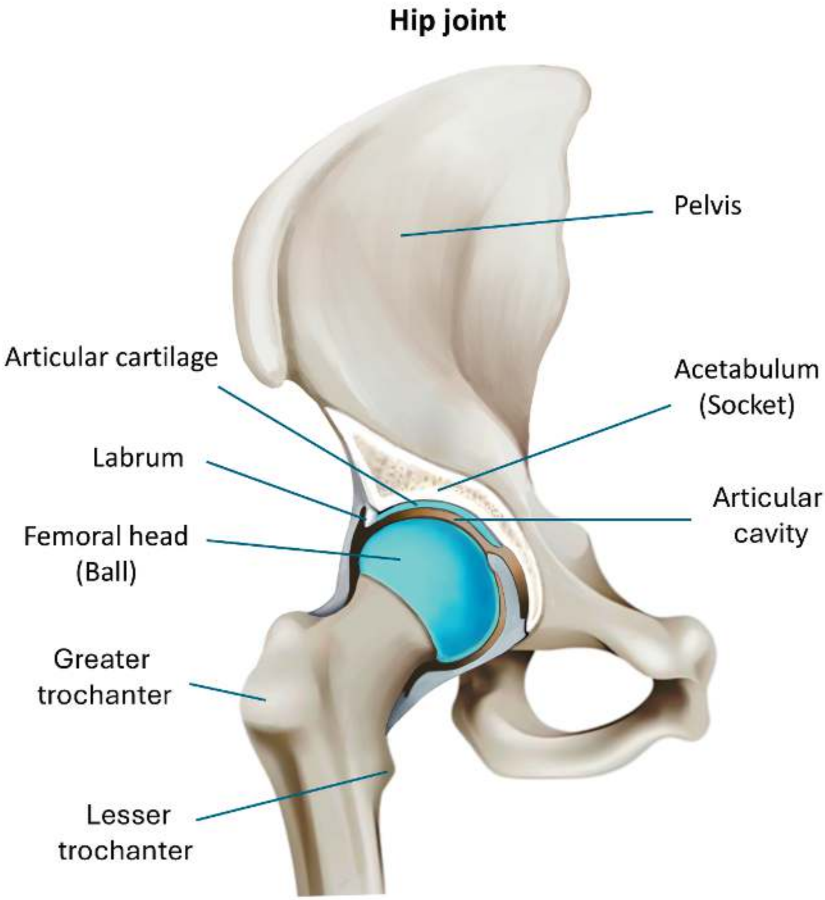


Figure 1. Structural diagram of the hip joint.

2. DEVELOPMENT OF THE HIP

The development of the acetabulum is a complex process involving three primary bones: the os pubis, os ilium, and os ischium. These bones are initially separated by hyaline cartilage and converge at a Y-shaped cartilage structure, known as the triradiate cartilage complex (**Figure 2**). During puberty, three secondary ossification centers appear within the triradiate cartilage, which contributes to the shape of the acetabulum. The secondary ossification center of the os pubis, sometimes referred to as the os acetabuli, forms the anterior wall of the acetabulum. The secondary ossification center of the os ilium and os ischium forms the superior and posterior wall of the acetabulum, respectively. Eventually, the triradiate cartilage fuses and forms the medial wall of the acetabulum. The triradiate cartilage closes at approximately 12 years of age in girls and

14 years in boys [1]. After the closure of the triradiate cartilage, the secondary ossification center of the os pubis continues to develop, which can potentially enhance the coverage of the acetabulum rim.

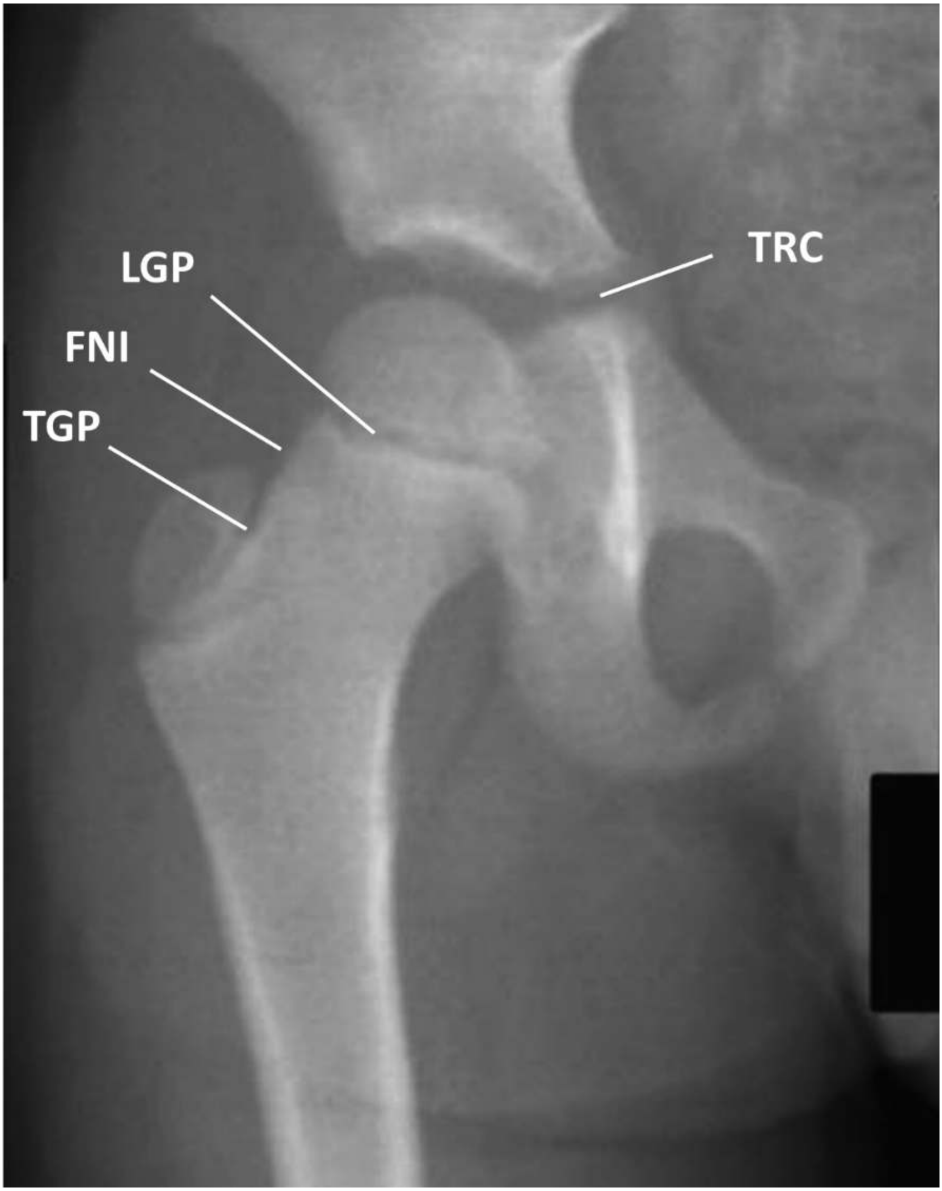


Figure 2. Growth plates of the proximal femur and the acetabulum on a dual-energy x-ray absorptiometry (DXA) image of the right hip in a 6-year-old child. TRC: triradiate cartilage; LGP: longitudinal growth plate; FNI: femoral neck isthmus; TGP: trochanteric growth plate.

The development of the proximal femur involves three critical growth plates that collectively determine its final shape and structure: longitudinal growth plate (LGP), trochanteric growth plate (TGP) and femoral neck isthmus (FNI) (**Figure 2**). The LGP is located at the femoral head-neck junction and is primarily responsible for the longitudinal growth of the femur. As children grow, the LGP gradually changes morphological shape. In younger children (ages 3 to 7 years), it appears as a horizontal or slightly irregular (corrugated) line. By the ages of 8 to 10 years, it begins to take on an arched shape. In older children (ages 11 to 13 years), it becomes a thin, arc-shaped convex line [2]. During skeletal maturation, growth plates dynamically adapt to mechanical loadings applied to the hip, potentially leading to changes in the shape and orientation of growth plates.

3. HIP OSTEOARTHRITIS (OA)

OA is the most common form of arthritis and a leading cause of chronic pain and disability worldwide [3, 4]. It is a multifactorial, degenerative joint disease characterized by the breakdown of cartilage and other joint tissues, which leads to pain, stiffness, swelling, and reduced mobility. OA most frequently affects hands and weight-bearing joints such as the knees, hips, and spine [3].

As populations age and obesity rates increase, the prevalence and burden of OA are expected to rise, posing growing challenges to individuals, healthcare systems, and societies worldwide [3, 5]. In 2020, an estimated 595 million people worldwide had osteoarthritis, representing 7.6% of the global population. This number is projected to rise significantly, with hip OA cases expected to increase by 78.6% by 2050 [6]. An Australian study found that the national healthcare costs related to OA were estimated to be over $2.1 billion (0.16% of $1,351 billion gross domestic product) in 2015 and are projected to exceed $2.9 billion by 2030 [7].

The treatments for OA, including medications, physical therapy, and surgical interventions like joint replacements, represent a substantial economic burden. Joint replacement surgeries, in particular, are costly procedures that are projected to increase significantly in the future [8, 9]. There are no disease-modifying therapies available for OA, therefore, current treatments focus on symptom management rather than halting or reversing disease progression. By targeting modifiable risk factors early and implementing evidence-based prevention strategies, we could reduce the prevalence of OA, improve population health outcomes, and alleviate healthcare costs over time.

The knee and hip joints are the most common sites of involvement in OA-related disability [10]. The development of hip OA results from a complex interplay of genetic, environmental, and lifestyle factors [3]. Several risk factors have been identified for the development of hip OA, including age, sex, genetics, high occupational loading, trauma and altered hip morphologies [11, 12]. Understanding the etiology of modifiable risk factors is essential for developing primary prevention strategies of hip OA.

4. FEMOROACETABULAR IMPINGEMENT SYNDROME

Femoroacetabular impingement (FAI) is a mechanical process in which anatomical abnormalities of the femoral head (ball of the hip) and/or acetabulum (hip joint socket) lead to repetitive, premature contact during hip motion. This abnormal contact generates excessive stress on the hip joint, particularly during movements like flexion and internal rotation, which may damage the labrum and cartilage over time. In 1965, Murray provided the first description of femoral morphology leading to hip osteoarthritis. Murray identified tilt deformities of the proximal femur, deformities of slipped capital femoral epiphysis (SCFE), and Perthes deformity as potential causes of hip osteoarthritis [13]. In the 1980s, Harris described the pistol grip deformity, which further advanced the understanding of femoral deformities associated with FAI [14]. Based on these earlier findings, Ganz and his colleagues significantly contributed to our understanding of FAI in the early 2000s. In 2003, Ganz et al. identified FAI as a pathological condition caused by abnormal contact between the femoral head and acetabulum, leading to joint damage and hip osteoarthritis [15]. They described two distinct types of FAI based on the pattern of chondral and labral lesions observed during surgical dislocation of the hip: cam and pincer impingement. Since the publication of Ganz's landmark paper, there has been an exponential rise in FAI-related research and literature. The concept of FAI as a cause of hip pain and early osteoarthritis has gained widespread acceptance in the orthopedic community, leading to significant advancements in the diagnosis and treatment of this condition.

When more and more research was performed, numerous terminologies have been used to describe FAI, such as "radiological FAI", "FAI morphology", "asymptomatic FAI" and "deformity or lesion", which caused confusion in both research and clinical practice. More importantly, many individuals exhibit cam and/or pincer morphology on imaging but do not experience any symptoms or complaints. This recognition highlighted the need to distinguish between morphological findings and clinically relevant diseases. To address these concerns, an international consensus statement involving 22 panel members from 9 countries (the Warwick Agreement in 2016) has provided uniform terminology, diagnosis and treatment principles relating to FAI syndrome [16]. It was agreed upon that FAI syndrome is "a motion-related clinical disorder of the hip with a triad of symptoms, clinical signs and imaging findings. It represents symptomatic premature contact between the proximal femur and the acetabulum". Two types of morphological variants of FAI syndrome include cam and pincer morphology **(Figure 3)**. As described in the statement, the diagnosis of FAI syndrome is not only dependent on imaging findings, but also on symptoms and clinical signs. Three elements must be present to diagnose FAI syndrome.

1. Symptoms. The main symptom of FAI syndrome is motion-related or position-related pain, which is typically described as a deep pain in the groin or hip. Patients often use the "C sign" to indicate the location of their discomfort, grasping the hip with their hand to demonstrate anterior and posterior pain. However, pain may also be perceived in the knee, thigh, buttock or back. In addition to pain, other sensations and symptoms associated with FAI syndrome include clicking, catching, locking, stiffness, restricted range of motion or giving way.
2. Clinical signs. When FAI syndrome is suspected in patients, physical examination, including gait, single leg control, muscle tenderness and hip range of motion, should be performed. The flexion adduction internal rotation (FADIR) test is widely used to evaluate FAI syndrome, which is sensitive but not specific. This means that the FADIR test is often positive in patients with FAI syndrome, but it can also be positive in patients with other hip conditions rather than FAI syndrome.
3. Imaging findings. Cam and pincer morphologies can be evaluated through radiographs and three-dimensional imaging, such as computed tomography (CT) and magnetic resonance imaging (MRI). It is suggested that the first imaging method should be with anteroposterior (AP) pelvis and lateral hip radiographs. As a further assessment, cross-sectional imaging is frequently utilized to develop an in-depth understanding of hip morphology and associated cartilage and labral lesions.

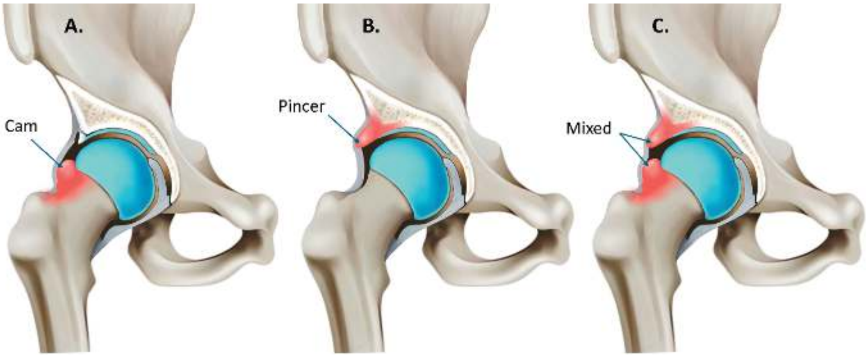


Figure 3. Different morphological variations of femoroacetabular impingement syndrome. A. Cam morphology. B. Pincer morphology. C. Mixed morphology.

5. PRIMARY CAM MORPHOLOGY

5.1 Definition

Cam morphology is characterized by a cartilage or bony prominence that alters the shape of the femoral head from spherical to aspherical. This prominence is usually located at the anterosuperior region of the femoral head-neck junction. Cam morphology can be classified as primary cam morphology (PCM) and secondary cam morphology. PCM develops during skeletal maturation as an adaptive response to mechanical loading. Secondary cam morphology arises due to existing conditions like SCFE, Legg-Calvé-Perthes disease, or post-traumatic deformities.

5.2 PCM measurement

PCM can be assessed using different measurement methods, including alpha angle [degrees], triangular index (TI) sign, femoral head-neck offset measure [mm], femoral head-neck offset ratio, and femoroacetabular excursion angle (beta angle). These measurements can be performed on dual-energy X-ray absorptiometry (DXA), radiographs, CT scans, and MRI, and reported as continuous and/or dichotomous outcomes based on specific thresholds. Each imaging modality determines the location where PCM is measured: AP pelvis and Dunn 45° radiographs measure PCM at the lateral and anterolateral aspect of the femoral head-neck junction, respectively, while three-dimensional imaging modalities (CT scans and MRI) enable measurement at multiple locations around the femoral head-neck junction.

The alpha angle (**Figure 4**) is one of the most common measures to define PCM on various imaging modalities and views. To date, the cut-off value of the alpha angle used to identify PCM varies widely across studies, ranging from 50° to 83°. Despite this variability, the most recent evidence, particularly from a systematic review [17], the Lisbon

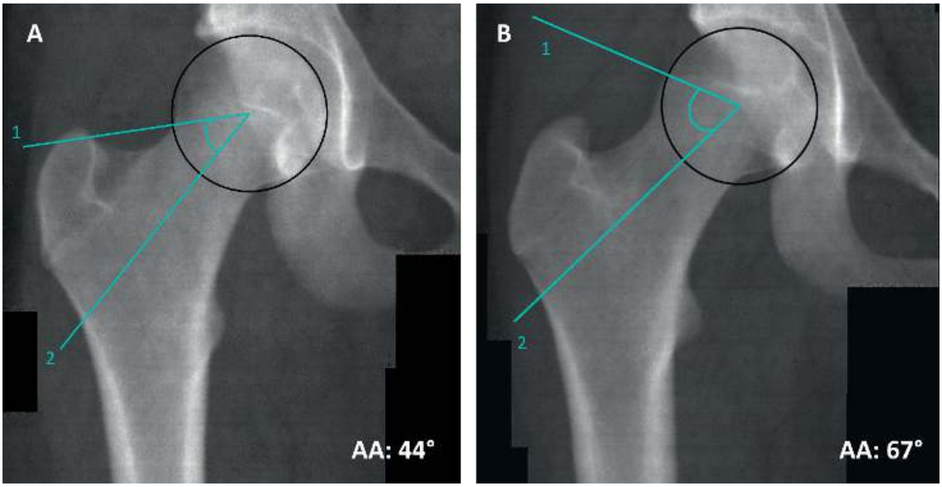


Figure 4. Measurement of the alpha angle (AA) on a dual-energy x-ray absorptiometry (DXA) image of the right hip. The alpha angle is formed between the intersection of two lines. The first line connects the center of the best-fitting circle around the femoral head to the point where the femoral head first departs from the margin of the best-fitting circle, and the second line connects the center of the best-fitting circle to the center of the femoral neck. (A). The alpha angle of 44° is shown, indicating a spherical femoral head. (B). The alpha angle of 67° is shown, indicating a primary cam morphology.

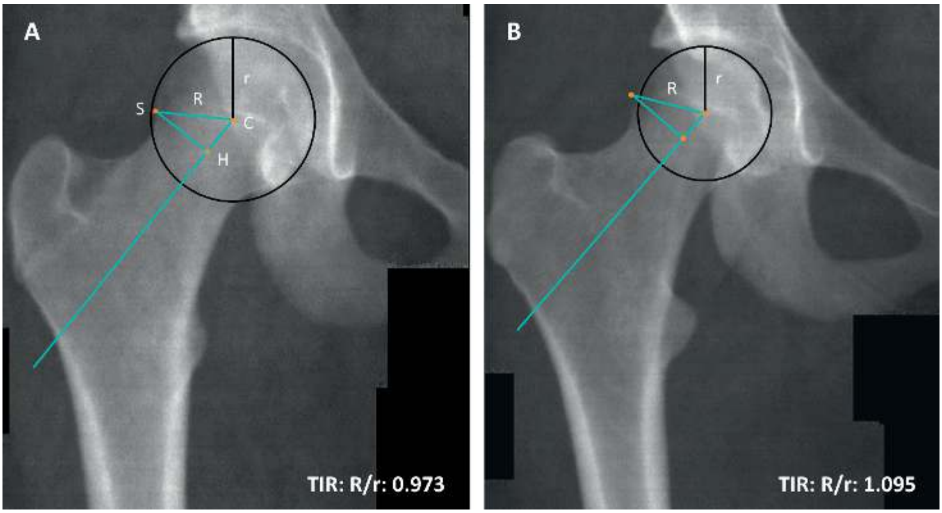


Figure 5. Measurement of the triangular index ratio (TIR) on a dual-energy x-ray absorptiometry (DXA) image of the right hip. (A). The center of the femoral head (point C) and the radius are determined by the best-fitting circle around the femoral head. From the midpoint of the radius (point H), a perpendicular line is generated to the superolateral cortex of the femoral head-neck junction (point S). The TIR of 0.973 in this sample is the ratio of the length of R from point S to point C and the length of r, the radius of the best-fitting circle, and represents a spherical femoral head. (B). A right hip with a TIR of 1.095, which represents a primary cam morphology.

agreement [18], the Oxford consensus [19], and a large cohort study reporting a bimodal distribution of alpha angles [20], supports the use of an alpha angle threshold of ≥ 60°.

Unlike the alpha angle, the triangular index ratio (TIR) assesses the lateral extension of the bone at a fixed point defined by half the radius of the femoral head along the axis of the femoral neck (**Figure 5**). The TIR [21] was derived from the TI [22] that was initially described by Gosvig et al. who defined PCM by a pathologically increased radius (R) ≥ natural radius (r) + 2 mm on an AP radiograph with 1.2 magnification in White adults. We converted the previously proposed TI threshold into a TIR threshold of ≥ 1.05 to define PCM. Combining alpha angle and TIR may allow for a more comprehensive evaluation of PCM on the AP view of the hip.

5.3 Prevalence and associated factors of PCM

5.3.1 Age and skeletal growth

To date, the knowledge on the age of onset of PCM in the general population is limited. Agricola et al. reported that osseous PCM was first identified on radiographs between the ages of 12 and 13 years in a cohort of 89 male elite soccer players [23]. In the same prospective cohort, it was shown that PCM develops gradually in size during adolescence until femoral head growth plate closure [24]. The finding that osseous PCM first appears between 12 and 13 years of age was confirmed by another cross-sectional study in male soccer players [25]. Interestingly, this study showed that soft tissue hypertrophy around the femoral head growth plate, where PCM normally develops, is already visible on MRI as early as 10 years old [25].

5.3.2 Sex

In the adult general population, the prevalence of PCM varies across studies, ranging from 15% to 35% in males and 2% to 10% in females.

In the Johnston County Osteoarthritis Project, Raveendran et al. included 2,596 individuals (mean age 63 years; 43% male) and used the AP pelvic radiograph to define PCM as alpha angle > 60° or the presence of triangular index sign (R ≥ r + 2mm). The prevalence of PCM was 25% in males and 10% in females [26]. In the Copenhagen osteoarthritis study, Gosvig et al. performed a cross-sectional study of 3,620 individuals (mean age 60 years; 37% male) and reported a prevalence of PCM of 19.6% in males and 5.2% in females, defined by the presence of triangular index sign (R ≥ r + 2mm) on the AP pelvic radiograph [27]. In the UK Biobank, Faber et al., in a cross-sectional study of 6,807 individuals (50% male) with a mean age of 63 years, reported a prevalence of PCM of 15.4% in males and 1.8% females using DXA scans of the left hip based on an alpha angle ≥ 60° [28].

In healthy young adults, PCM also has a male predilection. A Norwegian population-based cohort involving 2,081 participants (42% male) aged 17.2 to 20.1 years used AP pelvic radiographs to evaluate PCM as defined by the presence of pistol-grip deformity, focal prominence or flattening of the femoral head-neck junction and found a prevalence of 35% in males and 10.2% in females [29].

5.3.3 Ethnicity

In the general population, a large multi-ethnic cross-sectional study evaluated hip morphology by left hip DXA scans between 39,826 participants (mean age 63.7 years; 47.9% male) from the UK Biobank and 5,924 participants (mean age 63.4 years; 42.3% male) from the Shanghai Changfeng (SC) cohort [30]. PCM (alpha angle ≥ 60°) was more common in White UK Biobank males compared to Chinese SC males (16.5% vs. 6.3%). PCM was rarely observed in females of both populations, with a slightly higher prevalence in White UK Biobank females (1.5%) compared to Chinese SC females (0.9%). Similarly, a cross-sectional study involving 445 adult male soccer players assessed the prevalence of PCM among ethnic groups on the Dunn view radiograph [31]. East Asian players exhibited a notably lower prevalence (18.8%) of PCM defined by alpha angle > 60° compared to other groups including Arabic, Black, Persian, and White players, where the prevalence ranged from 57.5% to 71.7%.

5.3.4 Sport types

In adults, PCM is more prevalent among male athletes involved in high-impact sports, ranging from 55% to 90% in soccer [31-34], basketball [35], ice hockey [36-38], and American football [39]. Moreover, the development of PCM may be associated with certain types of sports and loading patterns. Philippon et al. found that male ice hockey players were 4.5 times more likely to develop PCM compared to skiers [38]. A longitudinal study involving 317 young participants (mean age 17.5 years; 53% male) examined the association between sport types and the development of PCM in the Iowa Bone Development Study [40]. Based on relative peak strain and ground reaction forces, sports were divided into power sports (basketball, cheerleading, football, gymnastics, soccer, and volleyball) and non-power sports (wrestling, baseball, cross-country or track and field, softball, or tennis). Power sport athletes had 2.93 times (95% confidence interval [CI], 1.04 – 8.27) higher odds of developing PCM within 6 years compared to non-athletes. However, no difference was observed between non-power sport athletes and non-athletes. The systematic review [41] by Doran et al. examined the prevalence of PCM among athletes across different sports and divided sports into six groups based on the mechanical loading on the hip: Cutting (Soccer and Basketball), Flexibility (Dance and Mixed martial arts), Contact (American football and Rugby), Impingement (Ice hockey, Rowing, Baseball catcher and Breaststroke swimming), Asymmetric (Baseball, Golf and Volleyball) and Endurance

(Track and field and Swimming) sports. They found that impingement (ice hockey), cutting (soccer, basketball) and contact (American football) sport types are associated with a higher prevalence of PCM. These sports involve frequent flexion and rotational movements of the hip, which were reported to stimulate bone formation at the femoral head-neck junction [42].

5.3.5 Physical activity levels

A dose-response relationship exists between the frequency of sports practice during adolescence and the development of PCM. A retrospective study of 63 adult male soccer players suggested that soccer players are at higher risk of developing PCM when they practiced soccer 4 or more times per week before age 12 years [43]. In a cross-sectional study involving 210 participants (103 male soccer players and 107 male and female controls) aged 9 to 18 years, Palmer et al. found that participants who played sports at a school or club level and at a national or international level had alpha angles of 4° and 7.7° greater than those who did not play sports [25]. Fernquest et al. followed up with the participants over three years and used the Physical Activity Questionnaire (PAQ) to assess physical activity levels from 1 (low) to 5 (high). Their findings indicated participants with a PAQ score between 3 and 4 and between 4 and 5 had an average change in alpha angle of 0.58° and 3.20° greater, respectively, than those with a PAQ score less than 2 [44].

5.3.6 Body mass index (BMI)

There is variation in the reported relationship between body weight and alpha angle in the literature, seemingly depending on the study population. Novais et al. reported that a higher BMI percentile was associated with higher alpha angles in a retrospective cross-sectional study based on pelvic CT from 128 adolescents aged 12 to 18 years without hip complaints [45]. However, other cross-sectional and longitudinal studies in adolescent elite male soccer players found no association between BMI and higher alpha angles [25, 44].

5.3.7 Radiographic parameters

Some specific radiographic parameters may be associated with PCM, such as epiphyseal extension (EE) and neck shaft angle (NSA) (**Figure 6**). A meta-analysis demonstrated lateral EE was strongly associated with higher alpha angles, with a pooled correlation coefficient of 0.68 (95% CI 0.63 – 0.73) [46]. Fernquest et al. observed a weak but positive association between changes in lateral EE and changes in the alpha angle over three years in adolescent participants [44]. However, in a 5-year follow-up of male soccer players, Van Klij et al. found that higher lateral EE and lower NSA were cross-sectionally associated with PCM but did not precede its development [47].

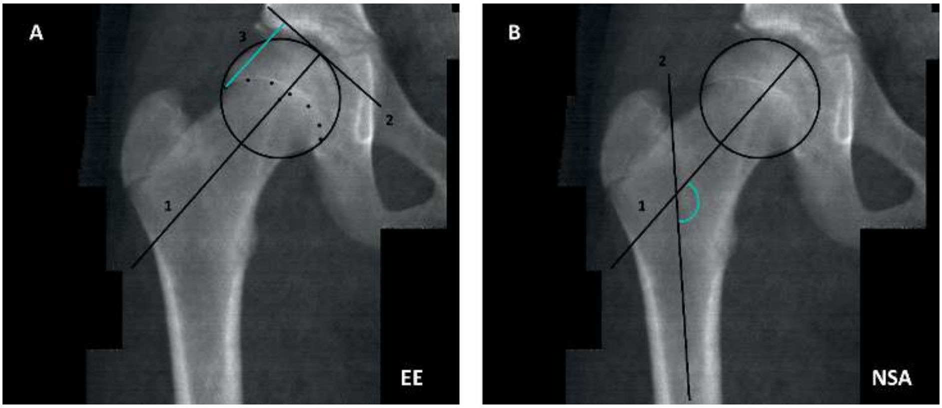


Figure 6. Measurement of lateral epiphyseal extension (EE) and neck shaft angle (NSA) on a dual-energy x-ray absorptiometry (DXA) image of the right hip. (A). The lateral EE is the ratio of the length of line 3 and the length of the femoral head radius. First, a perpendicular line (line 2) is generated from the femoral neck axis (line 1) to tangent the best-fitting circle. Line 3 is generated perpendicularly from line 2 to the lateral endpoint of the femoral head growth plate. (B). The NSA is the angle between line 1, the femoral neck axis, and line 2, the femoral shaft axis.

5.4 PCM and hip OA

PCM can lead to intra-articular damage [48,49] when repetitively forced into the acetabulum during hip motion, predisposing some individuals to FAI syndrome, and eventually to the development of hip OA. Multiple prospective cohort studies [21,50,51] have consistently demonstrated a strong association between PCM and the development of radiographic hip osteoarthritis (RHOA), with reported odds ratios (OR) ranging from 2.11 (95% CI 1.55 – 2.87) to 9.66 (95% CI 4.72 – 19.78). The OR value is influenced by the threshold of the alpha angle; specifically, a larger alpha angle corresponds to a more pronounced PCM and an increased risk of RHOA. These findings highlight the importance of potential preventive strategies in individuals with PCM to reduce the risk of developing FAI syndrome and hip OA.

6. PINCER MORPHOLOGY

6.1 Definition

Pincer morphology is characterized by acetabular overcoverage of the femoral head, which can be either focal or global. Focal pincer morphology typically results from acetabular retroversion, where the acetabulum is rotated backward. This condition is assessed using specific radiographic signs, such as the crossover sign, the posterior wall sign and the ischial spine sign. Global pincer morphology involves a generalized deepening of the acetabulum, affecting both anterior and posterior rims. It can be identified by coxa profunda, protrusio acetabuli, and quantitative measures such as the lateral center edge angle (LCEA) and the modified acetabular index. However, the crossover sign, the posterior wall sign and coxa profunda were reported to have poor reliability and specificity to define pincer morphology [52-54]. This thesis focuses on global pincer morphology.

6.2 Pincer morphology measurement

The LCEA (**Figure 7**) is one of the most commonly used, objective measurements to define pincer morphology, which quantifies the degree of acetabular bony coverage of the femoral head. Pincer morphology was defined as a LCEA threshold ≥ 39° [55, 56] or 40° [21, 51, 57, 58], while some studies used a higher LCEA threshold of ≥ 45° for pincer morphology [27, 28].

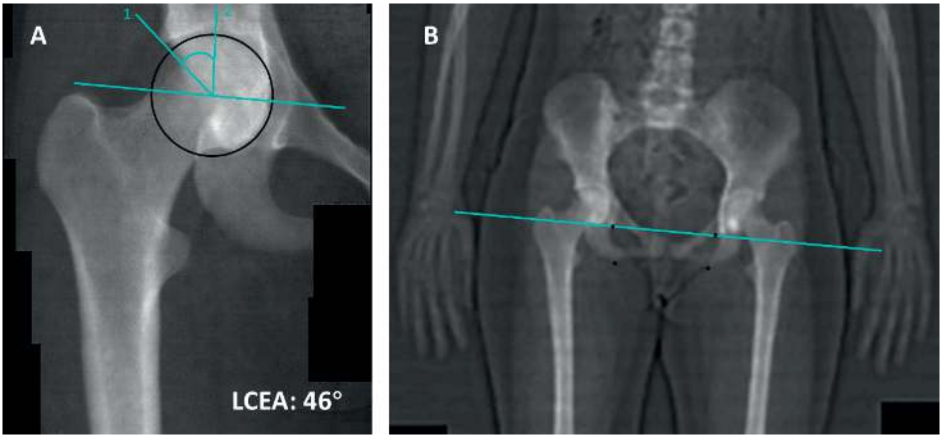


Figure 7. Measurement of lateral center edge angle (LCEA) on a dual-energy x-ray absorptiometry (DXA) image of the right hip. (A). The LCEA of 46° in this sample is formed by the intersection of two lines. The first line originates from the center of the femoral head and extends to the most lateral bony edge of the acetabulum. The second line is generated perpendicular to the horizontal pelvic reference line, as determined on the full-body DXA image. (B). Full-body DXA image depicts the horizontal pelvic reference line. This horizontal reference line was established to correct for pelvic obliquity and was determined based on the average of 2 lines between the most superior points of the obturator foramen and the most inferior points of the ischial tuberosity on both hips.

6.3 Prevalence and associated factors of pincer morphology

6.3.1 Age

Until now, the exact age at which pincer morphology starts to develop has not yet been determined. A retrospective study based on abdominal CT scans from 225 patients aged 2 to 19 without hip complaints reported that pincer morphology first developed at the age of 12 years [59].

6.3.2 Sex

In the adult general population, the prevalence of pincer morphology based on global pincer morphology ranges from 7% to 15% in males and 8% to 19% in females. A population-based study of 2,596 individuals (mean age 63 years; 43% male) in the U.S. found that 7% of males and 10% of females had pincer morphology as defined by a LCEA > 40° or the presence of acetabular protrusio on the AP pelvic radiograph [26]. Another population-based study involving 3,620 individuals (mean age 60 years; 37% male) found that pincer morphology defined by a LCEA ≥ 45° was present in 15.2% of males and 19.4% of females on the AP pelvic radiograph [27]. Faber et al. included 6,807 individuals (mean age 63 years; 50% male) from the UK Biobank in a cross-sectional study, where pincer morphology was defined as a LCEA ≥ 45° and present in 8.9% of males and 8.1% of females on the DXA images of left hips [28].

6.3.3 Ethnicity

A cross-sectional study compared the prevalence of pincer morphology between 39,826 participants (mean age 63.7 years; 47.9% male) from the UK Biobank and 5,924 participants (mean age 63.4 years; 42.3% male) from the SC cohort. The prevalence of pincer morphology, defined by a LCEA ≥ 45° on the left hip DXA image, was relatively similar among Chinese SC and White UK Biobank participants for both males (9.3% vs. 9.7%) and females (7.8% vs. 8.9%) [30]. In another cross-sectional study of adult male soccer players, the prevalence of pincer morphology (defined as a LCEA > 40° on the AP pelvic view radiograph) was low across all ethnicities, including 3.6% Arabic players, 2.3% Black players and 1.7% Persian players. No cases were found among White and East Asian players in this study [31].

6.3.4 Sporting activity

The prevalence of pincer morphology in athletes varies significantly across sport types and is less studied compared to PCM. A review has reported wide variations in the prevalence of pincer morphology in athletes, with some studies showing a prevalence as high as 74% in ballet dancers or 59.8% in elite ice hockey players [60]. However, these numbers often include focal pincer morphology. Since this thesis focuses on global pincer morphology, we reviewed its prevalence across different athletic populations.

A cross-sectional study consisted of 445 professional male soccer players (mean age 25 years) from diverse ethnic backgrounds and found that 3% of players had a LCEA > 40° on the AP pelvic view radiograph [31]. A cross-sectional study included 67 male collegiate American football players with a mean age of 21 years. The prevalence of pincer morphology (a LCEA > 40°) was 7% on the AP pelvic view radiograph [39]. A cohort study of 20 water polo players and synchronized swimmers (15 females, 5 males) aged 18 - 23 years showed that pincer morphology (a LCEA > 39°) was present in 22.5% of hips on MRI [61]. In a retrospective study of 37 professional female ice hockey players (mean age 25 years), 32% of hips exhibited pincer morphology as defined by a LCEA > 40° on the AP pelvic view radiograph [62].

6.3.5 BMI

The association between pincer morphology/higher LCEA and BMI has been explored in several studies. A cross-sectional study investigating 1,188 children at age 9 years within the Generation R study, which found that overweight and obesity were positively associated with higher LCEA [63]. Similarly, another cross-sectional study involving 107 elite male football players with a mean age of 22.7 years showed an association of BMI greater than 35 with the presence of global overcoverage as defined by a LCEA > 39° or an acetabular inclination < 0° [64]. However, a retrospective study involving 128 adolescents with a mean age of 15 years found no association between BMI percentiles and higher LCEA [45].

6.4 Pincer morphology and hip OA

Pincer morphology can result in repetitive impingement between the proximal femur and the acetabular rim during hip movement, which potentially causes damage to intra-articular structures [65, 66]. However, the relationship between pincer morphology and hip OA is complex and controversial. Multiple prospective cohort studies have found no association with pincer morphology and the development of hip OA [21, 51, 58]. A prospective study from the CHECK cohort reported no significant association between pincer morphology (a LCEA ≥ 40°) and incident RHOA over 2, 5, 8, and 10 years of follow-up unless hip pain was present [57]. A meta-analysis [67] of prospective studies concluded that pincer morphology (a LCEA > 39°) was not a significant risk factor for developing hip OA (OR 1.08 [95% CI 0.57 – 2.07]), highlighting its weaker association compared to other hip morphologies like PCM and hip dysplasia. In contrast, cross-sectional studies demonstrated a significant association between pincer morphology and hip OA, with an OR of 3.71 (95% CI 2.98 – 4.61) [67].

A recent study from the Worldwide Collaboration on OsteoArthritis prediCtion for the Hip (World COACH) consortium conducted a large-scale study involving 16,655 hips from 6 prospective cohort studies to study the association between pincer morphology and the development of hip OA within 8 years follow-up [68]. The consortium standardized the definition of pincer morphology (a LCEA ≥ 40° and a LCEA ≥ 45°) and RHOA, ensuring consistency across cohorts and reducing variability in how pincer morphology and RHOA were defined. Their findings demonstrated that hips with pincer morphology, defined as a LCEA ≥ 45°, had 1.59 times higher odds (OR 1.59 [95% CI 1.16 – 2.20]) of developing RHOA compared to those without pincer morphology [68]. This suggests that pincer morphology may be a risk factor for the development of hip OA. Thus, preventing pincer morphology at an early stage may reduce the risk of developing FAI syndrome and subsequent hip OA.

AIMS AND OUTLINE

To date, the prevalence and associated factors of PCM and pincer morphology are poorly understood in early adolescence – the period when these bony morphologies likely develop. Existing research has primarily focused on the etiology of PCM in athletic populations, identifying associations with male sex, ethnicity, high-impact sports practice and higher frequency of physical activity during skeletal maturation. However, these findings were largely derived from studies of male athletes, which had small sample sizes, limiting their generalizability to the general population. Moreover, there are no studies investigating the etiology of pincer morphology. It remains unclear whether associated factors of PCM in male athletes also holds for pincer morphology in the general population. This significant knowledge gap underscores the need to investigate the etiology of PCM and pincer morphology in the general adolescent population, as such insights may inform primary prevention strategies aimed at reducing the future burden of FAI syndrome and hip OA.

The aims of this thesis are to:

1. Determine the overall and sex-specific prevalence of PCM and pincer morphology in early adolescents from the general population
2. Investigate the factors associated with PCM and pincer morphology in early adolescents from the general population
3. Evaluate factors associated with the development of PCM in the general population

This thesis consists of three parts. **Part I** consists of **Chapters 2 and 3**, which estimated the overall and sex-specific prevalence of PCM and pincer morphology in early adolescents from the general population. Although the prevalence has been reported in adults, the prevalence of PCM and pincer morphology in early adolescence, when these morphologies may first develop, is poorly understood. **Part II** focuses on associated factors of PCM and pincer morphology in early adolescents from the general population. The current research on this topic of PCM predominantly focuses on male athletes. **Chapter 4** investigated demographic, anthropometric, and lifestyle factors associated with PCM and higher alpha angles in early adolescents from the general population. The etiology of pincer morphology remains largely unexplored, and it is unknown whether associated factors of PCM hold for pincer morphology as well. **Chapter 5** identified associated factors of pincer morphology and higher LCEA in early adolescents from the general population. **Part III** consists of **Chapter 6**, which investigated demographic, anthropometric, lifestyle, and radiographic factors at age 13 that are associated with the development of PCM within 5 years in the general population. In a subset of participants with DXA imaging at ages 9, 13, and 18, **Chapter 6** additionally investigated associated factors of PCM development within 8 years.

REFERENCES

1. Dimeglio A. Growth in pediatric orthopaedics. J Pediatr Orthop 2001; 21: 549-555.
2. Kandzierski G, Matuszewski L, Wojcik A. Shape of growth plate of proximal femur in children and its significance in the aetiology of slipped capital femoral epiphysis. Int Orthop 2012; 36: 2513-2520.
3. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019; 393: 1745-1759.
4. Glyn-Jones S, Palmer AJ, Agricola R, Price AJ, Vincent TL, Weinans H, et al. Osteoarthritis. Lancet 2015; 386: 376-387.
5. Hunter DJ, Schofield D, Callander E. The individual and socioeconomic impact of osteoarthritis. Nat Rev Rheumatol 2014; 10: 437-441.
6. Collaborators GBDO. Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Rheumatol 2023; 5: e508-e522.
7. Ackerman IN, Pratt C, Gorelik A, Liew D. Projected Burden of Osteoarthritis and Rheumatoid Arthritis in Australia: A Population-Level Analysis. Arthritis Care Res (Hoboken) 2018; 70: 877-883.
8. Singh JA, Yu S, Chen L, Cleveland JD. Rates of Total Joint Replacement in the United States: Future Projections to 2020-2040 Using the National Inpatient Sample. J Rheumatol 2019; 46: 1134-1140.
9. Sloan M, Premkumar A, Sheth NP. Projected Volume of Primary Total Joint Arthroplasty in the U.S., 2014 to 2030. J Bone Joint Surg Am 2018; 100: 1455-1460.
10. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 2014; 73: 1323-1330.
11. Allen KD, Thoma LM, Golightly YM. Epidemiology of osteoarthritis. Osteoarthritis Cartilage 2022; 30: 184-195.
12. Whittaker JL, Runhaar J, Bierma-Zeinstra S, Roos EM. A lifespan approach to osteoarthritis prevention. Osteoarthritis Cartilage 2021; 29: 1638-1653.
13. Murray RO. The aetiology of primary osteoarthritis of the hip. Br J Radiol 1965; 38: 810-824.
14. Harris WH. Etiology of osteoarthritis of the hip. Clin Orthop Relat Res 1986: 20-33.
15. Ganz R, Parvizi J, Beck M, Leunig M, Notzli H, Siebenrock KA. Femoroacetabular impingement: a cause for osteoarthritis of the hip. Clin Orthop Relat Res 2003: 112-120.
16. Griffin DR, Dickenson EJ, O'Donnell J, Agricola R, Awan T, Beck M, et al. The Warwick Agreement on femoroacetabular impingement syndrome (FAI syndrome): an international consensus statement. Br J Sports Med 2016; 50: 1169-1176.
17. van Klij P, Reiman MP, Waarsing JH, Reijman M, Bramer WM, Verhaar JAN, et al. Classifying Cam Morphology by the Alpha Angle: A Systematic Review on Threshold Values. Orthop J Sports Med 2020; 8: 2325967120938312.
18. Mascarenhas VV, Castro MO, Afonso PD, Rego P, Dienst M, Sutter R, et al. The Lisbon Agreement on femoroacetabular impingement imaging-part 2: general issues, parameters, and reporting. Eur Radiol 2021; 31: 4634-4651.
19. Dijkstra HP, Mc Auliffe S, Ardern CL, Kemp JL, Mosler AB, Price A, et al. Oxford consensus on primary cam morphology and femoroacetabular impingement syndrome: part 1-definitions, terminology, taxonomy and imaging outcomes. Br J Sports Med 2022; 57: 325-341.
20. Agricola R, Waarsing JH, Thomas GE, Carr AJ, Reijman M, Bierma-Zeinstra SM, et al. Cam impingement: defining the presence of a cam deformity by the alpha angle: data from the CHECK cohort and Chingford cohort. Osteoarthritis Cartilage 2014; 22: 218-225.

21. Nelson AE, Stiller JL, Shi XA, Leyland KM, Renner JB, Schwartz TA, et al. Measures of hip morphology are related to development of worsening radiographic hip osteoarthritis over 6 to 13 year follow-up: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2016; 24: 443-450.
22. Gosvig KK, Jacobsen S, Palm H, Sonne-Holm S, Magnusson E. A new radiological index for assessing asphericity of the femoral head in cam impingement. J Bone Joint Surg Br 2007; 89: 1309-1316.
23. Agricola R, Bessems JH, Ginai AZ, Heijboer MP, van der Heijden RA, Verhaar JA, et al. The development of Cam-type deformity in adolescent and young male soccer players. Am J Sports Med 2012; 40: 1099-1106.
24. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Cam morphology in young male football players mostly develops before proximal femoral growth plate closure: a prospective study with 5-yearfollow-up. Br J Sports Med 2019; 53: 532-538.
25. Palmer A, Fernquest S, Gimpel M, Birchall R, Judge A, Broomfield J, et al. Physical activity during adolescence and the development of cam morphology: a cross-sectional cohort study of 210 individuals. Br J Sports Med 2018; 52: 601-610.
26. Raveendran R, Stiller JL, Alvarez C, Renner JB, Schwartz TA, Arden NK, et al. Population-based prevalence of multiple radiographically-defined hip morphologies: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2018; 26: 54-61.
27. Gosvig KK, Jacobsen S, Sonne-Holm S, Palm H, Troelsen A. Prevalence of malformations of the hip joint and their relationship to sex, groin pain, and risk of osteoarthritis: a population-based survey. J Bone Joint Surg Am 2010; 92: 1162-1169.
28. Faber BG, Ebsim R, Saunders FR, Frysz M, Gregory JS, Aspden RM, et al. Cam morphology but neither acetabular dysplasia nor pincer morphology is associated with osteophytosis throughout the hip: findings from a cross-sectional study in UK Biobank. Osteoarthritis Cartilage 2021; 29: 1521-1529.
29. Laborie LB, Lehmann TG, Engesaeter IO, Eastwood DM, Engesaeter LB, Rosendahl K. Prevalence of radiographic findings thought to be associated with femoroacetabular impingement in a population-based cohort of 2081 healthy young adults. Radiology 2011; 260: 494-502.
30. Zheng J, Frysz M, Faber BG, Lin H, Ebsim R, Ge J, et al. Comparison between UK Biobank and Shanghai Changfeng suggests distinct hip morphology may contribute to ethnic differences in the prevalence of hip osteoarthritis. Osteoarthritis Cartilage 2025; 33: 473-481.
31. Mosler AB, Crossley KM, Waarsing JH, Jomaah N, Weir A, Holmich P, et al. Ethnic Differences in Bony Hip Morphology in a Cohort of 445 Professional Male Soccer Players. Am J Sports Med 2016; 44: 2967-2974.
32. Johnson AC, Shaman MA, Ryan TG. Femoroacetabular impingement in former high-level youth soccer players. Am J Sports Med 2012; 40: 1342-1346.
33. Gerhardt MB, Romero AA, Silvers HJ, Harris DJ, Watanabe D, Mandelbaum BR. The prevalence of radiographic hip abnormalities in elite soccer players. Am J Sports Med 2012; 40: 584-588.
34. Lahner M, Walter PA, von Schulze Pellengahr C, Hagen M, von Engelhardt LV, Lukas C. Comparative study of the femoroacetabular impingement (FAI) prevalence in male semiprofessional and amateur soccer players. Arch Orthop Trauma Surg 2014; 134: 1135-1141.
35. Siebenrock KA, Ferner F, Noble PC, Santore RF, Werlen S, Mamisch TC. The cam-type deformity of the proximal femur arises in childhood in response to vigorous sporting activity. Clin Orthop Relat Res 2011; 469: 3229-3240.
36. Ayeni OR, Banga K, Bhandari M, Maizlin Z, de Sa D, Golev D, et al. Femoroacetabular impingement in elite ice hockey players. Knee Surg Sports Traumatol Arthrosc 2014; 22: 920-925.

37. Lerebours F, Robertson W, Neri B, Schulz B, Youm T, Limpisvasti O. Prevalence of Cam-Type Morphology in Elite Ice Hockey Players. Am J Sports Med 2016; 44: 1024-1030.
38. Philippon MJ, Ho CP, Briggs KK, Stull J, LaPrade RF. Prevalence of increased alpha angles as a measure of cam-type femoroacetabular impingement in youth ice hockey players. Am J Sports Med 2013; 41: 1357-1362.
39. Kapron AL, Anderson AE, Aoki SK, Phillips LG, Petron DJ, Toth R, et al. Radiographic prevalence of femoroacetabular impingement in collegiate football players: AAOS Exhibit Selection. J Bone Joint Surg Am 2011; 93: e111(111-110).
40. Westermann RW, Scott EJ, Schaver AL, Schneider A, Glass NA, Levy SM, et al. Activity Level and Sport Type in Adolescents Correlate with the Development of Cam Morphology. JB JS Open Access 2021; 6: e21.00059.
41. Doran C, Pettit M, Singh Y, Sunil Kumar KH, Khanduja V. Does the Type of Sport Influence Morphology of the Hip? A Systematic Review. Am J Sports Med 2022; 50: 1727-1741.
42. Roels P, Agricola R, Oei EH, Weinans H, Campoli G, Zadpoor AA. Mechanical factors explain development of cam-type deformity. Osteoarthritis Cartilage 2014; 22: 2074-2082.
43. Tak I, Weir A, Langhout R, Waarsing JH, Stubbe J, Kerkhoffs G, et al. The relationship between the frequency of football practice during skeletal growth and the presence of a cam deformity in adult elite football players. Br J Sports Med 2015; 49: 630-634.
44. Fernquest S, Palmer A, Gimpel M, Birchall R, Broomfield J, Wedatilake T, et al. A longitudinal cohort study of adolescent elite footballers and controls investigating the development of cam morphology. Sci Rep 2021; 11: 18567.
45. Novais EN, Shefelbine SJ, Kienle KP, Miller PE, Bowen G, Kim YJ, et al. Body Mass Index Affects Proximal Femoral but Not Acetabular Morphology in Adolescents Without Hip Pathology. J Bone Joint Surg Am 2018; 100: 66-74.
46. Pettit M, Doran C, Singh Y, Saito M, Sunil Kumar KH, Khanduja V. How does the cam morphology develop in athletes? A systematic review and meta-analysis. Osteoarthritis Cartilage 2021; 29: 1117-1129.
47. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Clinical and radiological hip parameters do not precede, but develop simultaneously with cam morphology: a 5-year follow-up study. Knee Surg Sports Traumatol Arthrosc 2021; 29: 1401-1410.
48. Claes PAM, Hanff DF, Weir A, Riedstra NS, Weinans H, Eygendaal D, et al. The Association Between the Development of Cam Morphology During Skeletal Growth in High-Impact Athletes and the Presence of Cartilage Loss and Labral Damage in Adulthood: A Prospective Cohort Study With a 12-Year Follow-up. Am J Sports Med 2024; 52: 2555-2564.
49. Heerey J, Kemp J, Agricola R, Srinivasan R, Smith A, Pizzari T, et al. Cam morphology is associated with MRI-defined cartilage defects and labral tears: a case-control study of 237 young adult football players with and without hip and groin pain. BMJ Open Sport Exerc Med 2021; 7: e001199.
50. Agricola R, Heijboer MP, Bierma-Zeinstra SM, Verhaar JA, Weinans H, Waarsing JH. Cam impingement causes osteoarthritis of the hip: a nationwide prospective cohort study (CHECK). Ann Rheum Dis 2013; 72: 918-923.
51. Saberi Hosnijeh F, Zuiderwijk ME, Versteeg M, Smeele HT, Hofman A, Uitterlinden AG, et al. Cam Deformity and Acetabular Dysplasia as Risk Factors for Hip Osteoarthritis. Arthritis Rheumatol 2017; 69: 86-93.
52. Larson CM, Moreau-Gaudry A, Kelly BT, Byrd JW, Tonetti J, Lavallee S, et al. Are normal hips being labeled as pathologic? A CT-based method for defining normal acetabular coverage. Clin Orthop Relat Res 2015; 473: 1247-1254.

53. Zaltz I, Kelly BT, Hetsroni I, Bedi A. The crossover sign overestimates acetabular retroversion. Clin Orthop Relat Res 2013; 471: 2463-2470.
54. Nepple JJ, Lehmann CL, Ross JR, Schoenecker PL, Clohisy JC. Coxa profunda is not a useful radiographic parameter for diagnosing pincer-type femoroacetabular impingement. J Bone Joint Surg Am 2013; 95: 417-423.
55. Polat G, Arzu U, Dinc E, Bayraktar B. Prevalence of femoroacetabular impingement and effect of training frequency on aetiology in paediatric football players. Hip Int 2019; 29: 204-208.
56. Larson CM, Sikka RS, Sardelli MC, Byrd JW, Kelly BT, Jain RK, et al. Increasing alpha angle is predictive of athletic-related "hip" and "groin" pain in collegiate National Football League prospects. Arthroscopy 2013; 29: 405-410.
57. Riedstra NS, Boel F, van Buuren M, Eygendaal D, Bierma-Zeinstra S, Runhaar J, et al. Pincer Morphology Is Not Associated With Hip Osteoarthritis Unless Hip Pain Is Present: Follow-Up Data From a Prospective Cohort Study. Arthritis Care Res (Hoboken) 2024; 76: 644-651.
58. Agricola R, Heijboer MP, Roze RH, Reijman M, Bierma-Zeinstra SM, Verhaar JA, et al. Pincer deformity does not lead to osteoarthritis of the hip whereas acetabular dysplasia does: acetabular coverage and development of osteoarthritis in a nationwide prospective cohort study (CHECK). Osteoarthritis Cartilage 2013; 21: 1514-1521.
59. Monazzam S, Bomar JD, Dwek JR, Hosalkar HS, Pennock AT. Development and prevalence of femoroacetabular impingement-associated morphology in a paediatric and adolescent population: a CT study of 225 patients. Bone Joint J 2013; 95-B: 598-604.
60. van Klij P, Heerey J, Waarsing JH, Agricola R. The Prevalence of Cam and Pincer Morphology and Its Association With Development of Hip Osteoarthritis. J Orthop Sports Phys Ther 2018; 48: 230-238.
61. Langner JL, Black MS, MacKay JW, Hall KE, Safran MR, Kogan F, et al. The prevalence of femoroacetabular impingement anatomy in Division 1 aquatic athletes who tread water. J Hip Preserv Surg 2020; 7: 233-241.
62. Ross KA, Mojica ES, Lott A, Carter C, Gonzalez-Lomas G. Characterization of pincer-type Hip impingement in professional women's ice hockey players. Phys Sportsmed 2023; 51: 610-614.
63. Chung WK, De Vos-Jakobs S, Rivadeneira F, Bierma-Zeinstra SM, Waarsing JH. The association of BMI and physical activity on acetabular dysplasia in children. Osteoarthritis Cartilage 2021; 29: 50-58.
64. Nepple JJ, Brophy RH, Matava MJ, Wright RW, Clohisy JC. Radiographic findings of femoroacetabular impingement in National Football League Combine athletes undergoing radiographs for previous hip or groin pain. Arthroscopy 2012; 28: 1396-1403.
65. Pascual-Garrido C, Li DJ, Grammatopoulos G, Yanik EL, Clohisy JC, Group A. The Pattern of Acetabular Cartilage Wear Is Hip Morphology-dependent and Patient Demographic-dependent. Clin Orthop Relat Res 2019; 477: 1021-1033.
66. Beck M, Kalhor M, Leunig M, Ganz R. Hip morphology influences the pattern of damage to the acetabular cartilage: femoroacetabular impingement as a cause of early osteoarthritis of the hip. J Bone Joint Surg Br 2005; 87: 1012-1018.
67. Casartelli NC, Maffiuletti NA, Valenzuela PL, Grassi A, Ferrari E, van Buuren MMA, et al. Is hip morphology a risk factor for developing hip osteoarthritis? A systematic review with meta-analysis. Osteoarthritis Cartilage 2021; 29: 1252-1264.
68. Riedstra NS, Van Buuren MM, Boel F, Ahedi H, Arbabi V, Arden N, et al. Pincer Morphology Is A Risk Factor For Developing Radiographic Hip Osteoarthritis; Data From The World Coach Consortium. Osteoarthritis and Cartilage 2023; 31: S249-S250.

Chapter 2

The prevalence of primary cam morphology in early adolescents from the general population: a population-based study (Generation R)

Delong Chen, Fleur Boel, Pim van Klij, Michiel M.A. van Buuren,
Sita M.A. Bierma-Zeinstra, Rintje Agricola

Osteoarthritis Cartilage. 2025;33(5):633-637.

ABSTRACT

Objective

Small studies in athletes showed that primary cam morphology (PCM) gradually develops during skeletal growth. However, the prevalence of PCM in early adolescents is poorly understood. We aimed to estimate the overall and birth-assigned sex-specific prevalence of PCM in early adolescents from the general population.

Design

We cross-sectionally analyzed data from the Generation R cohort, an ongoing population-based prospective cohort study from early fetal life onward from Rotterdam, the Netherlands. High-resolution dual-energy x-ray absorptiometry (DXA) scans were performed on the right hip of participants around the age of 13 years. The alpha angle (AA) and triangular index ratio (TIR) were automatically measured. We defined PCM by a validated AA threshold ≥ 60° or a TIR threshold ≥ 1.05. The overall and birth-assigned sex-specific prevalence of PCM was reported as a percentage with 95% confidence interval (CI).

Results

The median age of the 4477 early adolescents included in this analysis was 13.5 years (2.5th - 97.5th percentile, 13.2 - 14.6) with 2166 (48.4%) being males. The overall prevalence of PCM (AA ≥ 60° or TIR ≥ 1.05) was 3.5% (95% CI, 2.9% – 4.0%). Male and female adolescents had a similar prevalence of PCM: 3.9% (95% CI, 3.1% – 4.7%) vs 3.0% (95% CI, 2.3% – 3.7%).

Conclusions

The overall prevalence of PCM was 3.5% in early adolescents from the general population in the Netherlands. The prevalence of PCM was similar between male and female early adolescents.

Keywords

Primary cam morphology; Osteoarthritis; Prevalence; Early adolescents; General population

INTRODUCTION

Osteoarthritis (OA) is a debilitating disorder that imposes a great challenge for society and has a considerable burden on healthcare systems. Prospective cohort studies have consistently shown that cam morphology is an important risk factor for hip OA [1].

Cam morphology refers to extra bone formation, usually at the anterolateral head-neck junction of the femur. This may result in abnormal contact between the proximal femur and acetabular rim during motion, and can cause progressive labral tears and cartilage defects, already in young adults [2]. Cam morphology is mostly acquired due to high-impact hip loading during skeletal growth, and is then referred to as primary cam morphology (PCM), with a consequently higher prevalence in adult athletes than non-athletes [3].

Current knowledge on the age of onset of PCM is limited and based on male athletes. PCM was first identified between the age of 12 and 13 years in young male elite soccer players [4]. It is also known that PCM develops gradually over time during adolescence, with a reported prevalence in the adult general population ranging 17% to 35% in males and 4% to 10% in females [5-7]. At present, studies on the prevalence of PCM in adolescents were performed on relatively small groups and mostly in male athletes participating in high-impact sports. There is a lack of epidemiological data on the prevalence of PCM in male and female adolescents from the general population. However, insight into when PCM first develops in the general population is essential for determining the timing of possible preventive strategies for PCM and subsequent hip OA later in life. Also, the latest Oxford consensus highlighted the need for more research focusing on females and prioritized sex-specific cohorts to investigate the development of PCM [8].

The aim of this study was to determine the prevalence of PCM in early adolescents from the general population and its distribution stratified by birth-assigned sex.

METHODS

Study population

We included participants from the Generation R cohort, a population-based, prospective cohort from Rotterdam, the Netherlands. An in-depth report provides details of the methodology of this cohort [9]. In total, 4929 participants attended the visit around the age of 13 years (Focus 13). Participants with a right hip dual energy x-ray absorptiometry (DXA) scan were eligible for inclusion in this study. Participants were excluded if the DXA image showed an incomplete femoral head or neck, movement artifacts, or artifacts in the region of interest that impeded measurements.

Given ethnicity and sports participation may influence the sex-specific prevalence of PCM, we conducted descriptive analyses of these variables to provide the context of the study population. According to the definition of Statistics Netherlands, the participants' ethnicity was determined by parental country of birth and categorized into four groups: European (Dutch, Turkish, European, Oceanian, and American Western), African (Cape Verdian, Moroccan, Dutch Antilles, Surinamese-Creole and other African), Asian (Indonesia, Surinamese-Hindustani, other Asian) and Other (Surinamese-Unspecified and American non-Western). Sports participation data were collected through self-reported questionnaires asking participants about weekly sports involvement, dichotomized as "no sports" or "sports participation".

The Medical Ethics Committee of the Erasmus Medical Center approved the study (MEC-2015-749). Written informed consent was obtained from all parents and their children.

DXA scans

A DXA scan of the right hip was obtained using General Electric (GE)-Lunar iDXA densitometer (GE Healthcare, Madison, WI, USA). For the DXA scan, participants lay supine with hands flat at their sides and legs slightly separated, positioned in internal rotation with the big toes touching. A Velcro strip was used to secure the feet in this position.

The status of proximal femoral physis

The timing of proximal femoral physis closure differs between males and females since females are, on average, more skeletal mature than males of the same age. This may influence the sex-specific prevalence of PCM. Therefore, we performed a description analysis of the proximal femoral physis status by sex, which was assessed manually (DC) on the right hip DXA images. A fully fused physis was scored as closed, while any remaining open portion was scored as open. Reliability assessments were conducted to ensure consistent and reproducible evaluations of proximal femoral physis status.

Primary cam morphology

The alpha angle (AA) and triangular index ratio (TIR) were used to define PCM on the right hip DXA images. They measure different aspects of PCM: the AA quantifies the deviation of the femoral head from sphericity, while the TIR assesses the lateral extension of the bone at a fixed point defined by half the radius of the femoral head along the axis of the femoral neck (**Supplementary Figure 1**). The TIR [10] was derived from the triangular index (TI) [11] that was initially described by Gosvig et al. who defined cam morphology by a pathologically increased radius (R) ≥ natural radius (r) + 2 mm on an anteroposterior (AP) radiograph with 1.2 magnification in white adults. We converted the previously proposed TI threshold into a TIR threshold of ≥ 1.05 to define PCM (see **Supplementary materials**).

PCM was defined by an AA ≥ 60° and/or a TIR ≥ 1.05. The AA and TIR were automatically calculated from a set of landmarks along the contour of the proximal femur using in-house developed software (**Supplementary Figure 1**). The landmarks were automatically placed on the DXA images using the BoneFinder® software (www.bone-finder.com; The University of Manchester, UK) and manually adjusted (DC and FB) for correct point placement when necessary. Reliability between the automated and manual measures was previously assessed by Boel et al., showing intraclass correlation coefficients (ICC) of 0.81 (95% confidence interval [CI], 0.46 – 0.92) for AA and 0.96 (95% CI, 0.91 – 0.98) for TIR [12].

Statistical analyses

Reliability assessments for proximal femoral physis status, including both interobserver and intraobserver reliability, were conducted using ICCs with 95% confidence interval (CI) in a two-way mixed-effects model with absolute agreement. Interobserver reliability involved two evaluators (DC and RA) examining a random subset of 100 DXA images, and intraobserver reliability was assessed by one evaluator (DC) reviewing the same images at one-month intervals. The distribution of AA and TIR in the total group and birth-assigned sex subgroup was presented in histograms. The prevalence of PCM was expressed as a percentage with 95% CI and presented for four groups: 1) an AA ≥ 60°; 2) a TIR ≥ 1.05; 3) an AA ≥ 60° or a TIR ≥ 1.05; and 4) both an AA ≥ 60° and a TIR ≥ 1.05. We performed a subgroup analysis and conducted a chi-square test to compare birth-assigned sex-specific prevalence. The prevalence of PCM was reported at the hip level. All analyses were conducted in R Statistical software (v4.2.1; R Core Team 2022). The binom package (v1.1-1.1) was used to compute 95% CIs, the ggplot2 package (v3.5.1) was used to create histograms, and the irr package (v0.84.1) was used to compute ICCs. Statistical significance was accepted at the level of $P < 0.05$.

RESULTS

Study population

A total of 4477 participants were included in this study (**Supplementary Figure 2**). The characteristics of the included participants are shown in **Table 1**.

Table 1. Demographic characteristics of included participants.

Characteristic	Included participants (n=4,477)	Males (n=2,166)	Females (n=2,311)
Age, years	13.5 (13.2-14.6)	13.5 (13.2-14.6)	13.5 (13.2-14.7)
Height, cm	164.2 (7.9)	165.0 (8.8)	163.4 (7.0)
BMI, kg/m^2	19.1 (15.2-29.2)	18.6 (15.5-27.5)	19.6 (15.4-30.4)
Ethnicity, %			
European	3,298 (75.3%)	1585 (73.2%)	1713 (74.1%)
African	693 (15.8%)	336 (15.5%)	357 (15.4%)
Asian	257 (5.9%)	128 (5.9%)	129 (5.9%)
Other	129 (3.0%)	73 (3.4%)	56 (2.4%)
Sports participation, %			
Yes	3206 (71.6%)	1590 (73.4%)	1616 (69.9%)
No	607 (13.6%)	234 (10.8%)	373 (16.1%)

Data are observed and presented as frequencies (percentages) for categorical variables, means (SD) for continuous normally distributed variables and medians (2.5th - 97.5th percentile) for continuous, non-normally distributed variables. Data on sport participation and ethnicity was missing in 644 and 100 participants, respectively. BMI: body mass index.

Proximal femoral physis status

Of the 4477 proximal femoral physes assessed, 1851 (41.3%) were closed, including 195 of 2166 (9.0%) in males and 1656 of 2,311 (71.7%) in females. The intraobserver and interobserver ICC for proximal femoral physis status were 0.90 (95% CI, 0.85 – 0.94) and 0.87 (95% CI, 0.78 – 0.92), respectively.

Prevalence of PCM

The distribution of AA and TIR in the total group and birth-assigned sex subgroup is shown in **Supplementary Figure 3**. The overall and birth-assigned sex-specific prevalence of PCM in early adolescents from the general population are shown in **Table 2**. Defined by an AA ≥ 60° or a TIR ≥ 1.05, the overall prevalence of PCM was 3.5% (95% CI, 2.9% – 4.0%), and the prevalence was similar in males (3.9%, [95% CI, 3.1% – 4.7%]) and females (3.0%, [95% CI, 2.3% – 3.7%]) ($p = 0.102$).

Table 2. The overall and birth-assigned sex-specific prevalence of primary cam morphology among early adolescents.

Charac-teristic	AA ≥ 60°				TIR ≥ 1.05				AA ≥ 60° or TIR ≥ 1.05				AA ≥ 60° and TIR ≥ 1.05			
	No. of cases	Prevalence, % (95% CI)	χ 2	P value	No. of cases	Prevalence, % (95% CI)	χ 2	P value	No. of cases	Prevalence, % (95% CI)	χ 2	P value	No. of cases	Prevalence, % (95% CI)	χ 2	P value
Overall	151	3.4% (2.8%-3.9%)			49	1.1% (0.8%-1.4%)			155	3.5% (2.9%-4.0%)			45	1.0% (0.7%-1.3%)		
Sex																
Male	84	3.9% (3.1%-4.7%)	3.29	0.07	26	1.2% (0.7%-1.7%)	0.44	0.51	85	3.9% (3.1%-4.7%)	2.68	0.102	25	1.2% (0.7%-1.6%)	0.93	0.333
Female	67	2.9% (2.2%-3.6%)			23	1.0% (0.6%-1.4%)			70	3.0% (2.3%-3.7%)			20	0.9% (0.5%-1.2%)		

AA: alpha angle; TIR: triangular index ratio; CI: confidence interval.

DISCUSSION

In this study, we estimated the overall and birth-assigned sex-specific prevalence of PCM of a large sample of early adolescents from the general population in Rotterdam, the Netherlands. The overall prevalence of PCM was 3.5% (95% CI, 2.9% – 4.0%) as defined by an AA ≥ 60° or a TIR ≥ 1.05. The prevalence was similar in males (3.9% [95% CI, 3.1% – 4.7%]) and females (3.0% [95% CI, 2.3% – 3.7%]).

A wide range of prevalence numbers for PCM have been reported in various studies. A Norwegian population-based cohort involving 2081 participants aged 17.2 to 20.1 years used AP pelvic radiograph to evaluate PCM as defined by pistol-grip deformity, focal prominence and flattening of the femoral head-neck junction and found a prevalence of 20.6% [5]. In contrast, our study found a relatively low prevalence of PCM (3.5%) in early adolescents. This discrepancy may be attributed the fact that PCM may not yet have developed by the age of 13 years. Secondly, our study assessed only the right hips based on DXA scans, whereas the Norwegian study assessed both hips using AP pelvic radiographs. Consequently, we presented a hip-level prevalence rather than a person-level prevalence due to the availability for only the right hip per person, which underestimates a person-level prevalence. Furthermore, the open physis observed in 59% of participants indicates ongoing skeletal development, and prospective studies have demonstrated that PCM gradually increases in size until the proximal femoral physis is closed [13]. Therefore, this prevalence is likely to increase when participants become older, influenced by mechanical loading (e.g., type and volume of loading) on the open proximal femoral physis during adolescence. The ongoing Generation R cohort will follow participants until young adulthood, providing future longitudinal data on the development of PCM in the general population.

The prevalence of PCM was similar between early adolescent males and females in our study, whereas other studies found that males are more likely to have cam morphology [6,7]. In older populations from the Copenhagen osteoarthritis study [7] and the Johnston Country Osteoarthritis Project (JoCoOA) [6], cam morphology was more common in males (17% – 25%) than in females (4% – 10%). Similarly, Laborie et al. reported a higher PCM prevalence in males (35%) compared to females (10.2%) in a Norwegian population-based study of 2081 young adults [5]. The lack of sex differences in our study may be due to earlier second growth spurt in females (between the ages of 12 to 13 years) than in males (between the ages of 14 to 15 years). Given this disparity in skeletal maturity (closed proximal femoral physis: 72% in females vs. 9% in males), males will be more likely to develop PCM in the follow-up than females in this cohort, as males still have skeletal growth potential. Although the engagement in sporting activities was similar between sexes in this study (73% in males vs. 70% in females), males are more likely to engage in impact sports that are associated with PCM development. Additionally, males close their proximal femoral physis later than females. This extended period of skeletal immaturity in males could expose them to a longer duration of sporting activities, thereby increasing the risk of PCM development.

The major strength of our study is the large sample size available to study PCM in early adolescents from the general population, allowing precise prevalence estimation. Moreover, the automated measurement of AA and TIR improves reproducibility and avoids reader bias. Some limitations should be discussed as well. First, our study population is representative of early adolescents, so the conclusions cannot be generalized to late adolescents as PCM could still develop over time in this cohort. Secondly, the prevalence of PCM could be underestimated due to the use of AP views of the right hip, as three-dimensional images are more sensitive in detecting PCM at the anterolateral aspect of the femoral head-neck junction. Thirdly, while DXA scans offer high-resolution images and low radiation exposure in children and adolescents, measurement differences may exist compared to radiographs. However, measurements on DXA scans and pelvic radiographs are similar in adults (The ICC was 0.72 (95% CI 0.68 – 0.75) for AA and 0.81 (95% CI 0.79 – 0.84) for TIR) [14]. Fourthly, our study reported hip-level rather than person-level prevalence. Analyzing only in right hips can lead to an underestimation in the person-level prevalence of PCM as it can also be present in left hips.

In conclusion, we found that the overall prevalence of PCM was 3.5% in early adolescents, as defined by an AA ≥ 60° or a TIR ≥ 1.05. Moreover, the prevalence of PCM was similar between male and female participants at this age. The low prevalence in this age category supports the notion from athletic populations that PCM gradually develops over time in adolescence. These findings provide valuable insights into the timing of potential primary preventive strategies which might start at or even before the age of 13 years, and even younger in females due to their earlier proximal femoral physis closure. However, further research should consider additional characteristics to identify those at highest risk of developing PCM.

REFERENCES

1. Agricola R, Heijboer MP, Bierma-Zeinstra SM, Verhaar JA, Weinans H, Waarsing JH. Cam impingement causes osteoarthritis of the hip: a nationwide prospective cohort study (CHECK). Ann Rheum Dis 2013; 72: 918-923.
2. Heerey J, Kemp J, Agricola R, Srinivasan R, Smith A, Pizzari T, et al. Cam morphology is associated with MRI-defined cartilage defects and labral tears: a case-control study of 237 young adult football players with and without hip and groin pain. BMJ Open Sport Exerc Med 2021; 7: e001199.
3. Frank JM, Harris JD, Erickson BJ, Slikker W, 3rd, Bush-Joseph CA, Salata MJ, et al. Prevalence of Femoroacetabular Impingement Imaging Findings in Asymptomatic Volunteers: A Systematic Review. Arthroscopy 2015; 31: 1199-1204.
4. Agricola R, Bessems JH, Ginai AZ, Heijboer MP, van der Heijden RA, Verhaar JA, et al. The development of Cam-type deformity in adolescent and young male soccer players. Am J Sports Med 2012; 40: 1099-1106.
5. Laborie LB, Lehmann TG, Engesaeter IO, Eastwood DM, Engesaeter LB, Rosendahl K. Prevalence of radiographic findings thought to be associated with femoroacetabular impingement in a population-based cohort of 2081 healthy young adults. Radiology 2011; 260: 494-502.
6. Raveendran R, Stiller JL, Alvarez C, Renner JB, Schwartz TA, Arden NK, et al. Population-based prevalence of multiple radiographically-defined hip morphologies: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2018; 26: 54-61.
7. Gosvig KK, Jacobsen S, Sonne-Holm S, Gebuhr P. The prevalence of cam-type deformity of the hip joint: a survey of 4151 subjects of the Copenhagen Osteoarthritis Study. Acta Radiol 2008; 49: 436-441.
8. Dijkstra HP, Mc Auliffe S, Ardern CL, Kemp JL, Mosler AB, Price A, et al. Oxford consensus on primary cam morphology and femoroacetabular impingement syndrome: part 2-research priorities on conditions affecting the young person's hip. Br J Sports Med 2022; 57: 342-358.
9. Kooijman MN, Kruithof CJ, van Duijn CM, Duijts L, Franco OH, van IMH, et al. The Generation R Study: design and cohort update 2017. Eur J Epidemiol 2016; 31: 1243-1264.
10. Nelson AE, Stiller JL, Shi XA, Leyland KM, Renner JB, Schwartz TA, et al. Measures of hip morphology are related to development of worsening radiographic hip osteoarthritis over 6 to 13 year follow-up: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2016; 24: 443-450.
11. Gosvig KK, Jacobsen S, Palm H, Sonne-Holm S, Magnusson E. A new radiological index for assessing asphericity of the femoral head in cam impingement. J Bone Joint Surg Br 2007; 89: 1309-1316.
12. Boel F, de Vos-Jakobs S, Riedstra NS, Lindner C, Runhaar J, Bierma-Zeinstra SMA, et al. Automated radiographic hip morphology measurements: An open-access method. Osteoarthr Imaging 2024; 4: 100181.
13. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Cam morphology in young male football players mostly develops before proximal femoral growth plate closure: a prospective study with 5-yearfollow-up. Br J Sports Med 2019; 53: 532-538.
14. Boel F, Wortel J, van Buuren MMA, Rivadeneira F, van Meurs JBJ, Runhaar J, et al. DXA images vs. Pelvic Radiographs: Reliability of Hip Morphology Measurements. Osteoarthritis Cartilage 2025; 33: 283-292.

SUPPLEMENTARY MATERIALS

Supplementary methods

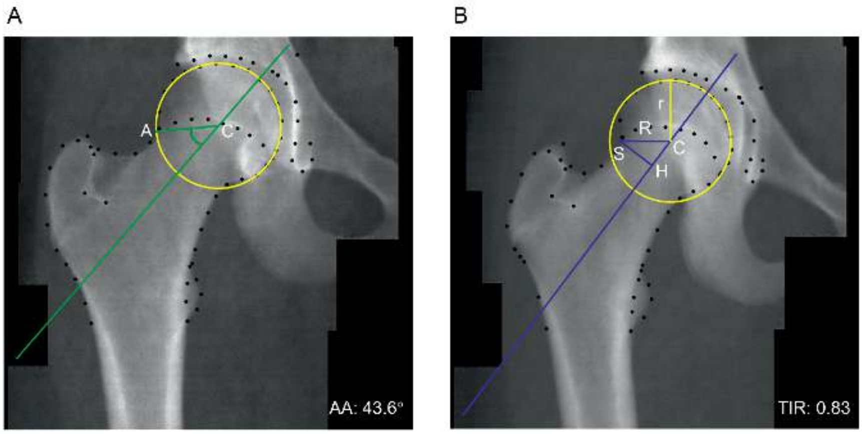
Triangular index ratio (TIR) threshold

The triangular index (TI) [1] proposed by Gosvig et al. uses a fixed threshold (+ 2mm) that does not depend on the size of the femoral head. However, since our study focused on adolescents, whose femoral head sizes vary and smaller than those of adults, we converted the TI into the TIR [2] using the radius of the best-fitting circle around the femoral head. This approach accounts for variability in femoral head size across age groups and populations. We referenced the average femoral head diameter of 57 mm in white adults as reported in the Johnston County Osteoarthritis Project (JoCoOA) [2]. The TI defined cam morphology using 1.2 magnification, while the JoCoOA did not use such magnification. To adjust for this difference, we divided the original threshold of 2 mm by 1.2 to obtain an adjusted threshold of 1.67 mm (i.e., 2 mm / 1.2 = 1.67 mm). Thus, we adjusted the TI to $R \geq r + 1.67$ mm. To calculate the TIR threshold for PCM, we used this adjusted threshold (1.67 mm) relative to the radius of the femoral head. Specifically, we determined the TIR as follows: $TIR \geq 1 + 1.67mm / r$, where r is the radius of the femoral head. Using the femoral head radius of 28.5 mm (i.e., 57mm / 2 = 28.5mm) from the JoCoOA study, the TIR threshold for PCM was determined to be 1.05.

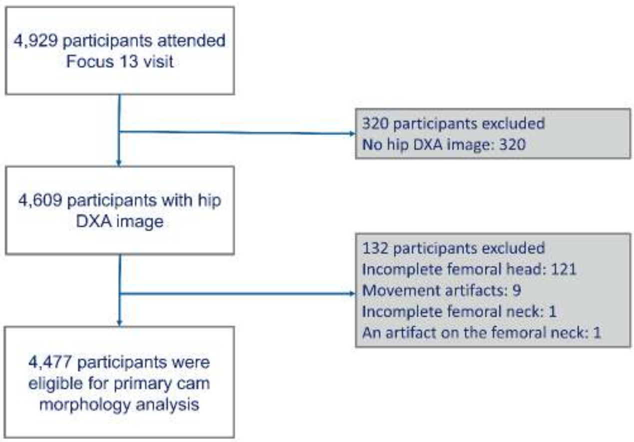
Supplementary references

1. Gosvig KK, Jacobsen S, Palm H, Sonne-Holm S, Magnusson E. A new radiological index for assessing asphericity of the femoral head in cam impingement. J Bone Joint Surg Br 2007; 89: 1309-1316.
2. Nelson AE, Stiller JL, Shi XA, Leyland KM, Renner JB, Schwartz TA, et al. Measures of hip morphology are related to development of worsening radiographic hip osteoarthritis over 6 to 13 year follow-up: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2016; 24: 443-450.

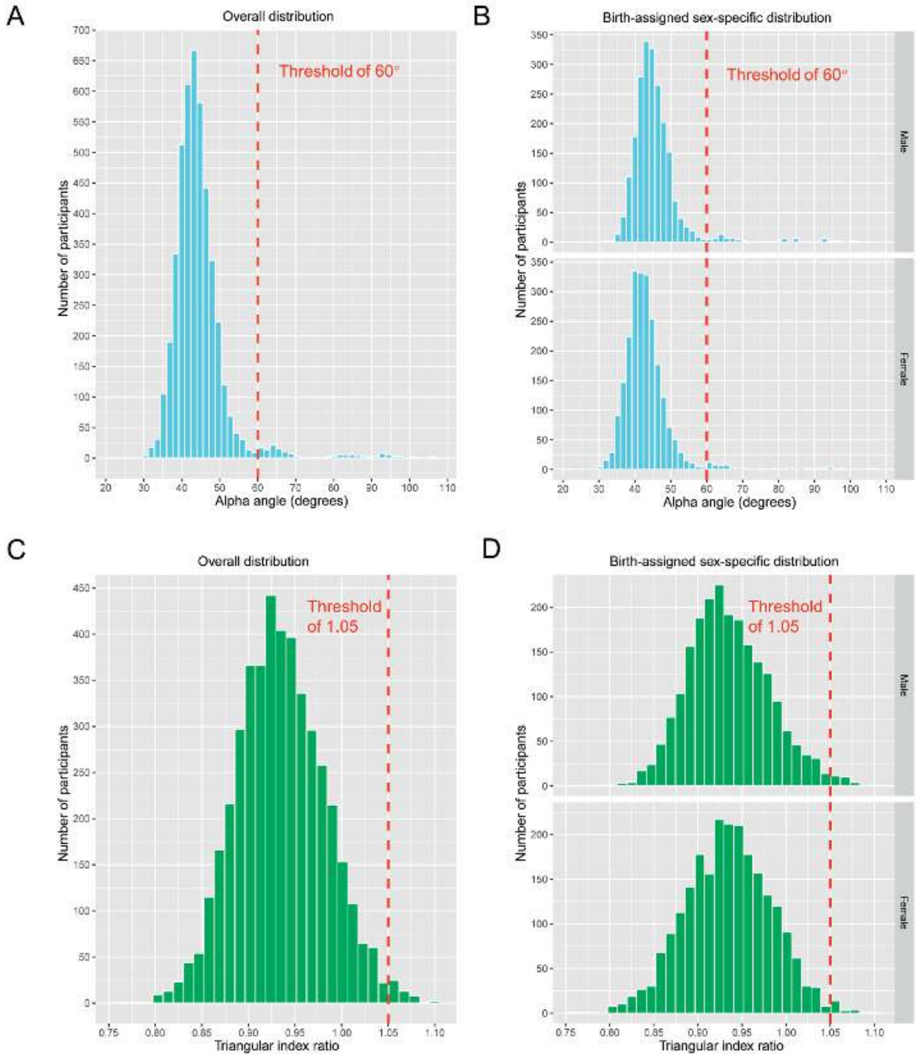
Supplementary figures



Supplementary Figure 1. Quantitative measurements of primary cam morphology. A. The alpha angle (AA) quantifies the deviation of the femoral head from sphericity. First, the best-fitting circle of the femoral head is generated based on the landmark points on the femoral head. From the center of the best-fitting circle (point C), one line is connected to the center of the femoral neck, and the other line is connected to the point where the femoral head first leaves the best-fitting circle (point A). The AA (green angle) is determined by the angle between these lines. B. The triangular index ratio (TIR) assesses the asphericity of the femoral head by measuring the lateral extension of the bone at a fixed point defined by the ½ radius (r) along the axis of the femoral neck. The center of the femoral head and the radius are determined by the best-fitting circle around the femoral head. From the midpoint of the radius (point H), a perpendicular line is generated to the superolateral cortex of the femoral head-neck junction (point S). The TIR is the ratio of the length of R from point S to point C and the length of r.



Supplementary Figure 2. Recruitment flowchart for the study. Abbreviations: DXA: dual-energy x-ray absorptiometry.



Supplementary Figure 3. The overall and birth-assigned sex-specific distribution of alpha angle and triangular index ratio. A-B. The overall (A) and sex-specific distribution (B) of alpha angle among the included participants. The red dashed line represents the 60° threshold of the alpha angle. C-D. The overall (C) and sex-specific distribution (D) of triangular index ratio among the included participants. The red dashed line represents the 1.05 threshold of the triangular index ratio.

Chapter 3

The prevalence of pincer morphology in early adolescents from the general population: a population-based study (Generation R)

Delong Chen, Fleur Boel, Suzanne de Vos-Jakobs, Pim van Klij, Michiel M.A. van Buuren, Sita M.A. Bierma-Zeinstra, Rintje Agricola

Arthritis Care Res (Hoboken). 2025;77(12):1436-1442.

ABSTRACT

Objective

Pincer morphology can lead to femoroacetabular impingement syndrome (FAIS) and may be a modifiable risk factor for hip osteoarthritis (OA). Currently, no studies investigate the prevalence of pincer morphology in early adolescence–the period when this bony shape likely develops. The purpose of this study was to estimate the prevalence and birth-assigned sex distribution of pincer morphology in early adolescents from the general population in the Netherlands.

Methods

This study was embedded in the Generation R study, a population-based prospective cohort in Rotterdam, the Netherlands. Around the age of 13 years, participants underwent high-resolution dual-energy x-ray absorptiometry (DXA) of their full-body and right hip. The lateral center edge angle (LCEA) was automatically determined based on landmarks outlining the hip contour, and pincer morphology was defined as a LCEA ≥ 40°. The overall and birth-assigned sex-specific prevalence was presented as a percentage with 95% confidence interval (CI).

Results

A total of 3,986 adolescents (median age 13.5 years [2.5th - 97.5th percentile, 13.2 - 14.6]; 46.8% males) were included. The overall prevalence of pincer morphology was 3.1% (95% CI 2.6% - 3.6%). The prevalence in male and female adolescents was 3.0% (95% CI 2.2% - 3.7%) and 3.3% (95% CI 2.5% - 4.0%), respectively.

Conclusion

Among early adolescents from the general population in the Netherlands, the estimated prevalence of pincer morphology was 3.1%. Male and female adolescents had a similar prevalence of pincer morphology. These findings could inform the timing of prevention strategies for pincer morphology, potentially reducing the risk of FAIS and hip OA.

Keywords

Pincer impingement; Femoroacetabular impingement syndrome; Hip osteoarthritis; Prevalence; General population

SIGNIFICANCE AND INNOVATIONS

- Based on a cross-sectional analysis of 3,986 adolescents aged 13 years in a population-based cohort (Generation R), we found that the overall prevalence of pincer morphology was 3.1% (95% CI 2.6% - 3.6%), with similar prevalence in male (3.0% [95% CI 2.2% - 3.7%)] and female adolescents (3.3% [95% CI 2.5% - 4.0%)].
- Given the relatively low prevalence in this population of early adolescents, pincer morphology might also develop further during skeletal maturation of the hip like cam morphology.
- Our findings could inform the timing of prevention strategies for pincer morphology, potentially reducing the risk of femoroacetabular impingement syndrome and hip osteoarthritis.

INTRODUCTION

Osteoarthritis (OA) is a major cause of disability worldwide,[1,2] and femoroacetabular impingement syndrome (FAIS) is an important risk factor of hip OA.[3] FAIS is a motion-related disorder that affects the hip joint and results from abnormal contact between the acetabulum and the femoral head.[4] Depending on the anatomical morphology, FAIS can be distinguished based on the presence of cam and/or pincer morphology. Cam morphology involves an extra bone formation at the anterolateral femoral head-neck junction, while pincer morphology exhibits either focal or global overcoverage of the femoral head by the acetabulum. Pincer morphology is not only associated with FAIS but also may lead to labral tears and circumferential acetabular cartilage damage.[5,6] Although the relationship between pincer morphology and hip OA is controversial,[7-10] a recent study from the Worldwide Collaboration on OsteoArthritis prediCtion for the Hip (World COACH) consortium reported that hips with pincer morphology have a 1.59 (95% confidence interval (CI) 1.16 - 2.20) times higher odds of developing radiographic hip OA within eight years.[11]

Until now, the exact age at which pincer morphology starts to develop has not yet been determined. A retrospective study based on abdominal computed tomography scans from 225 patients aged 2 to 19 without hip complaints reported that pincer morphology first developed at the age of 12 years.[12] To the best of our knowledge, no large population-based epidemiological studies have examined the prevalence of pincer morphology in the early adolescent population. Interestingly, there are more studies available on the development of cam morphology, which show that cam morphology is an adaptive response to vigorous hip loading and develops gradually over time during adolescence.[13,14] However, it is unknown whether this concept holds for pincer morphology as well. Understanding the prevalence of pincer morphology in early adolescence could be critical for informing the timing of prevention strategies that may help slow its progression to hip OA.

We therefore aimed to estimate the overall and birth-assigned sex-specific prevalence of pincer morphology in a general population of 3,986 early adolescents.

METHODS

Study design and participants

The data used in this study were derived from the Generation R study, a population-based prospective cohort aiming to investigate the growth, development and health of children from fetal life onwards in Rotterdam, the Netherlands. A total of 9,778 pregnant women whose delivery was expected between April 2002 and January 2006 were enrolled in the study, and their children became part of the Generation R cohort. Detailed designs and methods on the Generation R cohort were previously described elsewhere.[15] Around the age of 5 (Focus 5), 9 (Focus 9), and 13 years (Focus 13), all participating children and their parents were invited to visit the Generation R research center in the Erasmus MC - Sophia Children's Hospital. For the current study, we included all participants who had both full-body and right hip high-resolution dual-energy x-ray absorptiometry (DXA) scans available at the Focus 13 visit. Exclusion criteria were: 1) participants with an incomplete acetabulum depicted on the DXA image; 2) the presence of movement artifacts; 3) the presence of an artifact in the region of interest. This study was approved by the Medical Ethical Committee of Erasmus Medical Center (MEC-2015-749) and written informed consents were obtained from the participants and their parents. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.[16]

DXA scan

All participants underwent DXA scans of their full-body and right hip by well-trained investigators using the General Electric (GE)-Lunar iDXA densitometer (GE Healthcare, Madison, WI, USA). The full-body and right hip DXA scans were done sequentially with the participants in the same position. Before scanning, all participants were required to remove heavy clothing, shoes and any metal accessories. Afterwards, they were placed in a supine position with the hands flat at their side. The legs were slightly separated and rotated internally, with the big toes touching. The feet were fastened in this position with a Velcro strip to avoid movement.

Pincer morphology

Pincer morphology was determined by the lateral center edge angle (LCEA) on the DXA images. The LCEA defines the bony coverage of the acetabulum by the femoral head. The presence of pincer morphology was defined as a LCEA ≥ 40°.[10, 12, 17] The LCEA was automatically calculated based on landmarks outlining the hip contour with in-house developed software (**Fig. 1**).[18] All landmarks were placed automatically using the Bone-Finder® software (www.bone-finder.com; The University of Manchester, UK).19 A visual inspection was conducted to ensure correct placement of landmarks and manual adjustments (DC and FB) were made when necessary. The LCEA was determined using the following steps: first, the center of the femoral head was automatically computed based on the best-fitting circle around the femoral head. Next, the LCEA was formed by the line from the center of the femoral head to the most lateral bony edge of the acetabulum, and the line from the center of the femoral head perpendicular to the horizontal reference line of the pelvis as determined on the full-body DXA image (Fig. 1).[18] Details of this method have been published previously and showed an intermethod reliability between automatic measurement and manual measurement of 0.95 (95% CI, 0.87 - 0.98).[18]

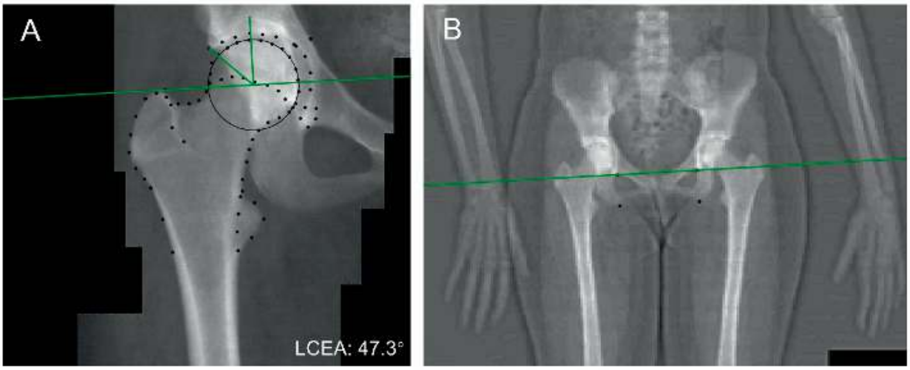


Figure 1. The measurement of lateral center edge angle (LCEA). On the hip dual-energy x-ray absorptiometry (DXA) image, we outlined the shape of the proximal femur and acetabulum with 80 landmarks. The center of the femoral head was automatically determined by the best-fitting circle, which was based on the landmarks outlining the femoral head. The LCEA of 47.3 degrees in this sample (A) is formed by the intersection of two lines: one from the center of the femoral head to the most lateral bony edge of the acetabulum, and the other from the center of the femoral head perpendicular to the horizontal reference line of the pelvis as determined on the full-body DXA image (B).

Data availability statement

The datasets used in the current study are available to researchers upon reasonable request to the management team of the Generation R Study. More detailed information is available on the following website (https://generationr.nl/researchers/collaboration/).

Statistical analyses

We compared the characteristics of included and excluded adolescents using Mann-Whitney U tests for non-normally distributed continuous data, Student's t-tests for normally distributed continuous data, and chi-square tests for categorical data. We estimated the prevalence of pincer morphology and presented it as a percentage with 95% CI stratified by sex. The 95% CI was computed assuming a binomial distribution. The chi-square test was used to examine the difference in birth-assigned sex-specific prevalence. The overall and birth-assigned sex-specific distribution of LCEA was assessed using histograms. To address potential selection bias on our findings, we calculated the weighted prevalence using inverse probability weighting (IPW) adjusting for birth-assigned sex, body mass index (BMI) and height.[20] We performed statistical analyses using R Statistical software (v4.2.1; R Core Team 2022). The 95% CIs were computed using the binom-package [21], histograms were generated using the ggplot2-package[22], and inverse probability of weights was computed using the ipw-package.[23] A p-value < 0.05 was considered as statistically significant.

RESULTS

Characteristics of study participants

A total of 4,929 participants attended the Focus 13 visit, of whom 3,986 participants (81%) had sufficient quality right hip and full-body DXA images available and were analyzed in this study (**Fig. 2**). Table 1 shows the characteristics of the included and excluded early adolescents. The median age of included adolescents was 13.5 years (2.5th - 97.5th percentile, 13.2 - 14.6), and 1,864 (46.8 %) were male adolescents. The median BMI of included adolescents was 19.2 kg/m^2 (2.5th - 97.5th percentile, 15.2 - 29.3), and the mean height was 164.0 cm (SD, 7.9). The excluded adolescents were more frequently males, slightly taller and had slightly lower BMI than the included adolescents (**Table 1**).

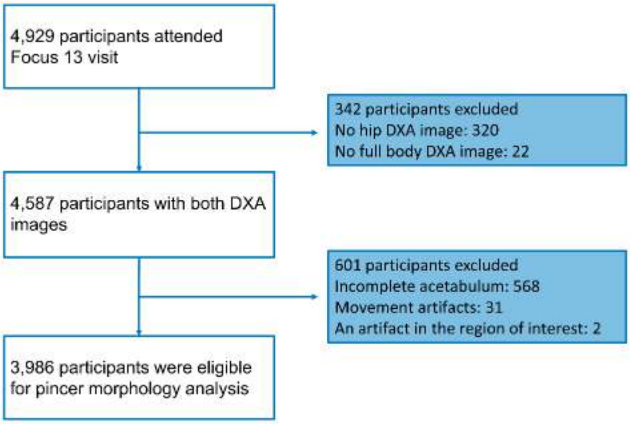


Figure 2. Flowchart of participants. DXA: dual-energy x-ray absorptiometry.

Table 1. Demographic characteristics of included and excluded adolescents.

Characteristic	Included adolescents (n=3,986)	Excluded adolescents (n=943)	P value
Age, years	13.5 (13.2-14.6)	13.6 (13.2-14.7)	0.567
Male, %	1,864 (46.8%)	556 (59.0%)	<0.001
Female, %	2,122 (53.2%)	387 (41.0%)	
BMI, kg/m2	19.2 (15.2-29.3)	18.9 (15.1-28.3)	0.003
Height, cm	164.0 (7.9)	165.9 (8.2)	<0.001

Data are presented as frequencies (percentages) for categorical variables, means (SD) for continuous normally distributed variables and medians (2.5th - 97.5th percentile) for continuous, non-normally distributed variables. BMI: body mass index.

Prevalence of pincer morphology

The overall and birth-assigned sex-specific LCEA distributions are presented in **Fig. 3**. The overall prevalence of pincer morphology was 3.1% (95% CI 2.6% - 3.6%) in early adolescents. In the sex subgroup analysis, the prevalence of pincer morphology was similar in male (3.0% [95%CI 2.2% - 3.7%]) and female participants (3.3% [95%CI 2.5% - 4.0%]) (**Table 2**). The weighted prevalence was similar to the unweighted prevalence in the total group and birth-assigned sex subgroup, as shown in **Table 2**.

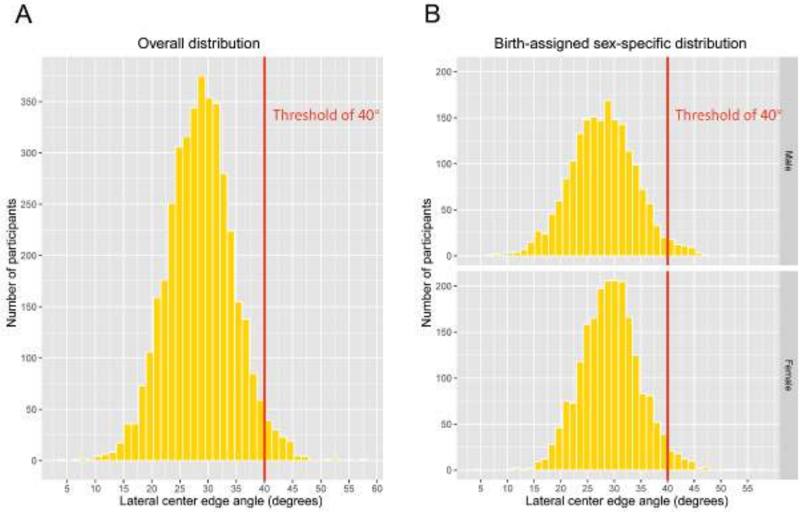


Figure 3. The overall (A) and birth-assigned sex-specific distribution (B) of the lateral center edge angle among the included early adolescents. The red solid line indicates the 40° threshold of the lateral center edge angle.

Table 2. The prevalence of pincer morphology among early adolescents stratified by birth-assigned sex.

Characteristic	LCEA ≥ 40°			
	No. of cases/ total No.	Prevalence, % (95% CI)	χ 2	P value
Unweighted prevalence				
Overall	124/3,986	3.1% (2.6%-3.6%)		
Sex				
Male	55/1,864	3.0% (2.2%-3.7%)	0.298	0.585
Female	69/2,122	3.3% (2.5%-4.0%)		
Weighted prevalence				
Overall	-	3.1% (2.6%-3.7%)		
Sex				
Male	-	3.0% (2.2%-3.8%)	0.203	0.653
Female	-	3.3% (2.5%-4.0%)		

LCEA: lateral center edge angle; CI: confidence interval.

DISCUSSION

This study included 3,986 early adolescents from the general population of Rotterdam, the Netherlands, and used high-resolution DXA scans to determine the prevalence of pincer morphology. We found that the overall prevalence of pincer morphology was 3.1% (95% CI 2.6% - 3.6%) and that it was similar in male (3.0% [95% CI 2.2% - 3.7%]) and female participants (3.3% [95% CI 2.5% - 4.0%]).

The previously reported prevalence of pincer morphology varies widely in literature due to different study populations and inconsistent definitions. To date, there is a paucity of literature on the prevalence of pincer morphology in early adolescents. A population-based study of 2,081 participants (mean age, 18.6 years) in Norway found that 24% of them had a pincer morphology as defined by the presence of a posterior wall sign, crossover sign or excessive acetabular coverage on the anteroposterior (AP) pelvic radiograph.[24] In a cross-sectional study of 6,807 individuals with a mean age of 62.7 years from the UK Biobank, pincer morphology was defined as a LCEA ≥ 45° and found in 8.5% of participants using DXA scans of the left hip.[25] Our results showed the prevalence of pincer morphology was 3.1% in early adolescents, lower than most of the previously reported prevalences in adults. Several factors could explain this result. First, the coverage of the acetabulum may still increase during skeletal maturation, which could lead to the development of pincer morphology. Some prospective studies have investigated the development of cam morphology, and revealed it gradually increases in size during adolescence.[13, 14] Interestingly, the low prevalence of pincer morphology in our study suggests that it might also gradually develop during skeletal growth similar to cam morphology. Prospective studies are needed to confirm this observation. Secondly, we only utilized the LCEA, one of the most commonly used objective measures, to quantify pincer morphology. Other definitions, such as the crossover sign, posterior wall sign and coxa profunda, have also been reported to determine pincer morphology. However, previous studies on these measures reported a poor reliability and specificity.[26-28] The definition of pincer morphology lacks a validated measure and accompanying thresholds, such as for the LCEA. In adults, the LCEA threshold to define pincer morphology varies across studies. Some large prospective studies used a threshold of 33.7° or 40° [10, 29] to investigate the association of pincer morphology and hip OA, while other studies used a threshold of 45°.[11, 25] The recent Lisbon Agreement provided guidance and criteria for defining pincer morphology, including global overcoverage identified by the presence of protrusio acetabuli or a Wiberg center edge angle (WCEA) ≥ 40° (or ≥ 35° with an acetabular index < 0°).[30] We used the same threshold value but chose to use the LCEA instead of the WCEA in this study since pincer impingement usually occurs between the femoral head-neck junction and the most lateral bony edge of the acetabulum.

Research on sex differences in the prevalence of pincer morphology has yielded inconclusive results. A population-based study of 2,596 participants (mean age, 63 years) in the U.S. found that 7% of male participants and 10% of female participants had pincer morphology as defined by a LCEA ≥ 40° or acetabular protrusio in the AP pelvic radiograph.[31] Faber et al. included 6,807 participants (mean age, 62.7 years) from UK biobank in a cross-sectional study, where pincer morphology was defined as LCEA ≥ 45° and present in 8.9% of male participants and 8.1% of female participants on the DXA images of left hips.[25] Our results are in line with these findings and also indicate the similar prevalence of pincer morphology between males and females at a mean age of 13 years. However, results from other studies are contrary to our findings. In a Norwegian population-based cohort study, Laborie et al. studied the AP pelvic radiograph of 2,081 subjects aged 17.2 to 20 years. They found that 34.3% of male participants had at least one sign of pincer morphology (posterior wall sign, crossover sign or excessive acetabular coverage) compared to 16.6% of female participants.[24] The reason for these inconsistent results, which complicate direct comparison, are the heterogeneous populations, diverse imaging modalities (radiographs vs. DXA scans), and variety in definitions for pincer morphology (LCEA thresholds or specific radiographic signs). Although our study found the similar prevalence of pincer morphology between sexes in early adolescence, follow-up of the current cohort can reveal if these sex-specific differences become apparent during or after skeletal maturation.

Selection bias is a critical consideration in this study, as 19% (943/4,929) of adolescents who visited the Generation R research center were excluded due to missing DXA scans or LCEA measurements. To address this selection bias, we applied IPW using a logistic regression model adjusting for sex, BMI, and height—factors that showed statistically significant differences between included and excluded participants (**Table 1**). The similarity between weighted and unweighted prevalence estimates suggests that the selection bias had a limited impact on our findings. However, generalizability to the broader Dutch population requires caution as our study did not weight results to the entire Dutch adolescent population.

The major strength of this study is the population-based design with a large sample size in an early adolescent population. Moreover, automated measurement is fast and highly reproducible for LCEA calculation which helps eliminate observer bias that is inherently present with manual measurement. Our study has some limitations that should be addressed. First, our study only included the right hips for analyses, so the prevalence of pincer morphology was based on hip level rather than person level. Moreover, it is important to note that analyzing only in right hips underestimates the prevalence of pincer morphology at the person level since participants may have unilateral pincer morphology in their left hips. Secondly, DXA is a less common imaging modality for determining pincer morphology. However, it provides sufficient resolution to identify hip morphologies with less radiation burden than radiographs and has been validated against AP pelvic radiographs in adults (intraclass correlation coefficient for LCEA: 0.93 [95% CI 0.91 - 0.94]).[32] Unlike three-dimensional imaging modalities or additional lateral radiographs, the anterior center edge angle could not be obtained from the AP DXA hip images, so this may lead to an underestimation of the prevalence of pincer morphology.[33] Thirdly, care should be taken when generalizing our results to late adolescents due to the potential for further development of pincer morphology when the study population becomes older.

In conclusion, our study provides a large-scale objective evaluation of pincer morphology among early adolescents from the general population in the Netherlands. Pincer morphology was present in 3.1% of early adolescents, and is similarly prevalent in male and female participants. Our study provides valuable data for this age group, serving as a reference for investigating the development of pincer morphology in males and females throughout adolescence. Given its higher prevalence in adults, pincer morphology might also develop further during skeletal maturation of the hip like cam morphology. Our findings could inform the timing of prevention strategies for pincer morphology, potentially reducing the risk of FAIS and hip OA.

REFERENCES

1. Collaborators GBDO. Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Rheumatol 2023; 5(9): e508-e522.
2. Glyn-Jones S, Palmer AJ, Agricola R, Price AJ, Vincent TL, Weinans H, et al. Osteoarthritis. Lancet 2015; 386(9991): 376-387.
3. Agricola R, van Buuren MMA, Kemp JL, Weinans H, Runhaar J, Bierma-Zeinstra SMA. Femoroacetabular impingement syndrome in middle-aged individuals is strongly associated with the development of hip osteoarthritis within 10-year follow-up: a prospective cohort study (CHECK). Br J Sports Med 2024; 58(18): 1061-1067.
4. Griffin DR, Dickenson EJ, O'Donnell J, Agricola R, Awan T, Beck M, et al. The Warwick Agreement on femoroacetabular impingement syndrome (FAI syndrome): an international consensus statement. Br J Sports Med 2016; 50(19): 1169-1176.
5. Beck M, Kalhor M, Leunig M, Ganz R. Hip morphology influences the pattern of damage to the acetabular cartilage: femoroacetabular impingement as a cause of early osteoarthritis of the hip. J Bone Joint Surg Br 2005; 87(7): 1012-1018.
6. Pascual-Garrido C, Li DJ, Grammatopoulos G, Yanik EL, Clohisy JC, Group A. The Pattern of Acetabular Cartilage Wear Is Hip Morphology-dependent and Patient Demographic-dependent. Clin Orthop Relat Res 2019; 477(5): 1021-1033.
7. Nelson AE, Stiller JL, Shi XA, Leyland KM, Renner JB, Schwartz TA, et al. Measures of hip morphology are related to development of worsening radiographic hip osteoarthritis over 6 to 13 year follow-up: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2016; 24(3): 443-450.
8. Nicholls AS, Kiran A, Pollard TC, Hart DJ, Arden CP, Spector T, et al. The association between hip morphology parameters and nineteen-year risk of end-stage osteoarthritis of the hip: a nested case-control study. Arthritis Rheum 2011; 63(11): 3392-3400.
9. Saberi Hosnijeh F, Zuiderwijk ME, Versteeg M, Smeele HT, Hofman A, Uitterlinden AG, et al. Cam Deformity and Acetabular Dysplasia as Risk Factors for Hip Osteoarthritis. Arthritis Rheumatol 2017; 69(1): 86-93.
10. Agricola R, Heijboer MP, Roze RH, Reijman M, Bierma-Zeinstra SM, Verhaar JA, et al. Pincer deformity does not lead to osteoarthritis of the hip whereas acetabular dysplasia does: acetabular coverage and development of osteoarthritis in a nationwide prospective cohort study (CHECK). Osteoarthritis Cartilage 2013; 21(10): 1514-1521.
11. Riedstra NS, Van Buuren MM, Boel F, Ahedi H, Arbabi V, Arden N, et al. Pincer Morphology Is A Risk Factor For Developing Radiographic Hip Osteoarthritis; Data From The World Coach Consortium. Osteoarthritis and Cartilage 2023; 31: S249-S250.
12. Monazzam S, Bomar JD, Dwek JR, Hosalkar HS, Pennock AT. Development and prevalence of femoroacetabular impingement-associated morphology in a paediatric and adolescent population: a CT study of 225 patients. Bone Joint J 2013; 95-B(5): 598-604.
13. Agricola R, Heijboer MP, Ginai AZ, Roels P, Zadpoor AA, Verhaar JA, et al. A cam deformity is gradually acquired during skeletal maturation in adolescent and young male soccer players: a prospective study with minimum 2-year follow-up. Am J Sports Med 2014; 42(4): 798-806.
14. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Cam morphology in young male football players mostly develops before proximal femoral growth plate closure: a prospective study with 5-yearfollow-up. Br J Sports Med 2019; 53(9): 532-538.

15. Kooijman MN, Kruithof CJ, van Duijn CM, Duijts L, Franco OH, van IMH, et al. The Generation R Study: design and cohort update 2017. Eur J Epidemiol 2016; 31(12): 1243-1264.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 2007; 147(8): 573-577.
17. Riedstra NS, Boel F, van Buuren M, Eygendaal D, Bierma-Zeinstra S, Runhaar J, et al. Pincer Morphology Is Not Associated With Hip Osteoarthritis Unless Hip Pain Is Present: Follow-Up Data From a Prospective Cohort Study. Arthritis Care Res (Hoboken) 2024; 76(5): 644-651.
18. Boel F, de Vos-Jakobs S, Riedstra NS, Lindner C, Runhaar J, Bierma-Zeinstra SMA, et al. Automated radiographic hip morphology measurements: An open-access method. Osteoarthr Imaging 2024; 4(2): 100181.
19. Lindner C, Thiagarajah S, Wilkinson JM, arc OC, Wallis GA, Cootes TF. Fully automatic segmentation of the proximal femur using random forest regression voting. IEEE Trans Med Imaging 2013; 32(8): 1462-1472.
20. Sayon-Orea C, Moreno-Iribas C, Delfrade J, Sanchez-Echenique M, Amiano P, Ardanaz E, et al. Inverse-probability weighting and multiple imputation for evaluating selection bias in the estimation of childhood obesity prevalence using data from electronic health records. BMC Med Inform Decis Mak 2020; 20(1): 9.
21. Dorai-Raj S. binom: Binomial Confidence Intervals for Several Parameterizations. 2022.
22. Wickham H. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York 2016.
23. van der Wal WM and Geskus RB. {ipw}: An {R} Package for Inverse Probability Weighting. Journal of Statistical Software. 2011; 43(13): 1-23.
24. Laborie LB, Lehmann TG, Engesaeter IO, Eastwood DM, Engesaeter LB, Rosendahl K. Prevalence of radiographic findings thought to be associated with femoroacetabular impingement in a population-based cohort of 2081 healthy young adults. Radiology 2011; 260(2): 494-502.
25. Faber BG, Ebsim R, Saunders FR, Frysz M, Gregory JS, Aspden RM, et al. Cam morphology but neither acetabular dysplasia nor pincer morphology is associated with osteophytosis throughout the hip: findings from a cross-sectional study in UK Biobank. Osteoarthritis Cartilage 2021; 29(11): 1521-1529.
26. Larson CM, Moreau-Gaudry A, Kelly BT, Byrd JW, Tonetti J, Lavallee S, et al. Are normal hips being labeled as pathologic? A CT-based method for defining normal acetabular coverage. Clin Orthop Relat Res 2015; 473(4): 1247-1254.
27. Zaltz I, Kelly BT, Hetsroni I, Bedi A. The crossover sign overestimates acetabular retroversion. Clin Orthop Relat Res 2013; 471(8): 2463-2470.
28. Nepple JJ, Lehmann CL, Ross JR, Schoenecker PL, Clohisy JC. Coxa profunda is not a useful radiographic parameter for diagnosing pincer-type femoroacetabular impingement. J Bone Joint Surg Am 2013; 95(5): 417-423.
29. Thomas GE, Palmer AJ, Batra RN, et al. Subclinical deformities of the hip are significant predictors of radiographic osteoarthritis and joint replacement in women. A 20 year longitudinal cohort study. Osteoarthritis Cartilage 2014; 22(10): 1504-1510.
30. Mascarenhas VV, Castro MO, Afonso PD, Rego P, Dienst M, Sutter R, et al. The Lisbon Agreement on femoroacetabular impingement imaging—part 2: general issues, parameters, and reporting. Eur Radiol 2021; 31(7): 4634-4651.
31. Raveendran R, Stiller JL, Alvarez C, Renner JB, Schwartz TA, Arden NK, et al. Population-based prevalence of multiple radiographically-defined hip morphologies: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2018; 26(1): 54-61.

32. Boel F, Wortel J, van Buuren MMA, Rivadeneira F, van Meurs JBJ, Runhaar J, et al. DXA images vs. Pelvic Radiographs: Reliability of Hip Morphology Measurements. Osteoarthritis Cartilage 2025; 33(2):283-292.
33. Herfkens J, van Buuren MMA, Riedstra NS, Verhaar JAN, Mascarenhas VV, Agricola R. Adding false-profile radiographs improves detection of developmental dysplasia of the hip, data from the CHECK cohort. J Hip Preserv Surg 2022; 9(1): 3-9.

Chapter 4

Associated factors of primary cam morphology in 4,477 early adolescents: a multi-ethnic, population-based, cross-sectional study (Generation R)

Delong Chen, Fleur Boel, Pim van Klij, Jos Runhaar, Fernando Rivadeneira, Sita M.A. Bierma-Zeinstra, Rintje Agricola

Orthopaedic Journal of Sports Medicine. 2025; 13(12): 23259671251394027.

ABSTRACT

Background

Multiple prospective cohort studies have consistently shown a strong association between cam morphology and the development of hip osteoarthritis. However, associated factors of primary cam morphology (PCM) in the general adolescent population remain largely unexplored.

Purpose

To investigate associated factors of the presence of PCM and increased alpha angle in early adolescents from the general population.

Study Design

Cross-sectional study; Level of evidence, 3.

Methods

We included 4,477 participants with high-resolution dual-energy X-ray absorptiometry (DXA) scans of the right hip from the population-based Generation R cohort in Rotterdam, the Netherlands. The alpha angle was automatically measured using validated methods. PCM was defined as an alpha angle ≥ 60°. We used multivariable logistic and linear regression models to investigate associated factors (demographic, anthropometric, lifestyle factors and proximal femoral physis status) of PCM and increased alpha angle, respectively.

Results

Of the included participants (median age 13.5 years [2.5th - 97.5th percentile, 13.2 - 14.6], 51.6% female, 73.7% European), 151 participants (3.4%) had PCM. Male sex (adjusted odds ratio [aOR] 2.56; 95% CI 1.62 – 4.04) and closed proximal femoral physis (aOR 3.28; 95% CI 2.05 – 5.24) were associated with higher odds of PCM, whereas underweight (aOR 0.42; 95% CI 0.18 – 0.97) was associated with lower odds of PCM. Male sex (β coefficient 2.99; 95% CI 2.40 – 3.58), closed proximal femoral physis (β coefficient 1.22; 95% CI 0.61 – 1.82), cutting sport type (β coefficient 1.07; 95% CI 0.30 – 1.85), overweight (β coefficient 0.89; 95% CI 0.22 – 1.55) and obesity (β coefficient 1.81; 95% CI 0.57 – 3.04) were associated with increased alpha angle. Ethnicity and physical activity frequency were not associated with PCM or increased alpha angle.

Conclusion

Among Dutch early adolescents, male sex and proximal femoral physis closure were associated factors of both PCM and increased alpha angle; while cutting sport type, overweight and obesity were additional modifiable factors of increased alpha angle. These findings could inform potential primary prevention strategies for PCM.

Keywords

Primary cam morphology; hip osteoarthritis; associated factors; early adolescents; general population

What is known about the subject

Primary cam morphology (PCM) develops primarily during adolescence due to physical loading when the proximal femoral physis is open, and thus a potential modifiable risk factor for future hip osteoarthritis (OA). High-impact sports practice has been shown to be associated with PCM, with a dose-response relationship existing between physical activity levels and its development. The current research on the aetiology of PCM predominantly focused on male athletes with small sample sizes. There is a lack of epidemiological studies evaluating the aetiology of PCM in females and amongst multi-ethnic populations.

What this study adds to existing knowledge

This population-based study among 4,477 Dutch early adolescents showed that male sex and closed proximal femoral physis constitute associated factors for both PCM and increased alpha angle; while cutting sport type, overweight, and obesity are additional associated factors for increased alpha angle. This study could inform the development of primary prevention strategies for PCM during this critical period of skeletal maturity, potentially reducing the burden of PCM and its long-term consequences, such as femoroacetabular impingement syndrome and hip OA.

INTRODUCTION

Osteoarthritis (OA) is a common and chronic degenerative disease driven by mechanical, inflammatory, and metabolic factors that is getting increasing attention due to its patient burden [24,25]. Multiple risk factors predispose individuals to hip OA, including genetic predisposition, high-impact sports, high occupational loading and altered hip morphologies [51]. Growing evidence suggests that hip morphology plays an important role in the development of hip OA [2,39,41,45,47]. One of the bony hip morphologies associated with hip OA is cam morphology, which refers to an aspherical femoral head with a bony prominence at the femoral head-neck junction [12]. This bony prominence is most commonly evaluated by the alpha angle in different imaging modalities and planes [12]. When symptoms and clinical signs co-exist, it is known as femoroacetabular impingement syndrome (FAIS) [20]. Cam morphology can lead to intra-articular damage [8,21] when repetitively forced into the acetabulum during hip motion, predisposing some individuals to FAIS, and eventually to the development of hip OA later in life.

Primary cam morphology refers to cam morphology that develops as an adaptive bone response to mechanical loading during various athletic activities in adolescence [12]. Small studies in male athletes reported that it gradually develops from 12 to 13 years onwards [1,37], but its aetiology in early adolescence is not completely understood. In adults, some cross-sectional studies have reported that a higher prevalence of PCM was present in male athletes, particularly in cutting and impingement sports, such as ice hockey [30,38], soccer [18,27,29] and basketball [43]. A dose-response relationship between sporting activity and PCM development has been observed in some studies [16,37,44]. A small retrospective study found male elite soccer players who trained at least four times per week before age 12 were at greater risk of PCM [44]. A cross-sectional study by Palmer et al. demonstrated that adolescent elite soccer athletes had significantly higher alpha angles than amateur athletes and non-athletes [37]. Fernquest et al. confirmed this dose-response relationship in a 3-year longitudinal follow-up, showing that adolescents with higher physical activity levels experienced greater increases in alpha angles [16].

In addition to physical loading from sports participation, ethnicity may be another associated factor. A cross-sectional study involving 445 elite male soccer players found that East Asian players had a lower prevalence of PCM compared to other ethnicities [33]. These ethnic differences may reflect underlying genetic predispositions. However, the current research on the aetiology of PCM is predominantly focused on male athletes with small sample sizes. Associated factors of PCM in the general adolescent population remain largely unexplored. Moreover, there is a lack of epidemiological studies evaluating the aetiology of PCM in females and amongst multi-ethnic populations, which aligns with the priorities set by the latest Oxford Consensus [14]. Understanding modifiable factors of PCM during skeletal maturity may offer a potential window for primary prevention strategies of PCM before it leads to hip OA later in life.

The first aim of our study was to determine factors associated with PCM in early adolescents from the general population. Our second aim was to determine factors associated with increased alpha angle.

METHODS

Study design and participants

We performed a cross-sectional analysis within the Generation R cohort, an ongoing multi-ethnic, population-based, prospective cohort in Rotterdam, the Netherlands, which followed participants from foetal life onwards. The study was approved by the Medical Ethical Committee of the Erasmus University Medical Center (MEC-2015-749), and written informed consent was obtained from all participating adolescents and their parents. More detailed information on the Generation R cohort is available elsewhere [28]. In total, 4,929 participants attended the visit around the age of 13 years (Focus 13), of whom participants with dual-energy x-ray absorptiometry (DXA) scans of their right hips were included in this study. We excluded participants if they lacked alpha angle measurements due to incomplete depiction of the femoral head or neck, movement artifacts and artifacts in the region of interest. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline [50].

DXA scans

In studies involving healthy childhood or adolescent populations where minimizing radiation exposure is a priority, a DXA scan offers a lower-radiation alternative for hip morphology assessment than radiographs. The anteroposterior DXA scans of the right hip of all participants were performed by well-trained investigators using General Electric (GE)-Lunar iDXA densitometer (iDXA Scanner, GE Healthcare, Madison, Wisconsin, USA, 2008). The participants were positioned supine on the scanning table with their legs slightly separated and internally rotated and their big toes touching. The feet were secured in this position using a Velcro strip [7].

Measurements of alpha angle

We defined PCM as an alpha angle ≥ 60° [4,7,49]. To increase statistical power to detect associations, we also used the alpha angle as a continuous outcome, aligning with recommendations from the Oxford consensus that emphasize using continuous measures for research on PCM aetiology [13].

The alpha angle was automatically measured based on landmarks using open-access, in-house developed, validated software [5]. These landmarks outlining the bony contour of the hip were automatically placed on the right hip DXA images using BoneFinder® software [31] (www.bone-finder.com; The University of Manchester, UK). The alpha angle quantifies the deviation of the femoral head from sphericity and is formed between two lines (**Figure 1**). The first line connects the center of the best-fitting circle around the femoral head to the point where the femoral head first departs from the margin of the best-fitting circle, and the second line connects the center of the best-fitting circle

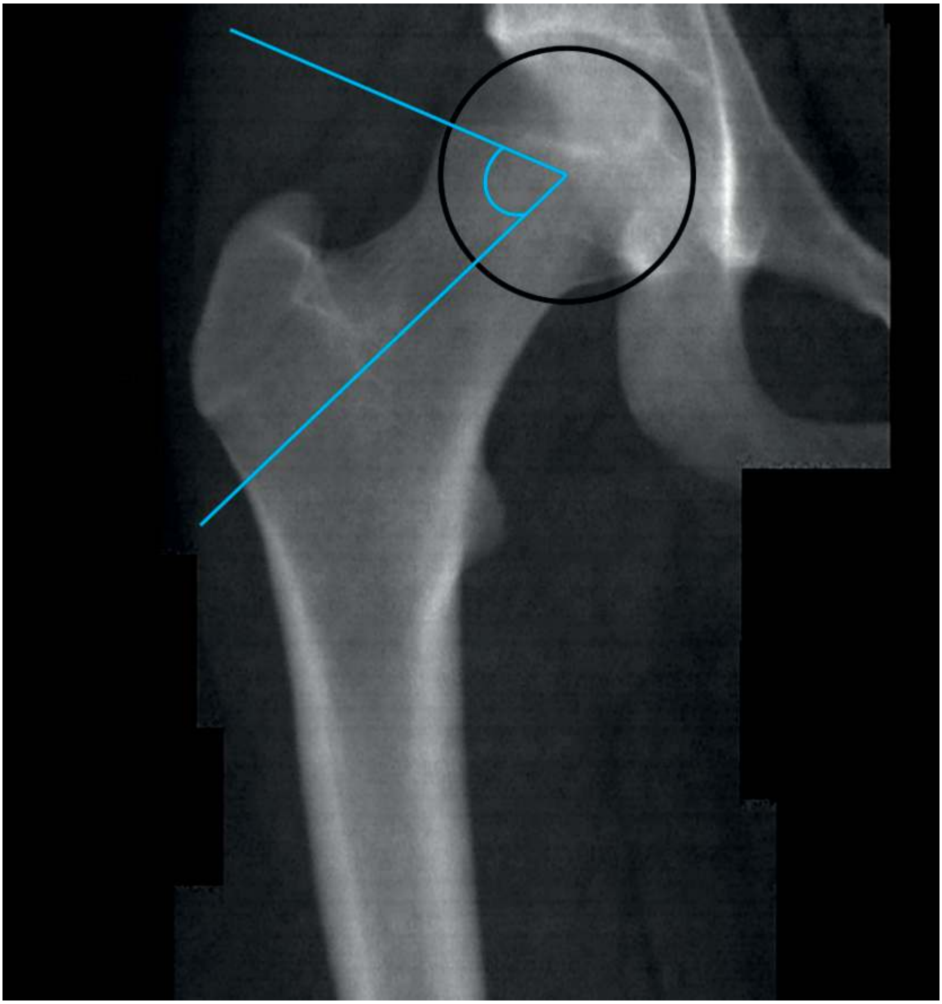


Figure 1. Measurement of alpha angle on a dual-energy x-ray absorptiometry image of the right hip. The alpha angle is formed by the intersection of two lines. From the best-fitting circle center around the femoral head, one line extends to the point where the femoral head first departs from the margin of the best-fitting circle, and the second line extends to the femoral neck center.

to the center of the femoral neck. Detailed methods of measurement were previously described by Boel et al., and a good intermethod reliability (0.81 [95% confidence interval (CI) 0.46 – 0.92]) between manual measurement and the automated method was observed [5] . Furthermore, recent research has demonstrated that alpha angle measurements performed on the supine DXA images are comparable to those on weight-bearing pelvic radiographs in adults, with good reliability (0.72 [95% CI 0.68 – 0.75]) between the two imaging modalities [6].

Associated factors

Demographic factors. The participant's sex assigned at birth was obtained from hospital registries and medical records. The age of participants was calculated at the date of DXA scans. According to the official definition of the Dutch Central Bureau of Statistics, the ethnicity of participants was determined based on the country of birth of their parents, on which information was collected from questionnaires. We categorized the ethnicity of participants into four groups: European (Dutch, Turkish, European, Oceanian, and American Western [including North American]), African (Cape Verdian, Moroccan, Dutch Antilles, Surinamese-Creole and other African), Asian (Indonesia, Surinamese-Hindustani, other Asian) and Other (Surinamese-Unspecified and American non-Western [including South American and Central American]) [10,26].

Proximal femoral physis status. The skeletal maturity of the femoral head was assessed by one investigator (DC) and was determined by the status of the proximal femoral physis (open or closed) on the right hip DXA images. Complete fusion of the physis indicates skeletal maturity, while an open physis indicates skeletal immaturity. The intraobserver and interobserver reliability of the proximal femoral physis evaluation were 0.90 (95% CI 0.85 – 0.94) and 0.87 (95% CI 0.78 – 0.92), respectively [7].

Anthropometric factor. The body mass index (BMI; in kg/m^2) was used to categorize the weight status of adolescents based on their height and weight, which were measured at the research center. Based on the age- and sex-specific BMI cut-offs proposed by the International Obesity Task Force (IOTF) [9], adolescent's weight was categorized into four groups: underweight, normal weight, overweight, and obesity. The specific IOTF BMI cut-offs for the median age of 13.5 years of our study population were as follows: underweight (< 16.11 kg/m^2 for males, < 16.55 kg/m^2 for females), overweight (> 22.24 kg/m^2 for males, >22.90 kg/m^2 for females), and obesity (> 27.26 kg/m^2 for males, > 28.03 kg/m^2 for females).

Lifestyle factors. Detailed information on sport types and physical activity frequency was obtained by self-reported questionnaires. Sport was categorized into seven groups

4

based on the mechanical loading placed on the hip [22,34]: cutting, flexibility, asymmetric, impingement, endurance, contact, or other sports (**Table 1**). For participants involved in two or more sports, the sport with the most time spent was considered as the primary sport, which was then categorized into one of the seven groups mentioned above. Participants were grouped into mixed sports if equal time was spent across multiple sport categories. Due to the limited sample size, contact sport type (N = 21) was grouped into cutting sport type because they share similar movements involving sudden directional changes during sporting activity. We determined the frequency of the physical activity based on the number of days per week that participants were physically active at least one hour, and dichotomized it into two categories: high frequency (four or more days per week) and low frequency (less than four days per week) [44].

Table 1. Sport categories based on mechanical loading on the hip.

Categories	Specific sports
Cutting	Soccer, Hockey, Basketball, Korfball, Handball, Skiing, Surfing, Skateboarding, Longboarding
Flexibility	Dancing, Judo/ (Kick) Boxing/ Martial arts, Gymnastics, Free running, Rock climbing, Synchronized swimming, Figure skating, Yoga, Combat sport
Asymmetric	Baseball, Softball, Tennis, Volleyball, Badminton, Table tennis, Cricket, Golf, Squash, Sword fighting
Impingement	Horseback riding, Water polo, Rowing, CrossFit, Skating, Ice hockey, Weight lifting, Gym, Fitness
Endurance	Athletics, Running, Swimming, Cycling/Mountain biking
Contact	Rugby, Football
Other	Sailing, Archery, Diving, Darts, Scootering, Karting

Statistical analyses

We used multivariable logistic and linear regression models to examine factors associated with PCM and increased alpha angle in the general population. The reference groups selected for each categorical variable were female sex, European ethnicity, open proximal femoral physis, normal weight, low physical activity frequency and no participation in sports. Effect estimates were reported as adjusted odds ratios (aOR) for binary outcomes or adjusted β coefficients for continuous outcomes with corresponding 95% CI, which were visualized with forest plots. We examined linear regression model assumptions (normality, homoscedasticity and multicollinearity) and did not find violations.

Missing data for ethnicity (2.2% missing), sport types (17.7% missing), and physical activity frequency (31.7% missing) were assumed to be missing at random. To maintain statistical power and minimize potential bias from missing data, we handled missing data using the multiple imputations by chained equations (MICE) method in which 40 datasets with 30 iterations were created, and reported the pooled results. We found no major differences in participant characteristics between the observed and the imputed datasets (**Supplemental Table 1**). To assess the robustness of our findings, we conducted two sensitivity analyses. First, we repeated analyses in the complete cases dataset to evaluate whether missing data patterns influence the primary findings. Secondly, we excluded mixed sports from our analysis to assess the impact of a single sport type on PCM. We conducted statistical analyses using R Statistical Software (v4.2.1; R Core Team 2022), constructed forest plots using "forest plot" package [19], and performed multiple imputations using "mice" package [46].

RESULTS

Participant characteristics

Figure 2 shows the flowchart of participants. A total of 4,477 participants were included in the current analyses. **Table 2** shows the characteristics of the included participants. The median alpha angle was 43.4 degrees (2.5th - 97.5th percentile, 35.4 - 64.0). The overall prevalence of PCM was 3.4% (N = 151; 84 males and 67 females) in early adolescents [7].

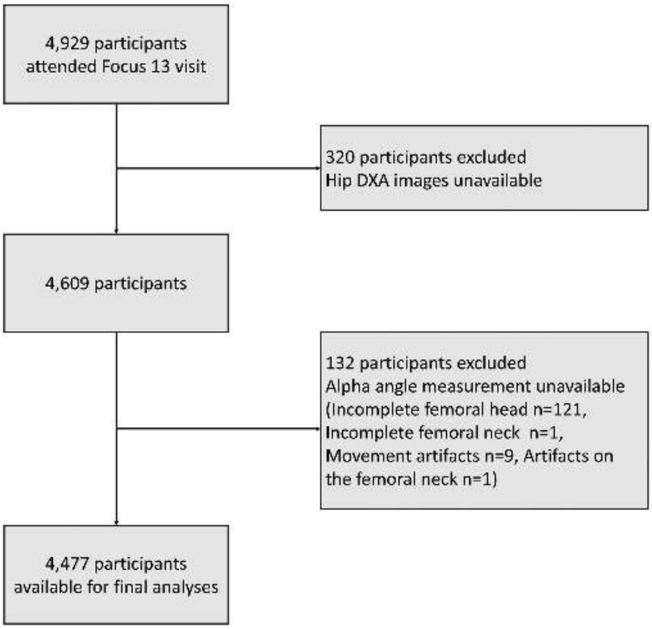


Figure 2. Flowchart of participants included for analyses. DXA: dual-energy x-ray absorptiometry.

Table 2. Characteristics of the study population.

Characteristic	Adolescents in study (N = 4,477)
Age, years	13.5 (13.2-14.6)
Sex	
Female	2,311 (51.6%)
Male	2,166 (48.4%)
Ethnicity	
European	3,368 (75.2%)
African	713 (15.9%)
Asian	264 (5.9%)
Other	132 (2.9%)
Proximal femoral physis status	
Open	2,626 (58.7%)
Closed	1,851 (41.3%)
Weight categories	
Underweight	468 (10.4%)
Normal weight	3,280 (73.3%)
Overweight	578 (12.9%)
Obesity	151 (3.4%)
Physical activity frequency	
Low	1,526 (34.1%)
High	2,951 (65.9%)
Sport types	
None	761 (17.0%)
Cutting	1,720 (38.4%)
Flexibility	587 (13.1%)
Asymmetric	274 (6.1%)
Impingement	276 (6.2%)
Endurance	284 (6.4%)
Other	41 (0.9%)
Mixed	534 (11.9%)
Primary cam morphology	151 (3.4%)
Alpha angle, degrees	43.4 (35.4-64.0)

Note: Values are medians (2.5th - 97.5th percentile) or frequencies (percentages) based on imputed data. The percentages of missing values before multiple imputation were 2.2% (N = 100) for ethnicity, 17.7% (N = 792) for sport types and 31.7% (N = 1,419) for physical activity frequency.

Associated factors of primary cam morphology among early adolescents

Characteristic	aOR (95%CI)	P value
Age	1.19 (0.82, 1.73)	0.360
Sex		
Female	1 (Ref.)	
Male	2.56 (1.62, 4.04)	<0.001
Ethnicity		
European	1 (Ref.)	
African	0.86 (0.54, 1.37)	0.525
Asian	0.65 (0.28, 1.53)	0.327
Other	1.34 (0.57, 3.14)	0.502
Proximal femoral physis status		
Open	1 (Ref.)	
Closed	3.28 (2.05, 5.24)	<0.001
Weight categories		
Underweight	0.42 (0.18, 0.97)	0.043
Normal weight	1 (Ref.)	
Overweight	0.89 (0.55, 1.44)	0.629
Obesity	1.03 (0.43, 2.45)	0.944
Physical activity frequency		
Low	1 (Ref.)	
High	1.32 (0.85, 2.07)	0.219
Sport types		
None	1 (Ref.)	
Cutting	1.08 (0.62, 1.87)	0.783
Flexibility	0.57 (0.26, 1.22)	0.147
Asymmetric	0.75 (0.31, 1.86)	0.540
Impingement	0.56 (0.20, 1.52)	0.254
Endurance	1.11 (0.51, 2.44)	0.792
Other	2.54 (0.69, 9.31)	0.160
Mixed	0.84 (0.40, 1.76)	0.642

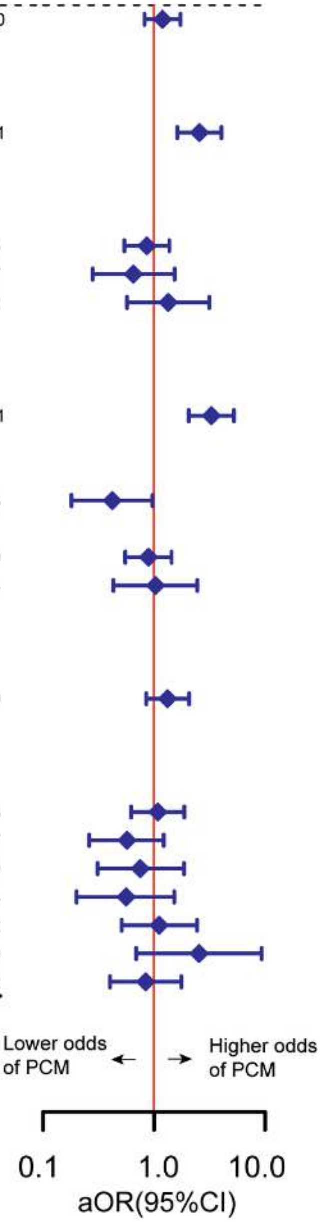


Figure 3. Associated factors of primary cam morphology among early adolescents. The multivariable logistic regression analysis was based on the imputed dataset and was the pooled result of 40 datasets. CI: confidence interval; aOR: adjusted odds ratio; PCM: primary cam morphology.

Associated factors of PCM

In the multivariable logistic regression analysis model, male sex (aOR 2.56, 95% CI 1.62 – 4.04) and closed proximal femoral physis (aOR 3.28, 95% CI 2.05 – 5.24) were associated with higher odds of PCM, and underweight (aOR 0.42, 95% CI 0.18 – 0.97) was associated with lower odds of PCM in this study population (**Figure 3**).

Associated factors of increased alpha angle among early adolescents

Characteristic	Adjusted β (95%CI)	P value
Age	0.53 (−0.06, 1.13)	0.079
Sex		
Female	0 (Ref.)	
Male	2.99 (2.40, 3.58)	<0.001
Ethnicity		
European	0 (Ref.)	
African	−0.41 (−1.04, 0.22)	0.198
Asian	−0.55 (−1.52, 0.41)	0.263
Other	0.29 (−1.03, 1.61)	0.667
Proximal femoral physis status		
Open	0 (Ref.)	
Closed	1.22 (0.61, 1.82)	<0.001
Weight categories		
Underweight	−1.08 (−1.81, −0.35)	0.004
Normal weight	0 (Ref.)	
Overweight	0.89 (0.22, 1.55)	0.009
Obesity	1.81 (0.57, 3.04)	0.004
Physical activity frequency		
Low	0 (Ref.)	
High	0.39 (−0.18, 0.95)	0.176
Sport types		
None	0 (Ref.)	
Cutting	1.07 (0.30, 1.85)	0.007
Flexibility	−0.38 (−1.28, 0.51)	0.401
Asymmetric	0.36 (−0.80, 1.52)	0.547
Impingement	−0.36 (−1.50, 0.77)	0.530
Endurance	0.96 (−0.25, 2.17)	0.119
Other	0.93 (−1.61, 3.48)	0.472
Mixed	0.42 (−0.53, 1.38)	0.384

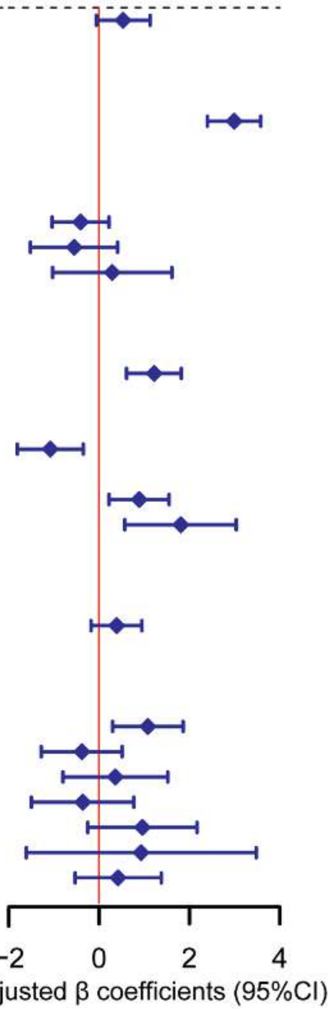


Figure 4. Associated factors of increased alpha angle among early adolescents. The multivariable linear regression analysis was based on the imputed dataset and was the pooled result of 40 datasets. CI: confidence interval.

Associated factors of increased alpha angle

In the multivariable linear regression model, male adolescents had an alpha angle that was on average 2.99° (95% CI 2.40 – 3.58; p-value < 0.001) higher than female adolescents (Figure 4). Participants with closed proximal femoral physis had an alpha angle that was on average 1.22° (95% CI 0.61 – 1.82; p-value < 0.001) higher than those with an open proximal femoral physis. Compared to adolescents with normal weight, those with underweight had an alpha angle that was on average 1.08° (95% CI -1.81 – -0.35) lower, and those with overweight and those with obesity had an alpha angle that was on average 0.89° (95% CI 0.22 – 1.55; p-value = 0.009) and 1.81° (95% CI 0.57 – 3.04; p-value = 0.004) higher, respectively. Adolescents who played cutting sports had an alpha angle that was on average 1.07° (95% CI 0.30 – 1.85; p-value = 0.007) higher than those who did not play sports.

Sensitivity analyses

When we repeated the analyses using the complete cases dataset (N = 2,874), we observed similar directions and strengths of the effect estimates in most variables (**Supplemental Table 2 and Supplemental Table 3**). However, the associations of increased alpha angle with overweight and obesity were attenuated and became statistically non-significant (**Supplemental Table 3**). When we excluded mixed sports from our analyses (**Supplemental Table 4 and Supplemental Table 5**), the association between overweight and increased alpha angle became statistically non-significant, while the association for obesity remained significant (**Supplemental Table 5**).

4

DISCUSSION

In this multi-ethnic population-based study, we observed that male sex and closed proximal femoral physis were associated with higher odds, and underweight with lower odds of PCM in early adolescents from the general population. In addition, male sex, closed proximal femoral physis, cutting sport type, overweight, and obesity were associated with increased alpha angle.

Due to its high prevalence, PCM is frequently studied within male athletic populations [32,35,52]. In adults, Doran et al. compared the prevalence of PCM across sport types in a systematic review and suggested that athletes participating in cutting, impingement and contact sports had a higher prevalence of PCM [15]. Moreover, Philippon et al. found that male ice hockey players were 4.5 times more likely to develop PCM than skiers [38]. This indicated that specific sport types and hip loading patterns significantly influence the development of PCM. We observed an association between increased alpha angle and cutting sport type in early adolescents from the general population, which might be primarily driven by the high rotational and shear forces exerted on the proximal femoral physis during rapid changes of direction. A finite element analysis revealed that there is a trigger for extra bone formation at the anterolateral head-neck junction when loading patterns of external rotation and flexion are applied to a hip with an open proximal femoral physis [40].

There is variation in the reported relationship between body weight and alpha angle in the literature, seemingly depending on the study population. In this study, overweight and obesity were associated with increased alpha angle in early adolescents from the general population in the main analysis, but these associations became non-significant in the sensitivity analysis of the complete cases. These findings were supported by Novais et al., who found that a higher BMI percentile was associated with increased alpha angle in a retrospective study based on pelvic computed tomography from 128 male and female adolescents aged 12 to 18 years without hip complaints [36]. The mechanism of association between higher weight categories and increased alpha angle is unclear and may involve multiple factors such as altered metabolic and hormonal profiles and increased mechanical loading [42]. However, some cross-sectional and longitudinal studies have found no association between BMI and increased alpha angle in male athletes [16,37]. This discrepancy could be attributed to the different loading patterns and physical demands between the athletic and general populations. Athletes experience high-impact and repetitive loading on their hips due to sport-specific movements (e.g. hip flexion and rotation), which may lead to the development of PCM independently of BMI. In contrast, the general population experienced less sport-specific hip loading, and they may be more influenced by overall body weight. The sensitivity analysis in our study showed that the relationship between alpha angle and overweight and obesity became non-significant when the sample size decreased, suggesting that this association might be weak. Therefore, larger cohort studies are needed to validate this association across different demographic groups.

Some small prospective studies in male athletes have shown that PCM gradually increases until proximal femoral physis closure [3,48]. A cross-sectional study of 210 individuals (103 male soccer players and 107 controls) aged 9 to 18 years found that individuals with a closed proximal femoral physis exhibited a maximum cartilage alpha angle 13 degrees higher than those with an open proximal femoral physis on MRI [37]. Fernquest et al. performed a 3-year longitudinal study of 140 individuals (69 male soccer players and 71 controls) and observed no significant increase in alpha angle in individuals with a closed proximal femoral physis at baseline [16]. Similarly, our study suggested that skeletal maturity of the femoral head (closed proximal femoral physis) was associated with the presence of PCM and increased alpha angle in the general population. This implies that the process of femoral head skeletal maturity is a critical window during which adolescents may be at increased risk for the development of PCM. In this study, the participants with an open proximal femoral physis still have the potential to develop PCM when they become older. The timing of potential primary prevention strategies for PCM in the general population should therefore precede the closure of the proximal femoral physis.

To our knowledge, this is the first study to identify associated factors of PCM in the general population. The presence of PCM is common in the general population [11,17], and is known to be a strong and potentially modifiable risk factor for hip OA. Our results are of aetiological and potentially preventive interest, but they may not directly be applied to clinical settings, where patients typically present due to symptoms. Primary prevention of PCM probably involves avoiding early sport specialization or reducing the axial loading as the development of PCM is strongly associated with cutting and impingement sports practicing (e.g. soccer, basketball, ice hockey) and higher levels of physical activity during skeletal growth. However, primary prevention presents several significant challenges [23]. First, while PCM develops during adolescence, intraarticular damages related to PCM may not occur until young adulthood [8,21]. A large proportion of individuals with PCM remain asymptomatic during adolescence. This raises concerns about overdiagnosis and unnecessary interventions, as not all cases will progress to FAIS and hip OA. Secondly, recommendations to reduce external loading during adolescence may conflict with guidelines promoting regular physical activity for overall health and development. Thirdly, the specific types and volume of loading contribute to the development of PCM remain unclear. Without this knowledge, it may be premature to implement primary prevention strategies. Future longitudinal studies are needed to identify which individuals are at higher risk for symptomatic progression or hip OA, and to develop targeted preventive strategies accordingly.

The major strengths of our study include a multi-ethnic, population-based design with a large sample size in early adolescents and the use of automated measures of the alpha angle to define PCM. Our study also had limitations. First, causal inferences cannot be drawn from the cross-sectional design of this study. Secondly, we only obtained DXA scans of the right hip, which underestimates the presence of PCM as it can be present in the left hips. Thirdly, our study only provided the AP view of the right hip, which might result in an underestimation of the prevalence of PCM compared to the Dunn view and three-dimensional imaging (e.g. magnetic resonance imaging) since cam morphology is a three-dimensional entity that typically develops at the anterolateral femoral head-neck junction of the hip. Fourthly, using the alpha angle as a continuous outcome may reduce its clinical relevance. In particular, small increments of increase in low alpha angles (e.g. between 35° and 45°) may not be meaningful in clinical practice and are unlikely to be associated with FAIS and hip OA. Fifthly, by focusing only on the self-reported sport types and the frequency of physical activity, our study may not capture the full impact of physical activity on PCM. Using objective measurement tools in future studies could provide a more comprehensive, objective assessment of physical activity and its relationship to PCM than questionnaires. Another limitation is a relatively high percentage of missing data on sport types (17.7%) and physical activity frequency (31.7%). This may lead to the potential of biased estimates although we utilized MICE to handle the missingness. Moreover, our study captures only a snapshot of early adolescence, and the results may not be generalized to young adults. Since PCM develops over time in adolescence, additional participants could still develop PCM in the future. Therefore, these findings should be generalized cautiously beyond this age group, and be followed up in the future. Lastly, although our study considered multiple associated factors, other important factors — such as acetabular morphology, femoral torsion, and other factors contributing to hip instability — were not included in the current analysis. These factors may influence PCM in early adolescents and warrant further investigation in future studies.

In conclusion, our cross-sectional analyses from the Generation R study found a PCM prevalence of 3.4% and associations of male sex, closed proximal femoral physis and underweight with the presence of PCM in early adolescents. Male sex, closed proximal femoral physis, cutting sport type, overweight and obesity were associated with increased alpha angle in early adolescents from the general population. These findings could inform potential primary prevention strategies for PCM in the general population during critical growth periods. Future longitudinal studies are required to explore the causality of these associations.

REFERENCES

1. Agricola R, Bessems JH, Ginai AZ, et al. The development of Cam-type deformity in adolescent and young male soccer players. *Am J Sports Med.* 2012;40(5):1099-1106.
2. Agricola R, Heijboer MP, Bierma-Zeinstra SM, et al. Cam impingement causes osteoarthritis of the hip: a nationwide prospective cohort study (CHECK). *Ann Rheum Dis.* 2013;72(6):918-923.
3. Agricola R, Heijboer MP, Ginai AZ, et al. A cam deformity is gradually acquired during skeletal maturation in adolescent and young male soccer players: a prospective study with minimum 2-year follow-up. *Am J Sports Med.* 2014;42(4):798-806.
4. Agricola R, Waarsing JH, Thomas GE, et al. Cam impingement: defining the presence of a cam deformity by the alpha angle: data from the CHECK cohort and Chingford cohort. *Osteoarthritis Cartilage.* 2014;22(2):218-225.
5. Boel F, de Vos-Jakobs S, Riedstra NS, et al. Automated radiographic hip morphology measurements: An open-access method. *Osteoarthr Imaging.* 2024;4(2):100181.
6. Boel F, Wortel J, van Buuren MMA, et al. DXA images vs. pelvic radiographs: Reliability of hip morphology measurements. *Osteoarthritis Cartilage.* 2025;33(2):283-292.
7. Chen D, Boel F, van Klij P, et al. The prevalence of primary cam morphology in early adolescents from the general population: A population-based study (Generation R). *Osteoarthritis Cartilage.* 2025;33(5):633-637.
8. Claes PAM, Hanff DF, Weir A, et al. The Association Between the Development of Cam Morphology During Skeletal Growth in High-Impact Athletes and the Presence of Cartilage Loss and Labral Damage in Adulthood: A Prospective Cohort Study With a 12-Year Follow-up. *Am J Sports Med.* 2024;52(10):2555-2564.
9. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatr Obes.* 2012;7(4):284-294.
10. den Hollander WJ, Schalekamp-Timmermans S, Holster IL, et al. Helicobacter pylori colonization and pregnancies complicated by preeclampsia, spontaneous prematurity, and small for gestational age birth. *Helicobacter.* 2017;22(2).
11. Dickenson EJ, Wall PDH, Hutchinson CE, Griffin DR. The prevalence of cam hip morphology in a general population sample. *Osteoarthritis Cartilage.* 2019;27(3):444-448.
12. Dijkstra HP, Ardern CL, Serner A, et al. Primary cam morphology; bump, burden or bog-standard? A concept analysis. *Br J Sports Med.* 2021;55(21):1212-1221.
13. Dijkstra HP, Mc Auliffe S, Ardern CL, et al. Oxford consensus on primary cam morphology and femoroacetabular impingement syndrome: part 1-definitions, terminology, taxonomy and imaging outcomes. *Br J Sports Med.* 2022;57(6):325-341.
14. Dijkstra HP, Mc Auliffe S, Ardern CL, et al. Oxford consensus on primary cam morphology and femoroacetabular impingement syndrome: part 2-research priorities on conditions affecting the young person's hip. *Br J Sports Med.* 2022;57(6):342-358.
15. Doran C, Pettit M, Singh Y, Sunil Kumar KH, Khanduja V. Does the Type of Sport Influence Morphology of the Hip? A Systematic Review. *Am J Sports Med.* 2022;50(6):1727-1741.
16. Fernquest S, Palmer A, Gimpel M, et al. A longitudinal cohort study of adolescent elite footballers and controls investigating the development of cam morphology. *Sci Rep.* 2021;11(1):18567.
17. Frank JM, Harris JD, Erickson BJ, et al. Prevalence of Femoroacetabular Impingement Imaging Findings in Asymptomatic Volunteers: A Systematic Review. *Arthroscopy.* 2015;31(6):1199-1204.
18. Gerhardt MB, Romero AA, Silvers HJ, et al. The prevalence of radiographic hip abnormalities in elite soccer players. *Am J Sports Med.* 2012;40(3):584-588.

19. Gordon M LT. forestplot: Advanced Forest Plot Using 'grid' Graphics. 2023.
20. Griffin DR, Dickenson EJ, O'Donnell J, et al. The Warwick Agreement on femoroacetabular impingement syndrome (FAI syndrome): an international consensus statement. *Br J Sports Med.* 2016;50(19):1169-1176.
21. Heerey J, Kemp J, Agricola R, et al. Cam morphology is associated with MRI-defined cartilage defects and labral tears: a case-control study of 237 young adult football players with and without hip and groin pain. *BMJ Open Sport Exerc Med.* 2021;7(4):e001199.
22. Heerey JJ, Kemp JL, Mosler AB, et al. What is the Prevalence of Hip Intra-Articular Pathologies and Osteoarthritis in Active Athletes with Hip and Groin Pain Compared with Those Without? A Systematic Review and Meta-Analysis. *Sports Med.* 2019;49(6):951-972.
23. Heerey JJ, van Klij P, Agricola R, et al. Preventing hip osteoarthritis in athletes: is it really a mission impossible? *Br J Sports Med.* 2024;58(9):465-467.
24. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet.* 2019;393(10182):1745-1759.
25. Hunter DJ, Schofield D, Callander E. The individual and socioeconomic impact of osteoarthritis. *Nat Rev Rheumatol.* 2014;10(7):437-441.
26. Jansen MAE, Beth SA, van den Heuvel D, et al. Ethnic differences in coeliac disease autoimmunity in childhood: the Generation R Study. *Arch Dis Child.* 2017;102(6):529-534.
27. Johnson AC, Shaman MA, Ryan TG. Femoroacetabular impingement in former high-level youth soccer players. *Am J Sports Med.* 2012;40(6):1342-1346.
28. Kooijman MN, Kruithof CJ, van Duijn CM, et al. The Generation R Study: design and cohort update 2017. *Eur J Epidemiol.* 2016;31(12):1243-1264.
29. Lahner M, Walter PA, von Schulze Pellengahr C, et al. Comparative study of the femoroacetabular impingement (FAI) prevalence in male semiprofessional and amateur soccer players. *Arch Orthop Trauma Surg.* 2014;134(8):1135-1141.
30. Lerebours F, Robertson W, Neri B, et al. Prevalence of Cam-Type Morphology in Elite Ice Hockey Players. *Am J Sports Med.* 2016;44(4):1024-1030.
31. Lindner C, Thiagarajah S, Wilkinson JM, et al. Fully automatic segmentation of the proximal femur using random forest regression voting. *IEEE Trans Med Imaging.* 2013;32(8):1462-1472.
32. Morris WZ, Li RT, Liu RW, Salata MJ, Voos JE. Origin of Cam Morphology in Femoroacetabular Impingement. *Am J Sports Med.* 2018;46(2):478-486.
33. Mosler AB, Crossley KM, Waarsing JH, et al. Ethnic Differences in Bony Hip Morphology in a Cohort of 445 Professional Male Soccer Players. *Am J Sports Med.* 2016;44(11):2967-2974.
34. Nawabi DH, Bedi A, Tibor LM, Magennis E, Kelly BT. The demographic characteristics of high-level and recreational athletes undergoing hip arthroscopy for femoroacetabular impingement: a sports-specific analysis. *Arthroscopy.* 2014;30(3):398-405.
35. Nepple JJ, Vigdorchik JM, Clohisy JC. What Is the Association Between Sports Participation and the Development of Proximal Femoral Cam Deformity? A Systematic Review and Meta-analysis. *Am J Sports Med.* 2015;43(11):2833-2840.
36. Novais EN, Shefelbine SJ, Kienle KP, et al. Body Mass Index Affects Proximal Femoral but Not Acetabular Morphology in Adolescents Without Hip Pathology. *J Bone Joint Surg Am.* 2018;100(1):66-74.
37. Palmer A, Fernquest S, Gimpel M, et al. Physical activity during adolescence and the development of cam morphology: a cross-sectional cohort study of 210 individuals. *Br J Sports Med.* 2018;52(9):601-610.

38. Philippon MJ, Ho CP, Briggs KK, Stull J, LaPrade RF. Prevalence of increased alpha angles as a measure of cam-type femoroacetabular impingement in youth ice hockey players. *Am J Sports Med.* 2013;41(6):1357-1362.
39. Riedstra NS, Vinge R, Herfkens J, et al. Acetabular dysplasia and the risk of developing hip osteoarthritis at 2,5,8, and 10 years follow-up in a prospective nationwide cohort study (CHECK). *Semin Arthritis Rheum.* 2023;60:152194.
40. Roels P, Agricola R, Oei EH, et al. Mechanical factors explain development of cam-type deformity. *Osteoarthritis Cartilage.* 2014;22(12):2074-2082.
41. Saberi Hosnijeh F, Zuiderwijk ME, Versteeg M, et al. Cam Deformity and Acetabular Dysplasia as Risk Factors for Hip Osteoarthritis. *Arthritis Rheumatol.* 2017;69(1):86-93.
42. Shapses SA, Sukumar D. Bone metabolism in obesity and weight loss. *Annu Rev Nutr.* 2012;32:287-309.
43. Siebenrock KA, Ferner F, Noble PC, et al. The cam-type deformity of the proximal femur arises in childhood in response to vigorous sporting activity. *Clin Orthop Relat Res.* 2011;469(11):3229-3240.
44. Tak I, Weir A, Langhout R, et al. The relationship between the frequency of football practice during skeletal growth and the presence of a cam deformity in adult elite football players. *Br J Sports Med.* 2015;49(9):630-634.
45. Tang J, van Buuren MMA, Riedstra NS, et al. Cam morphology is strongly and consistently associated with development of radiographic hip osteoarthritis throughout 4 follow-up visits within 10 years. *Osteoarthritis Cartilage.* 2023;31(12):1650-1656.
46. van Buuren S G-OK. mice: Multivariate Imputation by Chained Equations in R. *Journal of Statistical Software.* 2011;45:1-67.
47. van Klij P, Heerey J, Waarsing JH, Agricola R. The Prevalence of Cam and Pincer Morphology and Its Association With Development of Hip Osteoarthritis. *J Orthop Sports Phys Ther.* 2018;48(4):230-238.
48. van Klij P, Heijboer MP, Ginai AZ, et al. Cam morphology in young male football players mostly develops before proximal femoral growth plate closure: a prospective study with 5-yearfollow-up. *Br J Sports Med.* 2019;53(9):532-538.
49. van Klij P, Reiman MP, Waarsing JH, et al. Classifying Cam Morphology by the Alpha Angle: A Systematic Review on Threshold Values. *Orthop J Sports Med.* 2020;8(8):2325967120938312.
50. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med.* 2007;147(8):573-577.
51. Whittaker JL, Runhaar J, Bierma-Zeinstra S, Roos EM. A lifespan approach to osteoarthritis prevention. *Osteoarthritis Cartilage.* 2021;29(12):1638-1653.
52. Zadpoor AA. Etiology of Femoroacetabular Impingement in Athletes: A Review of Recent Findings. *Sports Med.* 2015;45(8):1097-1106.

SUPPLEMENTARY MATERIALS

Supplementary Table 1. Observed and imputed characteristics of included participants (N = 4,477).

Characteristic	Observed dataset	Imputed dataset
Age, years	13.5 (13.1-14.6)	NA
Sex		
Female	2,311 (51.6%)	NA
Male	2,166 (48.4%)	NA
Ethnicity		
European	3,298 (75.3%)	3,368 (75.2%)
African	693 (15.8%)	713 (15.9%)
Asian	257 (5.9%)	264 (5.9%)
Other	129 (3.0%)	132 (3.0%)
Proximal femoral physis status		
Open	2,626 (58.7%)	NA
Closed	1,851 (41.3%)	NA
Weight categories		
Underweight	468 (10.4%)	NA
Normal weight	3,280 (73.3%)	NA
Overweight	578 (12.9%)	NA
Obesity	151 (3.4%)	NA
Physical activity frequency		
Low	1,004 (32.8%)	1,526 (34.1%)
High	2,054 (67.2%)	2,951 (65.9%)
Sport types		
None	598 (16.2%)	761 (17.0%)
Cutting	1,434 (38.9%)	1,720 (38.4%)
Flexibility	483 (13.1%)	587 (13.1%)
Asymmetric	229 (6.2%)	274 (6.1%)
Impingement	227 (6.2%)	276 (6.2%)
Endurance	232 (6.3%)	284 (6.4%)
Other	34 (0.9%)	41 (0.9%)
Mixed	448 (12.2%)	534 (11.9%)
Primary cam morphology	151 (3.4%)	NA
Alpha angle, degrees	43.4 (35.4-64.0)	NA

Note: Values are in medians (2.5th - 97.5th percentile) for continuous variables and frequencies (percentages) for categorical variables.

Supplementary Table 2. Associated factors of primary cam morphology among early adolescents in the complete case dataset (N = 2,874).

	Adjusted OR (95% CI)	**P value**
Age	1.18 (0.64, 2.01)	0.572
Sex		
Female	1 (Ref.)	
Male	2.09 (1.14, 3.88)	0.018
Ethnicity		
European	1 (Ref.)	
African	0.78 (0.35, 1.52)	0.496
Asian	0.81 (0.24, 2.03)	0.688
Other	1.34 (0.32, 3.82)	0.631
Proximal femoral physis status		
Open	1 (Ref.)	
Closed	3.01 (1.62, 5.62)	<0.001
Weight categories		
Underweight	0.20 (0.03, 0.64)	0.025
Normal weight	1 (Ref.)	
Overweight	0.68 (0.30, 1.36)	0.317
Obesity	0.45 (0.02, 2.17)	0.437
Physical activity frequency		
Low	1 (Ref.)	
High	1.38 (0.84, 2.35)	0.219
Sport types		
None	1 (Ref.)	
Cutting	1.06 (0.54, 2.17)	0.879
Flexibility	0.80 (0.32, 1.90)	0.612
Asymmetric	0.79 (0.25, 2.18)	0.664
Impingement	0.66 (0.18, 1.94)	0.482
Endurance	1.20 (0.46, 2.96)	0.704
Other	4.30 (0.90, 15.37)	0.038
Mixed	0.90 (0.37, 2.13)	0.806

Note: The multivariable logistic regression analysis was based on the completed case dataset. CI: confidence interval; OR: odds ratio.

Supplementary Table 3. Associated factors of increased alpha angle among early adolescents in the complete case dataset (N = 2,874).

	Adjusted β coefficient (95% CI)	P value
Age	-0.12 (-0.92, 0.69)	0.776
Sex		
Female	0 (Ref.)	
Male	2.88 (2.18, 3.58)	<0.001
Ethnicity		
European	0 (Ref.)	
African	-0.88 (-1.72, -0.04)	0.040
Asian	-0.76 (-1.93, 0.41)	0.202
Other	-0.16 (-1.81, 1.49)	0.848
Proximal femoral physis status		
Open	0 (Ref.)	
Closed	1.32 (0.59, 2.04)	<0.001
Weight categories		
Underweight	-1.07 (-1.91, -0.23)	0.012
Normal weight	0 (Ref.)	
Overweight	0.58 (-0.29, 1.45)	0.188
Obesity	1.15 (-0.72, 3.02)	0.229
Physical activity frequency		
Low	0 (Ref.)	
High	0.36 (-0.24, 0.96)	0.241
Sport types		
None	0 (Ref.)	
Cutting	0.95 (0.10, 1.80)	0.029
Flexibility	-0.14 (-1.15, 0.87)	0.791
Asymmetric	0.26 (-0.95, 1.47)	0.671
Impingement	-0.19 (-1.44, 1.06)	0.765
Endurance	1.08 (-0.13, 2.30)	0.080
Other	1.81 (-0.91, 4.54)	0.192
Mixed	0.48 (-0.56, 1.52)	0.362

Note: The multivariable linear regression analysis was based on the complete case dataset. CI: confidence interval.

Supplementary Table 4. Sensitivity analyses on associated factors of primary cam morphology among early adolescents excluding mixed sports.

	Adjusted OR (95% CI)	P value
Age	1.15 (0.71, 1.87)	0.559
Sex		
Female	1 (Ref.)	
Male	2.23 (1.29, 3.86)	0.004
Ethnicity		
European	1 (Ref.)	
African	0.92 (0.52, 1.62)	0.766
Asian	0.47 (0.14, 1.54)	0.213
Other	1.20 (0.43, 3.37)	0.726
Proximal femoral physis status		
Open	1(Ref.)	
Closed	3.30 (1.88, 5.78)	<0.001
Weight categories		
Underweight	0.26 (0.08, 0.84)	0.024
Normal weight	1 (Ref.)	
Overweight	0.56 (0.27, 1.12)	0.102
Obesity	1.05 (0.37, 3.02)	0.921
Physical activity frequency		
Low	1 (Ref.)	
High	1.15 (0.70, 1.91)	0.583
Sport types		
None	1 (Ref.)	
Cutting	1.00 (0.57, 1.76)	0.990
Flexibility	0.55 (0.25, 1.19)	0.129
Asymmetric	0.71 (0.28, 1.81)	0.476
Impingement	0.55 (0.20, 1.49)	0.241
Endurance	1.06 (0.49, 2.33)	0.875
Other	2.93 (0.79, 10.82)	0.107

Note: The multivariable logistic regression analysis was based on the imputed dataset and was the pooled result of 40 datasets. CI: confidence interval; OR: odds ratio.

Supplementary Table 5. Sensitivity analyses on associated factors of increased alpha angle among early adolescents excluding mixed sports.

	Adjusted β coefficient (95% CI)	P value
Age	0.40 (-0.34, 1.13)	0.292
Sex		
Female	0 (Ref.)	
Male	2.81 (2.14, 3.48)	<0.001
Ethnicity		
European	0 (Ref.)	
African	-0.44 (-1.20, 0.31)	0.275
Asian	-1.24 (-2.39, -0.09)	0.034
Other	0.08 (-1.39, 1.55)	0.918
Proximal femoral physis status		
Open	0 (Ref.)	
Closed	1.12 (0.42, 1.81)	0.002
Weight categories		
Underweight	-1.21 (-2.02, -0.39)	0.004
Normal weight	0 (Ref.)	
Overweight	0.31 (-0.49, 1.10)	0.450
Obesity	2.00 (0.46, 3.54)	0.011
Physical activity frequency		
Low	0 (Ref.)	
High	0.28 (-0.36, 0.91)	0.394
Sport types		
None	0 (Ref.)	
Cutting	1.07 (0.31, 1.83)	0.006
Flexibility	-0.35 (-1.24, 0.53)	0.432
Asymmetric	0.35 (-0.77, 1.47)	0.539
Impingement	-0.33 (-1.46, 0.80)	0.563
Endurance	0.96 (-0.16, 2.07)	0.093
Other	1.01 (-1.49, 3.51)	0.428

Note: The multivariable linear regression analysis was based on the imputed dataset and was the pooled result of 40 datasets. CI: confidence interval.

Chapter 5

Associated factors of pincer morphology in 3,986 early adolescents: a multi-ethnic population-based study in the Netherlands (Generation R)

Delong Chen, Fleur Boel, Suzanne de Vos-Jakobs, Pim van Klij, Jos Runhaar, Fernando Rivadeneira, Sita M.A. Bierma-Zeinstra, Rintje Agricola

Under review

ABSTRACT

Objectives

To determine factors associated with pincer morphology and lateral center edge angle (LCEA) in early adolescents from the general population.

Methods

Data from the population-based cohort study Generation R on participants aged 13 years who underwent dual-energy x-ray absorptiometry scans of the right hip and full-body were analyzed. The LCEA was automatically measured using a validated method. Pincer morphology was defined as a LCEA ≥ 40°. Multivariable logistic and linear regression models were used to identify demographic, anthropometric, lifestyle factors and triradiate cartilage status associated with pincer morphology and LCEA, respectively.

Results

A total of 3,986 participants had a 3.1% prevalence of pincer morphology and a mean LCEA of 28.7° (SD 5.9). Overweight (adjusted odds ratio [aOR] 2.35, 95% CI 1.50 – 3.68), obesity (aOR 4.73, 95% CI 2.54 – 8.84), and closed triradiate cartilage (aOR 5.27, 95% CI 2.55 – 10.92) were associated with higher odds of pincer morphology, while flexibility sport type (aOR 0.36, 95% CI 0.14 – 0.92) was associated with lower odds of pincer morphology. Overweight (β 1.04, 95% CI 0.51 – 1.57), obesity (β 2.24, 95% CI 1.27 – 3.21) and closed triradiate cartilage (β 3.36, 95% CI 2.86 – 3.85) were associated with higher LCEA, while flexibility sport type (β -0.72, 95% CI -1.43 – -0.01) was associated with low LCEA. Physical activity frequency, sex and ethnicity were not associated with pincer morphology or LCEA.

Conclusion

Overweight, obesity and flexibility sport type are modifiable factors of pincer morphology in early adolescents, providing insights into potential strategies for primary prevention.

Keywords

Pincer morphology; Femoroacetabular impingement; Hip osteoarthritis; Early adolescents; Associated factors; Epidemiology

INTRODUCTION

Osteoarthritis (OA) is a widespread and degenerative joint disease with a high patient and societal burden [1, 2], and femoroacetabular impingement syndrome (FAIS) is strongly associated with the development of hip OA [3]. FAIS is a clinical disorder characterized by abnormal contact between the acetabulum and the proximal femur during hip movements [4]. The diagnosis of FAIS is based on three key elements: symptoms, clinical signs, and imaging findings. Two distinct morphological variations can be identified on imaging: cam and pincer morphologies. Cam morphology is distinguished by an aspherical femoral head, while pincer morphology refers to an excessive overcoverage of the femoral head by the acetabulum. The lateral center edge angle (LCEA), an objective measure of acetabular bony coverage, is widely used to define pincer morphology. During hip movement, the proximal femur can impinge against the pincer morphology, potentially leading to structural hip damage (e.g., cartilage and labrum damage) [5, 6]. Over time, this repeated impingement and subsequent damage may accelerate the development of hip OA.

Unlike cam morphology, the relationship between pincer morphology and hip OA has been inconsistent and controversial in the previous studies [7, 8]. However, a recent large-scale study of 16,655 hips from the Worldwide Collaboration on OsteoArthritis prediCtion for the Hip (World COACH) consortium has provided robust evidence on this matter. This study, which used a consistent and harmonized definition of pincer morphology and radiographic hip OA, reported that pincer morphology (a LCEA ≥ 45°) at baseline was associated with a 1.59 times (95% confidence interval [CI] 1.16 - 2.20) higher odds of developing radiographic hip OA within eight-years follow-up, suggesting pincer morphology is a potentially modifiable risk factor for hip OA [9].

While studies have reported on the prevalence of pincer morphology across different populations [8], no studies investigated factors associated with pincer morphology in the general adolescent population. Compared to pincer morphology, associated factors of primary cam morphology, which refers to cam morphology that develops as an adaptive bone response to mechanical loading, have been studied more extensively in the athletic population. Associations with male sex, ethnicity, high-impact sports practice and physical activity levels during skeletal growth have been reported for primary cam morphology [10-15]. However, whether these associated factors also hold for pincer morphology and in the general population remains unclear. To our knowledge, no epidemiological studies are available on factors associated with pincer morphology in the general adolescent population. A greater understanding of these associations could inform primary preventive strategies in early adolescence, and possibly reduce the risks of FAIS and hip OA later in life.

Therefore, the first aim of our study was to determine associated factors of pincer morphology in early adolescents from the general population. Our second aim was to determine associated factors of the LCEA as a continuous outcome.

METHODS

Study population

The study population consisted of participants within the Generation R study, a population-based, multi-ethnic, prospective cohort study, which was established to investigate the growth and health of children from foetal life onwards in Rotterdam, the Netherlands. The cohort consists of 9,749 children who were born to 9,778 mothers, included between April 2002 and January 2006. In early adolescence, around the age of 13 years (Focus 13), 4,929 participants visited our dedicated research center at the Erasmus MC-Sophia Children's Hospital. In this study, we included participants who attended the Focus 13 visit and had high-resolution dual-energy x-ray absorptiometry (DXA) scans of their right hip and full-body. The selection of the right hip was based on the study protocol, and this was arbitrary. Participants were excluded if they had an incomplete acetabulum depicted on the hip DXA images, movement artifacts or artifacts present in the region of interest that impeded LCEA measurements. Written informed consent was obtained from all participants and their parents, and the study was approved by the Medical Ethical Committee of Erasmus MC, University Medical Center Rotterdam (MEC-2015-749). We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline [16].

DXA scans

The assessment of pincer morphology typically relies on radiographs in cohort studies, but a high-resolution DXA scan offers a suitable low-radiation alternative for the healthy and young adolescent population [17]. High-resolution DXA scans of participants' full-body and right hip were sequentially conducted using a General Electric (GE)-Lunar iDXA densitometer (GE Healthcare, Madison, WI, USA). Participants were scanned in a supine position with their legs slightly separated and internally rotated with their big toes touching. A Velcro strip was used to secure the feet in this position [18].

Measurement of LCEA

The LCEA quantifies the degree of acetabular bony coverage of the femora head. The presence of pincer morphology was defined by a LCEA ≥ 40 degrees [19-22]. Given a lack of a clear consensus on a threshold of LCEA for pincer morphology in early adolescents, we used the LCEA as a dichotomous outcome (a LCEA ≥ 40°) and a continuous outcome in this study.

The LCEA was calculated automatically with open-access, in-house developed, validated software [23] based on specific landmarks along the hip contour on the right hip DXA images. These landmarks were automatically placed by the BoneFinder® software [24] (www.bone-finder.com; The University of Manchester, UK). The LCEA is constructed by two lines (**Figure 1**). From the center of the femoral head, the first line extends to the most lateral bony edge of the acetabulum. The second line is perpendicular to the horizontal reference line of the pelvis, which we determined on the full-body DXA image. The inter-method reliability of LCEA between the automated method and manual measurement was assessed with intraclass correlation coefficients (ICC) and was 0.95 (95% CI 0.87 – 0.98) [23]. The LCEA measurement may differ between DXA scans and pelvic radiographs due to different positioning and imaging techniques, while a recent study demonstrated good reliability in adults, with an ICC of 0.93 (95% CI 0.91 – 0.94) [17].

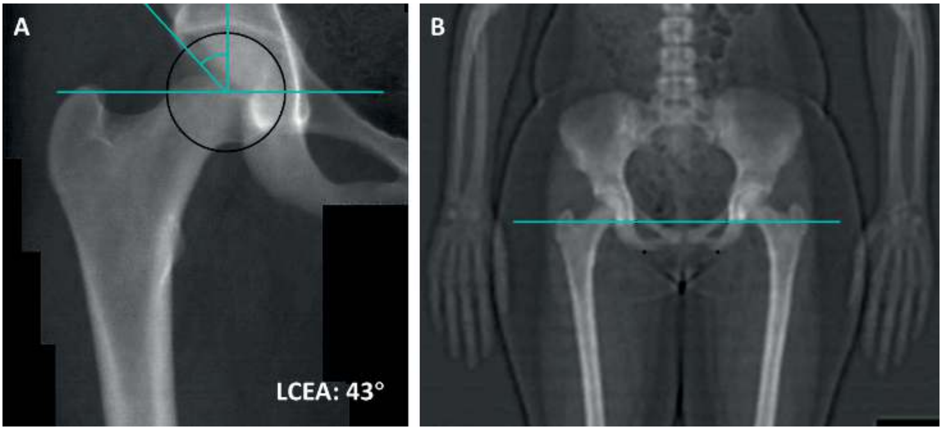


Figure 1. Measurement of lateral center edge angle (LCEA) on a dual-energy x-ray absorptiometry (DXA) image of the right hip. (A) The LCEA of 43° in this example is formed by the intersection of two lines. The first line originates from the center of the femoral head and extends to the most lateral bony edge of the acetabulum. The second line is generated perpendicular to the horizontal pelvic reference line, as determined on the full-body DXA image (B). This horizontal reference line was established to correct for pelvic obliquity and was determined based on the average of 2 lines between the superolateral point of the obturator foramen and the most inferior point of the ischial tuberosity on both hips.

Associated factors

Demographic factors. Participants' sex was assigned at birth and obtained from hospital registries and medical records. The age of participants was determined by calculating the difference between their birth dates and the dates of their DXA scans. The ethnicity of participants was collected by questionnaires and assessed by the parental countries of birth, using a classification from the Central Bureau of Statistics Netherlands. We divided ethnicity into four categories: Western (Dutch, Turkish, European, Oceanian, and American Western), African (Cape Verdian, Moroccan, Dutch Antilles, Surinamese-

Creole and other African), Asian (Indonesia, Surinamese-Hindustani, other Asian) and other (Surinamese-Unspecified and American non-Western) [25].

Triradiate cartilage status. A paediatric orthopaedic surgeon (SdVJ) scored the status of the triradiate cartilage (open or closed) on the right hip DXA images. The hips with a closed triradiate cartilage were considered as reaching acetabulum skeletal maturity.

Anthropometric factor. Participant's height (cm) and weight (kg) were measured following a standardized protocol, from which body mass index (BMI; in kg/m^2) was calculated. According to the International Obesity Task Force age- and sex-specific BMI cut-offs [26], BMI was classified into underweight, normal weight, overweight and obesity.

Lifestyle factors. Physical activity behaviours (type of sport and physical activity frequency) were evaluated with self-reported questionnaires. Type of sport was categorized into seven groups according to previous studies [27, 28]: cutting, flexibility, asymmetric, impingement, endurance, contact, or other sports (**Table 1**). These categories were mainly determined by the mechanical loading applied to the hip. For participants who engaged in multiple sports, the primary sport was determined as the one they spent the most time on and was categorized into one of the seven groups mentioned above. If participants spent equal time on two or more sports categories, they were grouped into mixed sports. Due to the limited sample size of contact sports (N = 19), they were grouped into cutting sports. The frequency of physical activity was evaluated by asking participants the number of days per week that involved a minimum of one hour of physical activity, and was categorized as two levels: low frequency (less than four days per week) and high frequency (four or more days per week) [15].

Table 1. Sport categories based on the mechanical loading on the hip.

Categories	Specific sports
Cutting	Soccer, Hockey, Basketball, Korfball, Handball, Skiing, Surfing, Skateboarding, Long-boarding
Flexibility	Dancing, Judo/ (Kick) Boxing/ Martial arts, Gymnastics, Free running, Rock climbing, Synchronized swimming, Figure skating, Yoga, Combat sport
Asymmetric	Baseball, Softball, Tennis, Volleyball, Badminton, Table tennis, Cricket, Golf, Squash, Sword fighting
Impingement	Horseback riding, Water polo, Rowing, CrossFit, Skating, Ice hockey, Weight lifting, Gym, Fitness
Endurance	Athletics, Running, Swimming, Cycling/Mountain biking
Contact	Rugby, Football
Other	Sailing, Archery, Diving, Darts, Scootering

Statistical analyses

Multivariable logistic and linear regression models were used to investigate factors (age, birth-assigned sex, ethnicity, triradiate cartilage status, weight category, type of sport, and physical activity frequency) associated with pincer morphology and LCEA, respectively. The reference group selected for each variable was female sex, Western ethnic background, open triradiate cartilage, normal weight, no sports and low physical activity frequency. All measures of association were visualized as a forest plot and shown as adjusted odds ratios (aOR) for the presence of pincer morphology or adjusted β coefficients for LCEA with their corresponding 95% CI. Linear regression model assumptions were tested and fulfilled, including normality, homoscedasticity and multicollinearity.

Missing data for associated factors ranged between 0.4% for triradiate cartilage status and 32.1% for the frequency of physical activity. We conducted multiple imputations by chained equations to create 40 datasets with 30 iterations for missing data, assuming missing at random structure. The LCEA was not imputed. We evaluated imputation and observed that the distribution of imputed data was similar to the observed data (**Table S1**), and convergence was reached. We presented pooled results of 40 imputed datasets. To assess the robustness of the findings, we performed two sensitivity analyses: (1) complete case analysis, and (2) excluding participants who engaged in mixed sports. Data analyses were conducted using R Statistical Software (v4.2.1; R Core Team 2022). Forest plots were created using "forestplot" package [29], and multiple imputation was performed using "mice" package [30].

RESULTS

Participant characteristics

After applying exclusion criteria, our study population consisted of 3,986 participants (**Figure 2**). **Table 2** presents the demographic characteristics of the participants. Pincer morphology was present in 3.1% (N = 124) of early adolescents. The mean LCEA was 28.7 degrees (SD, 5.9).

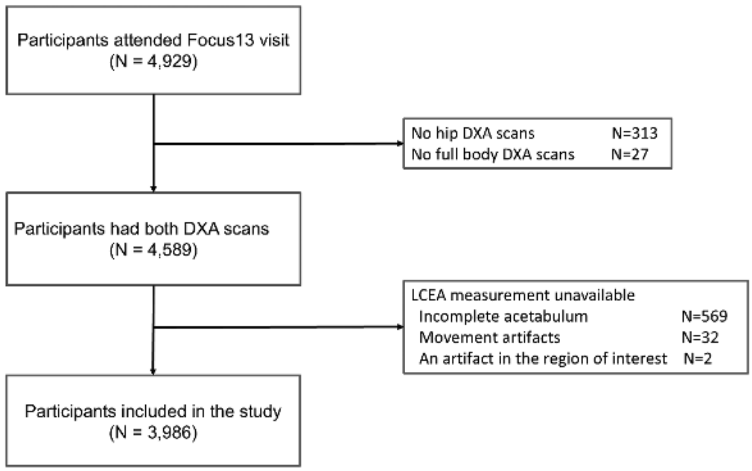


Figure 2. Flowchart of study participants. DXA, dual-energy x-ray absorptiometry; LCEA, lateral center edge angle.

Associated factors of pincer morphology and LCEA

Figure 3 shows overweight (aOR 2.35, 95% CI 1.50 – 3.68), obesity (aOR 4.73, 95% CI 2.54 – 8.84) and closed triradiate cartilage (aOR 5.27, 95% CI 2.55 – 10.92) being associated with higher odds of pincer morphology in early adolescents. Flexibility sport type (aOR 0.36, 95% CI 0.14 – 0.92) was associated with lower odds of pincer morphology. **Figure 4** shows participants with overweight and obesity having a higher LCEA of 1.04° (95% CI 0.51 – 1.57) and 2.24° (95% CI 1.27 – 3.21) than those with normal weight. Participants with closed triradiate cartilage had a higher LCEA of 3.36° (95% CI 2.86 – 3.85) than those with open triradiate cartilage. Adolescents who played flexibility sports had a lower LCEA of 0.72° (95% CI -1.43 – -0.01) than those who did not play sports.

Sensitivity analyses

Table S2 and **Table S3** show that the effect estimates were largely similar to those in the imputed datasets after restricting our analyses to complete cases (N = 2,540). No major differences of findings were present when mixed sport type was excluded from the multivariable logistic (**Table S4**) and linear (**Table S5**) regressions. However, the association between flexibility sport type and LCEA was attenuated and became statistically non-significant in multivariable linear regression models (**Table S3 and Table S5**).

Table 2. Demographic characteristics of included participants.

Characteristic	Included participants (N = 3,986)
Age, years	13.5 (13.2-14.6)
Sex	
Female	2,122 (53.2%)
Male	1,864 (46.8%)
Ethnicity	
Western	2,960 (74.3%)
African	663 (16.6%)
Asian	244 (6.1%)
Other	119 (3.0%)
Triradiate cartilage status	
Open triradiate cartilage	1,000 (25.1%)
Closed triradiate cartilage	2,986 (74.9%)
Weight category	
Underweight	406 (10.2%)
Normal weight	2,905 (72.9%)
Overweight	533 (13.4%)
Obesity	142 (3.6%)
Physical activity frequency	
Low	1,371 (34.4%)
High	2,615 (65.6%)
Type of sport	
None	685 (17.2%)
Cutting	1,538 (38.6%)
Flexibility	525 (13.2%)
Asymmetric	241 (6.0%)
Impingement	251 (6.3%)
Endurance	253 (6.4%)
Other	33 (0.8%)
Mixed	459 (11.5%)
Pincer morphology	124 (3.1%)
LCEA, degrees	28.7 (5.9)

Note: Values are in medians (2.5 - 97.5th percentile) or mean ± SD for continuous variables, frequencies (percentages) for categorical variables based on imputed data. LCEA, lateral center edge angle.

DISCUSSION

Results from this multi-ethnic population-based study suggested that overweight, obesity and closed triradiate cartilage were associated with the increased presence of pincer morphology and higher LCEA in early adolescents from the general population.

Assciated factors of pincer morphology among early adolescents

Characteristic	Adjusted OR (95%CI)	P value
Age	0.75 (0.46, 1.23)	0.252
Sex		
Female	1 (Ref.)	
Male	1.43 (0.96, 2.13)	0.078
Ethnicity		
Western	1 (Ref.)	
African	1.03 (0.64, 1.68)	0.896
Asian	0.73 (0.33, 1.64)	0.446
Other	0.50 (0.12, 2.08)	0.339
Triradiate cartilage status		
Open triradiate cartilage	1 (Ref.)	
Closed triradiate cartilage	5.27 (2.55, 10.92)	<0.001
Weight category		
Underweight	1.54 (0.79, 2.98)	0.201
Normal weight	1 (Ref.)	
Overweight	2.35 (1.50, 3.68)	<0.001
Obesity	4.73 (2.54, 8.84)	<0.001
Physical activity frequency		
Low	1 (Ref.)	
High	0.94 (0.57, 1.54)	0.805
Type of sport		
None	1 (Ref.)	
Cutting	0.80 (0.44, 1.45)	0.458
Flexibility	0.36 (0.14, 0.92)	0.033
Asymmetric	1.05 (0.46, 2.40)	0.905
Impingement	0.41 (0.13, 1.32)	0.135
Endurance	0.51 (0.18, 1.48)	0.216
Mixed	1.14 (0.57, 2.25)	0.713

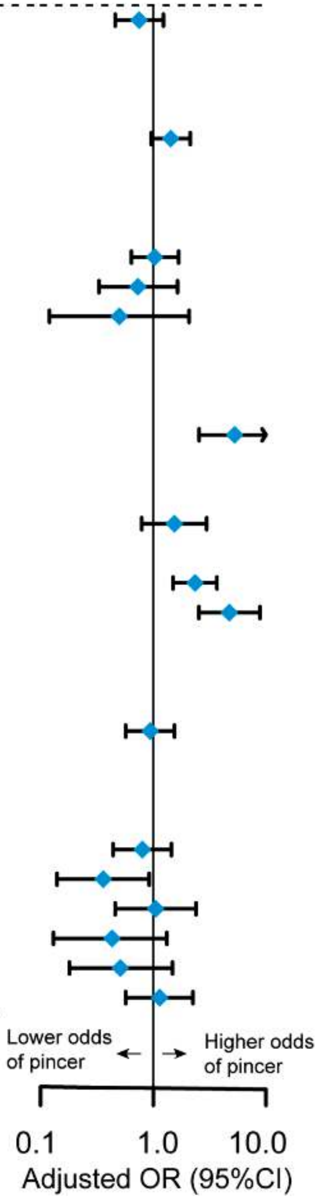


Figure 3. Associated factors of the presence of pincer morphology among early adolescents. The result was derived from multivariable logistic regression analysis and was the pooled result of 40 imputed datasets. The multivariable logistic regression model included age, sex, ethnicity, triradiate cartilage status, weight category, physical activity frequency and type of sport. The other sports category was analyzed but not presented in the forest plot due to complete separation (no pincer morphology cases). OR: odds ratio; CI: confidence interval.

Associated factors of LCEA among early adolescents

Characteristic	Adjusted β (95%CI)	P value
Age	−0.19 (−0.66, 0.29)	0.449
Sex		
Female	0 (Ref.)	
Male	0.12 (−0.31, 0.55)	0.583
Ethnicity		
Western	0 (Ref.)	
African	0.20 (−0.30, 0.70)	0.434
Asian	−0.21 (−0.98, 0.55)	0.585
Other	0.12 (−0.94, 1.17)	0.932
Triradiate cartilage status		
Open triradiate cartilage	0 (Ref.)	
Closed triradiate cartilage	3.36 (2.86, 3.85)	<0.001
Weight category		
Underweight	0.30 (−0.31, 0.90)	0.335
Normal weight	0 (Ref.)	
Overweight	1.04 (0.51, 1.57)	<0.001
Obesity	2.24 (1.27, 3.21)	<0.001
Physical activity frequency		
Low	0 (Ref.)	
High	−0.31 (−0.78, 0.16)	0.201
Type of sport		
None	0 (Ref.)	
Cutting	−0.24 (−0.85, 0.38)	0.454
Flexibility	−0.72 (−1.43, −0.01)	0.049
Asymmetric	−0.23 (−1.13, 0.66)	0.613
Impingement	−0.40 (−1.31, 0.51)	0.389
Endurance	−0.21 (−1.10, 0.69)	0.649
Other	1.40 (−0.81, 3.60)	0.215
Mixed	−0.55 (−1.31, 0.21)	0.157

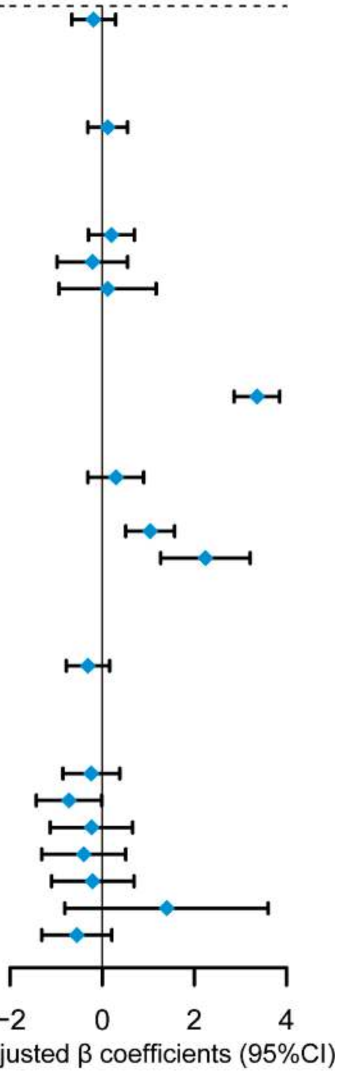


Figure 4. Associated factors of lateral center edge angle among early adolescents. The result was derived from multivariable linear regression analysis and was the pooled result of 40 imputed datasets. The multivariable linear regression model included age, sex, ethnicity, triradiate cartilage status, weight category, physical activity frequency and type of sport. CI: confidence interval; LCEA: lateral center edge angle.

Flexibility sport type was associated with the decreased presence of pincer morphology and lower LCEA.

In the current study, we observed that overweight and obese participants had higher odds of having pincer morphology at 13 years of age. This is in line with a cross-sectional study investigating 1,188 children at age 9 years within the Generation R study, which also found that overweight and obesity were associated with higher LCEA [31]. Similarly, another cross-sectional study involving 107 elite male soccer players with a mean age of 22.7 years showed an association of BMI greater than 35 with the presence of global overcoverage as defined by a LCEA > 39° or an acetabular inclination < 0° [32]. A potential mechanism for this association involves increased mechanical loading on the hip joint due to excessive body weight, which may stimulate adaptive bone formation at the acetabular rim, leading to femoral head overcoverage. However, a retrospective study involving 128 male and female adolescents with a mean age of 15 years found no association between BMI percentiles and the LCEA [33]. Differences in findings might be due to the smaller sample size that reduces statistical power in this retrospective study, or to variations in the LCEA measurement, as they measured the LCEA at the most lateral weight-bearing part of the sourcil.

The aetiology of pincer morphology in relation to high-impact sports is less frequently studied than primary cam morphology, which is an adaptive bone response to vigorous hip loading during adolescence. Although a high prevalence of pincer morphology was found in elite male and female ballet dancers (74%) [34], they defined pincer morphology including both focal and global overcoverage. Our study found flexibility sport type was associated with the decreased presence of pincer morphology in early adolescents from the general population. Due to the cross-sectional nature of our study design, this association could be interpreted in two ways: flexibility sport type may have a protective effect against pincer morphology in this age group, or reverse association, whereby adolescents with pincer morphology may be less likely to participate in flexibility sports. The aetiology of pincer morphology may differ from that of primary cam morphology, which is associated with vigorous sporting activities [10] and more common in high-impact cutting and impingement sports like soccer, basketball and ice hockey in young adults [35-38]. These sports involve repetitive flexion and external rotation of the hip, which could stimulate bone formation at the anterolateral aspect of the proximal femoral physis, leading to primary cam morphology [39]. However, our findings indicated no significant association of high physical activity frequency and cutting or impingement sport type with pincer morphology in early adolescents from the general population.

Our study suggested closed triradiate cartilage was associated with the increased presence of pincer morphology in early adolescents. This implies that early adolescents with open triradiate cartilage in this age group still have the potential to develop pincer morphology as their acetabulum matures. Furthermore, after triradiate cartilage closure, a secondary ossification center known as the os acetabuli contributes to further development of the lateral acetabular rim, potentially resulting in more acetabular coverage. In our study population, it was challenging to determine whether the os acetabuli was fused or had not yet appeared, as it is only visible for a few months (approximately 10 months [40]). While previous research on skeletal maturity and hip morphology has predominantly focused on primary cam morphology, particularly in athletic populations, there remains a gap in understanding towards this relationship in pincer morphology. Prospective studies in male athletes have shown that primary cam morphology gradually increases in size until the femoral head growth plate is closed [41, 42], suggesting that the development of primary cam morphology is associated with skeletal maturity of the femoral head. Future studies are needed to assess how pincer morphology develops with skeletal maturity of the acetabulum in the general population.

Our study has several strengths. To our knowledge, this is the first population-based study to investigate associated factors of pincer morphology in early adolescents from the general population. Moreover, its large sample size increases the statistical power of the study and allows for explore multiple associated factors. The use of automated measurement of LCEA to define pincer morphology is another strength. This precise and reproducible measurement reduces the potential bias of manual measurements. Some limitations need to be discussed. Firstly, only analyses on the right hips can lead to an underestimation of the presence of pincer morphology as it can be present in the left hips. Secondly, our study only involved sport types and the frequency of physical activity, without considering the intensity and volume of physical activity. Future research could employ objective measurement tools to quantify levels of physical activity. Thirdly, it is important to note that the prevalence of pincer morphology in our study was relatively low. Given that our study population consisted predominantly of early adolescents, it is likely that the presence of pincer morphology and average LCEA may increase as this population ages. Therefore, our findings are applicable to this age group and could not be generalized to young adults. Fourthly, we could not address the causality of these associations due to the inherent limitation of the cross-sectional study.

In conclusion, this population-based study in the general population of the Netherlands found that overweight, obesity and closed triradiate cartilage were associated with the increased presence of pincer morphology and higher LCEA in early adolescents from the general population, while flexibility sport type was associated with the decreased presence of pincer morphology and lower LCEA. Our study identified modifiable factors of pincer morphology in the young general population, which may assist towards the development of potential primary intervention strategies (e.g. overweight and obesity management) to prevent pincer morphology in early adolescence from developing into FAIS and hip OA later in life.

REFERENCES

1. Collaborators GBDO. Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Rheumatol 2023; 5: e508-e522.
2. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019; 393: 1745-1759.
3. Agricola R, van Buuren MMA, Kemp JL, Weinans H, Runhaar J, Bierma-Zeinstra SMA. Femoroacetabular impingement syndrome in middle-aged individuals is strongly associated with the development of hip osteoarthritis within 10-year follow-up: a prospective cohort study (CHECK). Br J Sports Med 2024; 58: 1061-1067.
4. Griffin DR, Dickenson EJ, O'Donnell J, Agricola R, Awan T, Beck M, et al. The Warwick Agreement on femoroacetabular impingement syndrome (FAI syndrome): an international consensus statement. Br J Sports Med 2016; 50: 1169-1176.
5. Pascual-Garrido C, Li DJ, Grammatopoulos G, Yanik EL, Clohisy JC, Group A. The Pattern of Acetabular Cartilage Wear Is Hip Morphology-dependent and Patient Demographic-dependent. Clin Orthop Relat Res 2019; 477: 1021-1033.
6. Beck M, Kalhor M, Leunig M, Ganz R. Hip morphology influences the pattern of damage to the acetabular cartilage: femoroacetabular impingement as a cause of early osteoarthritis of the hip. J Bone Joint Surg Br 2005; 87: 1012-1018.
7. Casartelli NC, Maffiuletti NA, Valenzuela PL, Grassi A, Ferrari E, van Buuren MMA, et al. Is hip morphology a risk factor for developing hip osteoarthritis? A systematic review with meta-analysis. Osteoarthritis Cartilage 2021; 29: 1252-1264.
8. van Klij P, Heerey J, Waarsing JH, Agricola R. The Prevalence of Cam and Pincer Morphology and Its Association With Development of Hip Osteoarthritis. J Orthop Sports Phys Ther 2018; 48: 230-238.
9. Riedstra NS, Van Buuren MM, Boel F, Ahedi H, Arbabi V, Arden N, et al. Pincer Morphology Is A Risk Factor For Developing Radiographic Hip Osteoarthritis; Data From The World Coach Consortium. Osteoarthritis and Cartilage 2023; 31: S249-S250.
10. Palmer A, Fernquest S, Gimpel M, Birchall R, Judge A, Broomfield J, et al. Physical activity during adolescence and the development of cam morphology: a cross-sectional cohort study of 210 individuals. Br J Sports Med 2018; 52: 601-610.
11. Mosler AB, Crossley KM, Waarsing JH, Jomaah N, Weir A, Holmich P, et al. Ethnic Differences in Bony Hip Morphology in a Cohort of 445 Professional Male Soccer Players. Am J Sports Med 2016; 44: 2967-2974.
12. Agricola R, Weinans H. What causes cam deformity and femoroacetabular impingement: still too many questions to provide clear answers. Br J Sports Med 2016; 50: 263-264.
13. Zadpoor AA. Etiology of Femoroacetabular Impingement in Athletes: A Review of Recent Findings. Sports Med 2015; 45: 1097-1106.
14. Westermann RW, Scott EJ, Schaver AL, Schneider A, Glass NA, Levy SM, et al. Activity Level and Sport Type in Adolescents Correlate with the Development of Cam Morphology. JB JS Open Access 2021; 6.
15. Tak I, Weir A, Langhout R, Waarsing JH, Stubbe J, Kerkhoffs G, et al. The relationship between the frequency of football practice during skeletal growth and the presence of a cam deformity in adult elite football players. Br J Sports Med 2015; 49: 630-634.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 2007; 147: 573-577.

17. Boel F, Wortel J, van Buuren MMA, Rivadeneira F, van Meurs JBJ, Runhaar J, et al. DXA images vs. pelvic radiographs: Reliability of hip morphology measurements. Osteoarthritis Cartilage 2025; 33: 283-292.
18. Chen D, Boel F, van Klij P, van Buuren MMA, Bierma-Zeinstra SMA, Agricola R. The prevalence of primary cam morphology in early adolescents from the general population: A population-based study (Generation R). Osteoarthritis Cartilage 2025; 33: 633-637.
19. Riedstra NS, Boel F, van Buuren M, Eygendaal D, Bierma-Zeinstra S, Runhaar J, et al. Pincer Morphology Is Not Associated With Hip Osteoarthritis Unless Hip Pain Is Present: Follow-Up Data From a Prospective Cohort Study. Arthritis Care Res (Hoboken) 2024; 76: 644-651.
20. Raveendran R, Stiller JL, Alvarez C, Renner JB, Schwartz TA, Arden NK, et al. Population-based prevalence of multiple radiographically-defined hip morphologies: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2018; 26: 54-61.
21. Saberi Hosnijeh F, Zuiderwijk ME, Versteeg M, Smeele HT, Hofman A, Uitterlinden AG, et al. Cam Deformity and Acetabular Dysplasia as Risk Factors for Hip Osteoarthritis. Arthritis Rheumatol 2017; 69: 86-93.
22. Chen D, Boel F, de Vos-Jakobs S, van Klij P, van Buuren MMA, Bierma-Zeinstra SMA, et al. The prevalence of pincer morphology in early adolescents from the general population: a population-based study (Generation R). Arthritis Care Res (Hoboken) 2025.
23. Boel F, de Vos-Jakobs S, Riedstra NS, Lindner C, Runhaar J, Bierma-Zeinstra SMA, et al. Automated radiographic hip morphology measurements: An open-access method. Osteoarthritis Imaging 2024; 4.
24. Lindner C, Thiagarajah S, Wilkinson JM, arc OC, Wallis GA, Cootes TF. Fully automatic segmentation of the proximal femur using random forest regression voting. IEEE Trans Med Imaging 2013; 32: 1462-1472.
25. Heppe DH, Medina-Gomez C, de Jongste JC, Raat H, Steegers EA, Hofman A, et al. Fetal and childhood growth patterns associated with bone mass in school-age children: the Generation R Study. J Bone Miner Res 2014; 29: 2584-2593.
26. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes 2012; 7: 284-294.
27. Shibata KR, Matsuda S, Safran MR. Arthroscopic Hip Surgery in the Elite Athlete: Comparison of Female and Male Competitive Athletes. Am J Sports Med 2017; 45: 1730-1739.
28. Heerey JJ, Kemp JL, Mosler AB, Jones DM, Pizzari T, Scholes MJ, et al. What is the Prevalence of Hip Intra-Articular Pathologies and Osteoarthritis in Active Athletes with Hip and Groin Pain Compared with Those Without? A Systematic Review and Meta-Analysis. Sports Med 2019; 49: 951-972.
29. Gordon M LT. forestplot: Advanced Forest Plot Using 'grid' Graphics. 2023.
30. van Buuren S G-OK. mice: Multivariate Imputation by Chained Equations in R. Journal of Statistical Software 2011; 45: 1-67.
31. Chung WK, De Vos-Jakobs S, Rivadeneira F, Bierma-Zeinstra SM, Waarsing JH. The association of BMI and physical activity on acetabular dysplasia in children. Osteoarthritis Cartilage 2021; 29: 50-58.
32. Nepple JJ, Brophy RH, Matava MJ, Wright RW, Clohisy JC. Radiographic findings of femoroacetabular impingement in National Football League Combine athletes undergoing radiographs for previous hip or groin pain. Arthroscopy 2012; 28: 1396-1403.

33. Novais EN, Shefelbine SJ, Kienle KP, Miller PE, Bowen G, Kim YJ, et al. Body Mass Index Affects Proximal Femoral but Not Acetabular Morphology in Adolescents Without Hip Pathology. J Bone Joint Surg Am 2018; 100: 66-74.
34. Harris JD, Gerrie BJ, Varner KE, Lintner DM, McCulloch PC. Radiographic Prevalence of Dysplasia, Cam, and Pincer Deformities in Elite Ballet. Am J Sports Med 2016; 44: 20-27.
35. Lerebours F, Robertson W, Neri B, Schulz B, Youm T, Limpisvasti O. Prevalence of Cam-Type Morphology in Elite Ice Hockey Players. Am J Sports Med 2016; 44: 1024-1030.
36. Siebenrock KA, Ferner F, Noble PC, Santore RF, Werlen S, Mamisch TC. The cam-type deformity of the proximal femur arises in childhood in response to vigorous sporting activity. Clin Orthop Relat Res 2011; 469: 3229-3240.
37. Johnson AC, Shaman MA, Ryan TG. Femoroacetabular impingement in former high-level youth soccer players. Am J Sports Med 2012; 40: 1342-1346.
38. Philippon MJ, Ho CP, Briggs KK, Stull J, LaPrade RF. Prevalence of increased alpha angles as a measure of cam-type femoroacetabular impingement in youth ice hockey players. Am J Sports Med 2013; 41: 1357-1362.
39. Roels P, Agricola R, Oei EH, Weinans H, Campoli G, Zadpoor AA. Mechanical factors explain development of cam-type deformity. Osteoarthritis Cartilage 2014; 22: 2074-2082.
40. Morris WZ, Chen JY, Cooperman DR, Liu RW. Characterization of ossification of the posterior rim of acetabulum in the developing hip and its impact on the assessment of femoroacetabular impingement. J Bone Joint Surg Am 2015; 97: e11.
41. Agricola R, Heijboer MP, Ginai AZ, Roels P, Zadpoor AA, Verhaar JA, et al. A cam deformity is gradually acquired during skeletal maturation in adolescent and young male soccer players: a prospective study with minimum 2-year follow-up. Am J Sports Med 2014; 42: 798-806.
42. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Cam morphology in young male football players mostly develops before proximal femoral growth plate closure: a prospective study with 5-yearfollow-up. Br J Sports Med 2019; 53: 532-538.

SUPPLEMENTARY MATERIALS

Supplementary Table 1. Observed and imputed characteristics of included participants (N = 3,986).

Characteristic	Data missing	Observed dataset	Imputed dataset
Age, years	-	13.5 (13.2-14.6)	-
Sex	-		-
Female	-	2,122 (53.2%)	-
Male	-	1,864 (46.8%)	-
Ethnicity	94 (2.4%)		-
Western	-	2,895 (74.4%)	2,960 (74.3%)
African	-	644 (16.5%)	663 (16.6%)
Asian	-	237 (6.1%)	244 (6.1%)
Other	-	116 (3.0%)	119 (3.0%)
Triradiate cartilage status	14 (0.4%)		-
Open triradiate cartilage	-	995 (25.1%)	1,000 (25.1%)
Closed triradiate cartilage	-	2,977 (74.9%)	2.986 (74.9%)
Weight category	-		-
Underweight	-	406 (10.2%)	-
Normal weight	-	2,905 (72.9%)	-
Overweight	-	533 (13.4%)	-
Obesity	-	142 (3.6%)	-
Physical activity frequency	1,280 (32.2%)		-
Low	-	888 (32.8%)	1,371 (34.4%)
High	-	1,818 (67.2%)	2,615 (65.6%)
Type of sport	709 (17.8%)		-
None	-	540 (16.5%)	685 (17.2%)
Cutting	-	1,278 (39.0%)	1,538 (38.6%)
Flexibility	-	431 (13.2%)	525 (13.2%)
Asymmetric	-	201 (6.1%)	241 (6.0%)
Impingement	-	208 (6.3%)	251 (6.3%)
Endurance	-	206 (6.3%)	253 (6.4%)
Other	-	27 (0.8%)	33 (0.8%)
Mixed	-	386 (11.9%)	459 (11.5%)
Pincer morphology	-	124 (3.1%)	-
LCEA, degrees	-	28.7(5.9)	-

Note: Values are in medians (2.5 - 97.5th percentile) or mean ± SD for continuous variables, frequencies (percentages) for categorical variables. LCEA, lateral center edge angle.

Supplementary Table 2. Sensitivity analyses on associated factors of pincer morphology among early adolescents in the complete case dataset (N = 2,540).

	Adjusted OR (95% CI)	P value
Age	0.34 (0.12, 0.83)	0.026
Sex		
Female	1 (Ref.)	
Male	1.09 (0.62, 1.88)	0.751
Ethnicity		
Western	1 (Ref.)	
African	1.01 (0.48, 1.96)	0.984
Asian	0.60 (0.14, 1.70)	0.408
Other	0.49 (0.03, 2.36)	0.487
Triradiate cartilage status		
Open triradiate cartilage	1(Ref.)	
Closed triradiate cartilage	3.76 (1.65, 9.73)	0.003
Weight category		
Underweight	2.06 (0.95, 4.11)	0.050
Normal weight	1 (Ref.)	
Overweight	2.24 (1.12, 4.20)	0.016
Obesity	5.79 (2.17, 13.75)	<0.001
Physical activity frequency		
Low	1 (Ref.)	
High	0.89 (0.52, 1.55)	0.662
Type of sport		
None	1 (Ref.)	
Cutting	0.74 (0.36, 1.55)	0.422
Flexibility	0.25 (0.06, 0.77)	0.030
Asymmetric	0.99 (0.34, 2.55)	0.984
Impingement	0.31 (0.05, 1.14)	0.127
Endurance	0.60 (0.17, 1.70)	0.372
Mixed	1.45 (0.66, 3.18)	0.355

Note: The result was derived from multivariable logistic regression analysis in the complete case dataset which adjusted for age, sex, ethnicity, triradiate cartilage status, weight category, physical activity frequency and type of sport. The other sports category was analysed but not presented in the table due to complete separation (no pincer morphology cases). OR: odds ratio; CI: confidence interval.

5

Supplementary Table 3. Sensitivity analyses on associated factors of lateral center edge angle among early adolescents in the complete case dataset (n = 2,540).

	Adjusted β coefficient (95% CI)	P value
Age	-0.55 (-1.23, 0.12)	0.107
Sex		
Female	0 (Ref.)	
Male	-0.08 (-0.62, 0.46)	0.761
Ethnicity		
Western	0 (Ref.)	
African	0.19 (-0.51, 0.88)	0.594
Asian	-0.04 (-1.00, 0.92)	0.932
Other	0.25 (-1.13, 1.63)	0.722
Triradiate cartilage status		
Open triradiate cartilage	0 (Ref.)	
Closed triradiate cartilage	3.06 (2.44, 3.67)	<0.001
Weight category		
Underweight	0.12 (-0.59, 0.83)	0.736
Normal weight	0 (Ref.)	
Overweight	1.32 (0.60, 2.04)	<0.001
Obesity	2.61 (1.07, 4.15)	<0.001
Physical activity frequency		
Low	0 (Ref.)	
High	-0.35 (-0.85, 0.16)	0.178
Type of sport		
None	0 (Ref.)	
Cutting	-0.13 (-0.84, 0.58)	0.715
Flexibility	-0.72 (-1.57, 0.13)	0.095
Asymmetric	-0.02 (-1.05, 1.00)	0.966
Impingement	-0.25 (-1.29, 0.79)	0.636
Endurance	-0.29 (-1.31, 0.73)	0.576
Other	0.07 (-2.40, 2.55)	0.954
Mixed	-0.46 (-1.33, 0.41)	0.302

Note: The result was derived from multivariable linear regression analysis in the complete case dataset which adjusted for age, sex, ethnicity, triradiate cartilage status, weight category, physical activity frequency and type of sport. CI: confidence interval.

Supplementary Table 4. Sensitivity analyses on associated factors of pincer morphology among early adolescents excluding mixed sports.

	Adjusted OR (95% CI)	P value
Age	0.59 (0.28, 1.24)	0.163
Sex		
Female	1 (Ref.)	
Male	1.05 (0.63, 1.75)	0.862
Ethnicity		
Western	1 (Ref.)	
African	0.84 (0.44, 1.59)	0.591
Asian	0.60 (0.21, 1.72)	0.345
Other	0.29 (0.04, 2.18)	0.232
Triradiate cartilage status		
Open triradiate cartilage	1(Ref.)	
Closed triradiate cartilage	4.01 (1.70, 9.42)	0.001
Weight category		
Underweight	1.88 (0.89, 3.97)	0.096
Normal weight	1 (Ref.)	
Overweight	2.59 (1.47, 4.57)	0.001
Obesity	4.05 (1.69, 9.67)	0.002
Physical activity frequency		
Low	1 (Ref.)	
High	0.84 (0.47, 1.50)	0.560
Type of sport		
None	1 (Ref.)	
Cutting	0.77 (0.41, 1.42)	0.398
Flexibility	0.26 (0.10, 0.71)	0.008
Asymmetric	1.07 (0.45, 2.51)	0.883
Impingement	0.33 (0.09, 1.12)	0.075
Endurance	0.47 (0.16, 1.39)	0.171

Note: The result was derived from multivariable logistic regression analysis and was the pooled result of 40 imputed datasets. The multivariable logistic regression model included age, sex, ethnicity, triradiate cartilage status, weight category, physical activity frequency and sport types except for mixed sports. The other sports category was analysed but not presented in the table due to complete separation (no pincer morphology cases). OR: odds ratio; CI: confidence interval.

Supplementary Table 5. Sensitivity analyses on associated factors of lateral center edge angle among early adolescents excluding mixed sports.

	Adjusted β coefficient (95% CI)	P value
Age	-0.26 (-0.86, 0.34)	0.395
Sex		
Female	0 (Ref.)	
Male	0.04 (-0.46, 0.54)	0.869
Ethnicity		
Western	0 (Ref.)	
African	0.12 (-0.48, 0.72)	0.699
Asian	-0.12 (-1.01, 0.78)	0.797
Other	0.11 (-1.06, 1.29)	0.852
Triradiate cartilage status		
Open triradiate cartilage	0 (Ref.)	
Closed triradiate cartilage	3.19 (2.61, 3.76)	0.001
Weight category		
Underweight	0.39 (-0.30, 1.08)	0.268
Normal weight	0 (Ref.)	
Overweight	1.04 (0.40, 1.68)	0.002
Obesity	2.26 (1.01, 3.51)	<0.001
Physical activity frequency		
Low	0 (Ref.)	
High	-0.40 (-0.92, 0.12)	0.130
Type of sport		
None	0 (Ref.)	
Cutting	-0.23 (-0.86, 0.40)	0.479
Flexibility	-0.72 (-1.45, 0.01)	0.053
Asymmetric	-0.26 (-1.19, 0.68)	0.590
Impingement	-0.34 (-1.26, 0.58)	0.470
Endurance	-0.16 (-1.08, 0.76)	0.731
Other	1.34 (-0.85, 3.53)	0.229

Note: The result was derived from multivariable linear regression analysis and was the pooled result of 40 imputed datasets. The multivariable linear regression model included age, sex, ethnicity, triradiate cartilage status, weight category, physical activity frequency and sport types except for mixed sports. CI: confidence interval.

Chapter 6

Development of primary cam morphology and associated factors: a longitudinal population-based study (Generation R)

Delong Chen, Fleur Boel, Pim van Klij, Jos Runhaar, Fernando Rivadeneira, Sita M.A. Bierma-Zeinstra, Rintje Agricola

Submitted

ABSTRACT

Objective

To investigate longitudinally (1) whether demographic, anthropometric, lifestyle, and radiographic factors at age 13 are associated with the development of primary cam morphology (PCM) by age 18 in the general population; and (2) whether the lateral epiphyseal extension (EE) is associated with PCM development in a subset of participants with imaging at ages 9, 13, and 18.

Design

This longitudinal study used data from the population-based cohort, Generation R. The primary analysis included participants who underwent anteroposterior dual-energy X-ray absorptiometry (DXA) imaging of the right hip at ages 13 and 18. We defined PCM as an alpha angle ≥ 60°. The associations of demographic, anthropometric, lifestyle, and radiographic factors were assessed using multivariate logistic regression. The secondary analysis focused on a subset with DXA imaging at ages 9, 13, and 18, evaluating lateral EE as a potential contributing factor.

Results

The primary analysis included 2,572 participants (baseline mean age 13.5 years; 56% female). Male sex, being underweight, cutting and impingement sport types, and a lower neck shaft angle at age 13 were associated with higher odds of PCM development within 5 years, while Asian ethnicity was associated with lower odds. The secondary analysis included 399 participants (baseline mean age 9.7 years; 53% female). Male sex, a higher lateral EE at age 9, and mostly being underweight from ages 9 to 18 were associated with PCM development within 8 years.

Conclusions

Being underweight and participating in cutting or impingement sports are modifiable factors associated with PCM development, indicating potential targets for PCM prevention.

Keywords

Primary cam morphology; Femoroacetabular impingement; Associated factors; General population; Aetiology; Epidemiology

INTRODUCTION

Cam morphology is characterised by a bony prominence at the anterolateral femoral head-neck junction [1]. Cam morphology can cause femoroacetabular impingement syndrome (FAIS) [2], if abnormal contact between the cam morphology and the acetabular rim during motion results in symptoms and functional limitations. The development of cam morphology in adolescents is also strongly associated with future acetabular cartilage damage in young adults [3,4] and hip osteoarthritis (OA) later in life [5-7].

Primary cam morphology (PCM) is thought to be an adaptive response to mechanical loading and gradually develops throughout adolescence [8], with minimal changes after femoral head growth plate (FHGP) closure [9,10]. The critical window for PCM development appears to be the second growth spurt, during which the FHGP is highly responsive to mechanical loading and may interact with growth and sex hormones [11].

The timing of the second growth spurt differs by sex, typically around 12-13 years of age in females and around 14-15 years of age in males [12]. Cross-sectional studies on male football players have reported that bony PCM was first identifiable around 12-13 years of age [13,14].

Current understanding of the aetiology of PCM is predominantly based on small cross-sectional and cohort studies involving male athletes, which limits the generalisability of findings to females and the general population. Evidence suggests that PCM development is multifactorial, influenced by biological sex, ethnicity, participation in high-impact sports during skeletal growth, and other yet-to-be-confirmed factors [7,11,15-19]. PCM is particularly prevalent among male athletes engaged in cutting and impingement sports, such as football and ice hockey [16,20-22]. In male football players, higher frequency of sporting activity during adolescence have been associated with increased PCM risk, demonstrating a dose-response relationship [10,14,23]. Additionally, a longitudinal study of 49 male football players found that greater lateral epiphyseal extension (EE) and a lower neck-shaft angle (NSA) were consistently associated with the presence of PCM [24]. However, to date, no population-based longitudinal studies have investigated the development of PCM, a research gap identified as a priority in the recent Oxford Consensus [25] to advance understanding of PCM aetiology and inform primary prevention strategies.

The primary aim of this study was to longitudinally assess associations between demographic, anthropometric, lifestyle, and radiographic factors at age 13 and PCM development within a 5-year follow-up period. To further explore the role of FHGP shape in PCM development, we conducted a secondary analysis in a subset of participants with DXA

6

imaging available at ages 9, 13, and 18. Due to the smaller sample size, we focused on a reduced set of variables, including lateral epiphyseal extension (EE) at age 9. Therefore, the secondary aim was to assess associations between selected early-life factors and PCM development within an 8-year follow-up period.

METHODS

Study population

The data were derived from the Generation R Study, a population-based, prospective cohort study from Rotterdam, the Netherlands [26]. The cohort consists of 9,749 children born between April 2002 and January 2006. These children were followed from foetal life onwards and were invited to visit the Generation R research centre at approximately 6, 9, 13, and 18 years of age. The primary analysis included participants with alpha angle (AA) measurements on dual-energy X-ray absorptiometry (DXA) images at ages 13 and 18 years, excluding participants who had PCM at age 13. The secondary analysis included participants with AA measurements on DXA images at ages 9, 13, and 18 years, excluding participants who had PCM at ages 9 and 13. Participants were also excluded from the analyses if they did not have DXA images, their DXA images exhibited (movement) artefacts, or the femoral head or neck was incompletely depicted. The Generation R study was approved by the Medical Ethics Committee of the Erasmus Medical Centre (MEC-2007-413, MEC-2012-165, MEC-2015-749). Written informed consent was obtained from all participants and their parents.

DXA scans

Although radiographs are commonly used to assess hip morphologies in epidemiological studies, DXA scans are a reliable alternative with a lower radiation burden (intermethod intraclass correlation coefficient [ICC] of 0.72 [95% confidence interval 0.68 – 0.75] for AA) [27].

Anteroposterior (AP) DXA scans of the right hip were obtained at ages 9, 13, and 18 years using a General Electric (GE)-Lunar iDXA densitometer (GE Healthcare, Madison, WI, USA). DXA scans of the right hip were taken in a random subset of participants who visited the centre at age 9 due to logistical constraints. All DXA scans were conducted following a previously published protocol [28].

DXA imaging measurements

An AA threshold ≥ 60° was used to define PCM at ages 9, 13, and 18 years [28-30]. In this study, AA, EE, and NSA were automatically measured using an in-house developed and validated method (**Figure 1**) [31]. The AA and NSA were measured at ages 9, 13, and 18 years, whereas the EE was only measured at age 9 years, as this measurement can only be performed when the FHGP is open.

The intermethod reliability of the automated method compared to manual measurements was an ICC of 0.81 (95% CI 0.46 – 0.92) for the AA and 0.57 (95% CI 0 – 0.86) for the NSA [31].

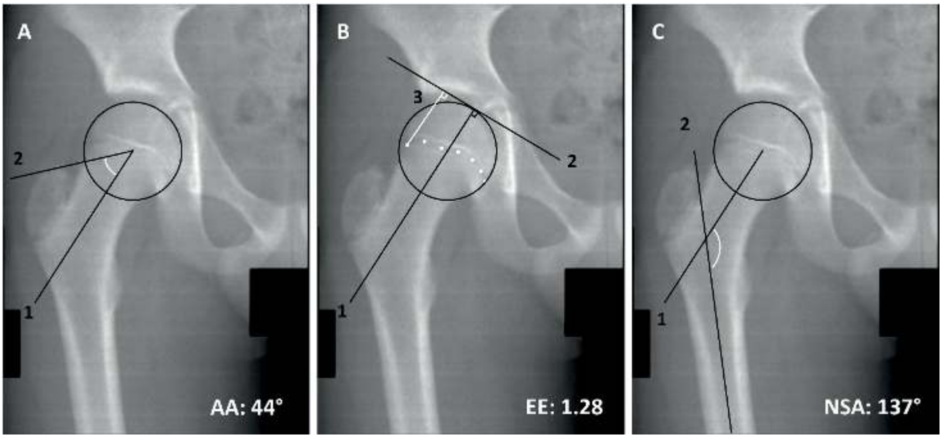


Figure 1: The measurements of alpha angle (AA), lateral epiphyseal extension (EE) and neck shaft angle (NSA) on the right hip DXA image. **A**: The AA is the angle between line 1, the femoral neck axis, connecting the best-fitting circle centre and the femoral neck centre, and line 2 from the best-fitting circle centre to the alpha point where the femoral head first departs from the margin of the best-fitting circle. **B**: The lateral EE is the ratio of the length of line 3 and the length of the femoral head radius. First, a perpendicular line (line 2) is generated to the femoral neck axis (line 1), which tangents the best-fitting circle. Line 3 is generated perpendicularly to line 2 to the lateral endpoint of the femoral head growth plate. **C**: The NSA is the angle between line 1, the femoral neck axis, and line 2, the femoral shaft axis.

Covariates

Information on covariates including demographic (birth-assigned sex and ethnicity), anthropometric (weight category), lifestyle factors (type of sport and physical activity frequency), and FHGP was described in the **Supplementary Materials**.

Equity, diversity and inclusion statement

The Generation R Study was designed to be conducted in a multi-ethnic population from Rotterdam, known for its diverse population. Our study included approximately equal numbers of male and female participants from diverse ethnic backgrounds (78.5% Western, 13.2% African, 5.3% Asian, and 3.0% other ethnic backgrounds). The author team includes five males and two females, comprising two junior and five senior clinical and academic researchers from different countries and disciplines.

Patient and public involvement

The Generation R cohort employs strategies to ensure participant involvement. These include regular email communications, telephone contact, transportation reimbursements, and home visits when necessary. To keep participants informed about the study's progress and findings, regular newsletters, social media and websites are utilised. The Generation R Parent and Child Group meets approximately twice a year, providing a platform for participants to share their experiences and offer feedback to improve the research process.

Statistical analysis

The hip-level prevalence of PCM was reported as a percentage with a 95% CI. For the primary analysis, multivariable logistic regression was used to identify factors at age 13 that are associated with PCM development at age 18. The variables of interest included age at baseline, birth-assigned sex, ethnicity, weight category, type of sport, physical activity frequency, and NSA at baseline. Females sex, Western ethnicity, normal weight, no sports participation, and <4 days/week of physical activity were used as reference categories, respectively. The FHGP status at age 13 was included as a confounder in the model.

The secondary analysis employed multivariable logistic regression to assess factors associated with PCM development within 8 years. The variables of interest included birth-assigned sex, weight category at ages 9, 13, and 18 years, sport type at ages 9, 13, and 18 years, and lateral EE at age 9. The FHGP status at age 13 was included as a confounder in the model. All analyses were performed in both sex-combined and male groups, but not in the female subgroup due to the limited number of PCM cases (Primary analysis: 34 cases; Secondary analysis: 9 cases). Results are presented as adjusted odds ratios (aOR) with 95% CIs. No multicollinearity was found between the variables in the primary and secondary analyses.

Missing covariates were handled using multivariate imputations by chained equations (MICE) [32] as detailed in the **Supplementary Materials**. The pooled MICE results were compared to observed results to assess the plausibility of the imputed results (**Supplementary Tables 1 and 2**). Sensitivity analyses using complete cases were conducted for the primary analysis to evaluate the robustness of our findings. Statistical analyses were performed in R Statistical Software (v4.2.1; R Core Team 2022) using the "mice" package [33] and the glm function. A p-value of < 0.05 was considered statistically significant.

RESULTS

Participants

In this study, 2,572 participants were included for the primary analysis (**Figure 2**). The mean age of the study population at baseline was 13.6 years (SD 0.3), and 55.9% were female (**Table 1**). The mean follow-up time was 4.8 ± 0.7 years. Excluded participants included proportionally fewer females and Western individuals, and they reported lower physical activity frequency at baseline compared to those who were included (**Supplementary Table 3**).

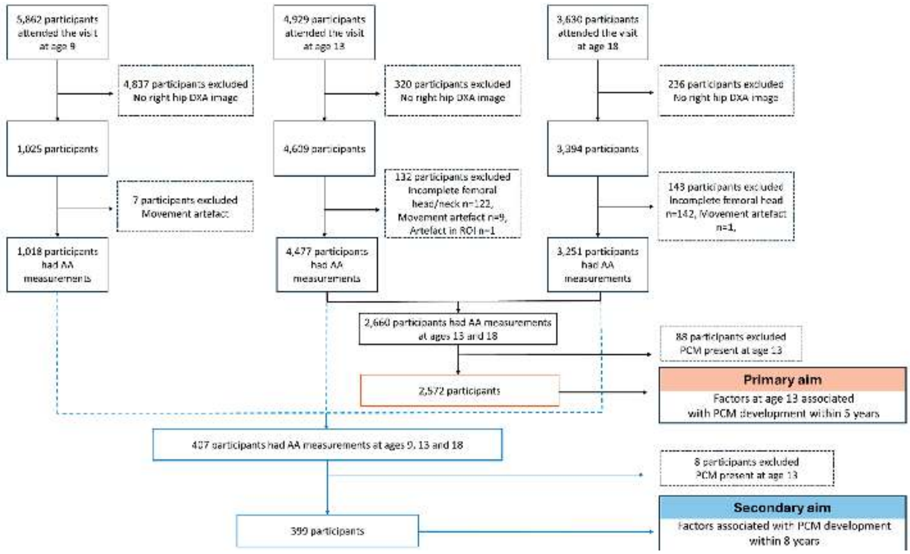


Figure 2. Flowchart of study participants. DXA, dual-energy x-ray absorptiometry; AA, alpha angle; PCM; primary cam morphology; ROI, region of interest.

Baseline factors associated with PCM development within 5 years

PCM developed in 311 participants (12.1%; 268 males and 43 females) within 5 years (**Supplementary Table 4**). In the sex-combined group, male sex (aOR 8.34, 95% CI 5.44 – 12.78), being underweight (aOR 1.46, 95% CI 1.00 – 2.12), participating in cutting sports (aOR 2.08, 95% CI 1.20 – 3.62) and impingement sports (aOR 2.67, 95% CI 1.22 – 5.86), and a decrease in NSA (aOR 1.04, 95% CI 1.02 – 1.08) were associated with higher odds of PCM development within 5 years, while Asian ethnicity (aOR 0.24, 95% CI 0.10 – 0.61) was associated with lower odds (**Table 2**).

In the male subgroup, being underweight (aOR 1.62, 95% CI 1.06 – 2.45), participating in cutting sports (aOR 2.25, 95% CI 1.20 – 4.24) and impingement sports (aOR 3.30, 95% CI 1.21 – 9.04), and a lower NSA (aOR 1.04, 95% CI 1.02 – 1.08) were also associated with higher odds of PCM development within 5 years, while Asian ethnicity (aOR 0.24, 95% CI 0.10 – 0.61) was associated with lower odds (**Table 2**).

Table 1. Baseline characteristics of included participants for the primary analysis (N = 2,572).

Characteristics	Combined (N = 2,572)	Male (N = 1,133)	Female (N = 1,439)
Age, years	13.6 (0.3)	13.6 (0.4)	13.6 (0.3)
Ethnicity			
Western	2,019 (78.5)	894 (78.9)	1,125 (78.2)
African	340 (13.2)	136 (12.1)	203 (14.1)
Asian	137 (5.3)	63 (5.5)	74 (5.1)
Other	76 (3.0)	40 (3.5)	37 (2.6)
Weight category			
Normal weight	1,921 (74.7)	871 (76.9)	1,050 (73.0)
Underweight	299 (11.6)	128 (11.3)	171 (11.9)
Overweight or Obesity	352 (13.7)	134 (11.8)	218 (15.1)
Type of sport			
None	431 (16.8)	141 (12.4)	290 (20.1)
Cutting	1,121 (43.6)	655 (57.8)	466 (32.4)
Flexibility	412 (16.0)	115 (10.2)	297 (20.6)
Asymmetric	201 (7.8)	89 (7.9)	112 (7.8)
Impingement	198 (7.7)	36 (3.2)	162 (11.3)
Endurance	176 (6.8)	73 (6.4)	103 (7.2)
Other	33 (1.3)	24 (2.1)	9 (0.6)
Physical activity frequency			
< 4 days/week	881 (34.2)	329 (29.0)	552 (38.3)
≥ 4 days/week	1,691 (65.8)	804 (71.0)	887 (61.7)
FHGP			
Open	1,487 (57.8)	1,048 (92.5)	439 (30.5)
Closed	1,085 (42.2)	85 (7.5)	1,000 (69.5)
Radiographic measurements			
NSA, degrees	131.9 (5.5)	131.6 (5.2)	132.1 (5.7)
AA, degrees	43.4 (4.5)	44.5 (4.1)	42.4 (4.5)

Note: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables based on imputed data. FHGP, femoral head growth plate; NSA, neck shaft angle; AA, alpha angle.

Table 2. Associated factors at age 13 and primary cam morphology development within 5 years.

Characteristics	Combined (N = 2,572)			Male (N = 1,133)			Female (N = 1,439)	
	PCM, N = 311	No PCM, N = 2,261	aOR (95% CI)	PCM, N = 268	No PCM, N = 865	aOR (95% CI)	PCM, N = 43	No PCM, N = 1,369
Age	13.6 (0.4)	13.6 (0.3)	1.08 (0.74, 1.58)	13.6 (0.4)	13.6 (0.4)	1.13 (0.74, 1.72)	13.6 (0.4)	13.6 (0.3)
Sex								
Female	43 (13.8)	1,396 (61.7)	1 (Ref.)	-		-	-	
Male	268 (86.2)	865 (38.3)	8.34 (5.44, 12.78) ***	-		-	-	
Ethnicity								
Western	259 (83.3)	1,760 (77.8)	1 (Ref.)	225 (84.0)	669 (77.3)	1 (Ref.)	35 (81.4)	1,090 (96.9)
African	36 (11.6)	304 (13.4)	0.96 (0.64, 1.45)	29 (10.8)	107 (12.4)	0.91 (0.58, 1.44)	6 (14.0)	197 (97.0)
Asian	5 (1.6)	132 (5.8)	0.24 (0.10, 0.61) **	4 (1.5)	59 (6.8)	0.21 (0.08, 0.59) **	1 (2.3)	73 (98.6)
Other	11 (3.5)	65 (2.9)	1.07 (0.53, 2.16)	10 (3.7)	30 (3.5)	1.07 (0.50, 2.28)	1 (2.3)	36 (97.3)
Weight category								
Normal weight	230 (74.0)	1,691 (74.8)	1 (Ref.)	201 (75.0)	670 (77.5)	1 (Ref.)	29 (67.4)	1,021 (97.2)
Underweight	47 (15.1)	252 (11.1)	1.46 (1.00, 2.12) *	42 (15.7)	86 (9.9)	1.62 (1.06, 2.45) *	5 (11.6)	165 (97.1)
Overweight or Obesity	34 (10.9)	318 (14.1)	1.09 (0.72, 1.65)	25 (9.3)	109 (12.6)	0.93 (0.57, 1.51)	9 (20.9)	209 (95.9)
Type of sport								
None	23 (7.4)	408 (18.0)	1 (Ref.)	18 (6.7)	123 (14.2)	1 (Ref.)	5 (11.6)	285 (98.3)
Cutting	188 (60.5)	933 (41.3)	2.08 (1.20, 3.62) **	173 (64.6)	482 (55.7)	2.25 (1.20, 4.24) *	15 (34.9)	451 (96.8)
Flexibility	31 (10.0)	381 (16.9)	1.58 (0.79, 3.15)	23 (8.6)	92 (10.6)	1.69 (0.75, 3.78)	8 (18.6)	289 (97.3)
Asymmetric	24 (7.7)	177 (7.8)	1.86 (0.91, 3.80)	18 (6.7)	71 (8.2)	1.69 (0.73, 3.90)	6 (14.0)	106 (94.6)
Impingement	18 (5.8)	180 (8.0)	2.67 (1.22, 5.86) *	12 (4.5)	24 (2.8)	3.30 (1.21, 9.04) *	6 (14.0)	156 (96.3)
Endurance	20 (6.4)	156 (6.9)	1.80 (0.83, 3.89)	17 (6.3)	56 (6.5)	2.03 (0.86, 4.79)	3 (7.0)	100 (97.1)
Other	7 (2.3)	26 (1.1)	2.25 (0.72, 7.03)	7 (2.6)	17 (2.0)	2.57 (0.77, 8.54)	0 (0.0)	9 (100)
Physical activity frequency								
< 4 days/week	78 (25.1)	803 (35.5)	1 (Ref.)	64 (23.9)	265 (30.6)	1 (Ref.)	14 (32.6)	538 (97.5)
≥ 4 days/week	233 (74.9)	1458 (64.5)	1.13 (0.80, 1.60)	204 (76.1)	600 (69.4)	1.12 (0.76, 1.65)	29 (67.4)	858 (96.7)
Radiographic measurements								
NSA	130.7 (4.6)	132.0 (5.6)	0.96 (0.93, 0.98) ***	130.7 (4.6)	132.0 (5.4)	0.96 (0.93, 0.98) **	131.2 (4.7)	132.1 (5.7)

Notes: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables based on imputed data. The effect estimates were derived from multivariable logistic regression based on the pooled result of 35 imputed datasets. This model included baseline age, sex, ethnicity, weight category, type of sport, physical activity frequency, NSA, and was adjusted for femoral head growth plate status. Due to the limited number of cases, no separate logistic regression analysis was performed in females. Abbreviation: PCM, primary cam morphology; aOR, adjusted odds ratios; CI, confidence interval; NSA, neck shaft angle. *P value < 0.05, ** P value < 0.01, *** P value < 0.001.

The sensitivity analysis using complete cases (N = 1,695) produced effect estimates similar to those from the imputed datasets. However, in the complete case analysis, the association for endurance sport type became statistically significant in the male subgroup, with an aOR of 2.81 (95% CI 1.05 – 7.85) (**Supplementary Table 5**).

Factors associated with PCM development within 8 years

The secondary analysis included 399 participants (189 males and 210 females), see Figure 2. Participants characteristics are shown in **Table 3**. The mean age at baseline was 9.7 ± 0.4 years, and the mean follow-up time was 8.1 ± 0.5 years.

PCM developed in 63 participants (15.8%; 54 males and 9 females) within 8 years. In the sex-combined group, male sex (aOR 6.64, 95% CI 2.70 – 16.32), a higher lateral EE at age 9 (aOR 6.58, 95% CI 2.98 – 1453.60), and mostly being underweight from ages 9 to 18 (aOR 2.44, 95% CI 1.04 – 5.74) were associated with higher odds of PCM development within 8 years (**Table 4**). No factors were found to be associated with PCM development within 8 years in the male subgroup analysis.

Table 3. Participants characteristics for the secondary analysis (N = 399).

Characteristics	Combined (N = 399)	Male (N = 189)	Female (N = 210)
Age, years	17.9 (0.5)	17.9 (0.5)	17.9 (0.5)
Weight pattern over time			
Normal weight	305 (76.4)	149 (78.8)	156 (74.3)
Underweight	38 (9.5)	20 (10.6)	18 (8.6)
Overweight or Obesity	56 (14.0)	20 (10.6)	36 (17.1)
Sport type pattern over time			
None	67 (16.8)	21 (11.1)	46 (21.9)
Cutting	154 (38.6)	93 (49.2)	61 (29.0)
Flexibility	46 (11.5)	18 (9.5)	28 (13.3)
Asymmetric	20 (5.0)	13 (6.9)	7 (3.3)
Impingement	19 (4.8)	3 (1.6)	16 (7.6)
Endurance	7 (1.8)	3 (1.6)	4 (1.9)
Other	86 (21.6)	38 (20.1)	48 (22.9)
FHGP age 13			
Open	254 (63.7)	178 (94.2)	76 (36.2)
Closed	145 (36.3)	11 (5.8)	134 (63.8)
EE	1.27 (0.11)	1.23 (0.11)	1.30 (0.10)

Note: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables based on imputed data. FHGP, femoral head growth plate; EE, epiphyseal extension.

Table 4. Factors associated with primary cam morphology development within 8 years (N = 399).

Characteristics	Combined (N = 399)			Male (N = 189)			Female (N = 210)	
	PCM N = 63	No PCM N = 336	aOR (95% CI)	PCM N = 54	No PCM N = 135	aOR (95% CI)	PCM N = 9	No PCM N = 201
Age	17.9 (0.5)	17.9 (0.5)	1.07 (0.56, 2.03)	17.9 (0.5)	17.9 (0.5)	1.20 (0.65, 2.20)	17.7 (0.5)	17.9 (0.5)
Sex								
Female	9 (14.3)	201 (59.8)	1 (Ref.)	-	-	-	-	-
Male	54 (85.7)	135 (40.2)	6.64 (2.70, 16.32) ***	-	-	-	-	-
Weight pattern over time								
Normal weight	47 (74.6)	258 (76.8)	1 (Ref.)	40 (74.1)	109 (80.7)	1 (Ref.)	7 (77.8)	149 (74.1)
Underweight	12 (19.0)	26 (7.7)	2.44 (1.04, 5.74) *	11 (20.4)	9 (6.7)	1.99 (0.90, 4.41)	1 (11.1)	17 (8.5)
Overweight or Obesity	4 (6.4)	52 (15.5)	0.53 (0.16, 1.72)	3 (5.6)	17 (12.6)	0.59(0.19, 1.87)	1 (11.1)	35 (17.4)
Sport type pattern over time								
None	6 (9.5)	61 (18.2)	1 (Ref.)	6 (11.1)	15 (11.1)	1 (Ref.)	0 (0)	46 (22.9)
Cutting	34 (54.0)	120 (35.7)	1.33 (0.43, 4.14)	29 (53.7)	64 (47.4)	1.29 (0.43, 3.88)	5 (55.6)	56 (27.9)
Flexibility	5 (7.9)	41 (12.2)	0.94 (0.20, 4.34)	5 (9.3)	13 (9.6)	0.82 (0.18, 3.64)	0 (0)	28 (13.9)
Asymmetric	3 (4.8)	17 (5.1)	0.86 (0.15, 4.85)	3 (5.5)	10 (7.4)	1.27 (0.24, 6.81)	0 (0)	7 (3.5)
Impingement	2 (3.2)	17 (5.1)	1.08 (0.10, 11.09)	1 (1.9)	2 (1.5)	0.49 (0.05, 4.78)	1 (11.1)	15 (7.5)
Endurance	1 (1.6)	6 (1.8)	2.76 (0.19, 40.57)	1 (1.9)	2 (1.5)	2.68 (0.20, 35.89)	0 (0)	4 (2.0)
Other	12 (19.0)	74 (22.0)	1.05 (2.86, 3.84)	9 (16.7)	29 (21.5)	0.96 (0.27, 3.39)	3 (33.3)	45 (22.4)
EE	1.27 (0.10)	1.27 (0.11)	6.58 (2.98, 1453.60) **	1.26 (0.11)	1.22 (0.11)	13.90 (0.77, 249.83)	1.32 (0.05)	1.30 (0.10)

Note: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables based on imputed data.
The effect estimates were derived from multivariable logistic regression based on the pooled result of 50 imputed datasets. This model included age, sex, weight pattern over time, type of sport played over time, epiphyseal extension, and was adjusted for femoral head growth plate status at age 13. Due to the limited number of PCM cases in females, no separate logistic regression analysis was performed in the female subgroup. Abbreviation: PCM, primary cam morphology; aOR, adjusted odds ratios; CI, confidence interval; EE, epiphyseal extension. *P value < 0.05, ** P value < 0.01, *** P value < 0.001.

DISCUSSION

In this longitudinal, population-based study, being underweight, participating in cutting and impingement sports, and a lower NSA at 13 years were associated with higher odds, while Asian ethnicity was associated with lower odds of PCM development within 5 years in both the total population and male subgroup. Moreover, male sex, mostly being underweight from ages 9 to 18, as well as a higher lateral EE at age 9 were associated with PCM development within 8 years in the secondary analysis.

Our results demonstrate marked sex differences in the development of PCM between ages 13 and 18, with 268 males (23.7%) developing PCM compared to only 43 females (3.0%). This pattern aligns with findings from the adult general population, where PCM prevalence in females (2%–10%) remains substantially lower than in males (15%–35%) [34-37]. One possible explanation for this disparity is the earlier closure of the FHGP in females; in our study, 70% of females had a closed FHGP by age 13, compared to 8% of males. Additionally, differences in sports participation may contribute to sex-specific PCM development. At age 13, females were less likely to engage in sports (79.9% vs. 87.6% in males) and less likely to participate in cutting sports (32.4% vs. 57.8% in males). These findings suggest that the timing and necessity of primary prevention strategies should differ by sex. In males, PCM prevalence increased markedly by 19.8% (from 3.9% to 23.7%) between ages 13 and 18, whereas in females, prevalence remained stable at 3.0% [28]. Supporting this, a 3-year longitudinal study involving 36 female controls found minimal changes in AA after age 12 [10]. Given the low PCM prevalence in females at age 18, population-level primary prevention may not be warranted for females and should instead focus on males. However, this advice could not be generalised to female athletes. Beyond sex, ethnicity also emerged as a non-modifiable factor influencing PCM development. Participants of Asian ethnicity had significantly lower odds of developing PCM, with a prevalence of 3.7%, compared to 12.9% in Western and 10.5% in African participants. These findings are consistent with a cross-sectional study of 445 male football players (mean age 25 years), which reported a lower PCM prevalence in East Asian players (18.8%) compared to other ethnic groups (57.5%–71.7%) despite comparable athletic backgrounds [16]. While the underlying mechanisms remain unclear, genetic predispositions may contribute to these ethnic differences in PCM development.

We also studied modifiable factors, namely sport type, physical activity frequency and weight category. Our study indicated that participation in cutting and impingement sports at age 13 years was associated with PCM development in both the sex-combined and male groups, while the frequency of physical activity did not appear to influence PCM development. Furthermore, being underweight was associated with higher odds of PCM development in both primary and secondary analyses. Previous, small cross-sectional studies in young adult athletes showed similar results, where athletes participating in cutting sports (e.g. football, basketball) and impingement sports (e.g. ice hockey) had a high prevalence of PCM (60%–90% in males [16, 20-22, 38] and 50%–84% in females [22, 39]). Therefore, primary prevention of PCM could target reducing cutting and impingement sport loads. Restricting sport participation is not advisable given the broader health benefits of physical activity. In this study, young adults who developed PCM were less likely to have participated in flexibility sports or to have been inactive during adolescence, compared to those who did not develop PCM. One potential preventive strategy would be to alternate cutting or impingement sports with flexibility sports during the adolescent period, thereby reducing the impact from cutting or impingement sports. Cutting sports are thought to involve repetitive high shear loads on the lateral FHGP during rapid changes of hip direction, while impingement sports involve deep hip flexion with internal rotation [40]. Finite element analysis showed that these specific movement patterns could increase shear stresses at the lateral FHGP, which triggers extra bone formation at the anterolateral femoral head-neck junction [41]. However, this possible strategy still warrants further exploration since it could result in decreased engagement in sports if children cannot participant in their preferred sport, and approximately 10% of adolescents participating in flexibility sports still developed PCM.

Radiographic measurements could play a role in identifying adolescents at risk of developing PCM, since a higher lateral EE at age 9 and a lower NSA at age 13 were associated with PCM development. A higher lateral EE indicates that the FHGP extends more toward the femoral neck. Although the association of a lateral EE with PCM development has been investigated in the athletic population[10, 14, 24, 42, 43], this is the first study showing the association in the general population. Additionally, the varus hip orientation (a lower NSA) may contribute to PCM development through altered hip biomechanics. Our finding suggests that these radiographic measurements may serve as factors for predicting PCM development in the general population. However, a 5-year longitudinal study of 49 male football players found that higher lateral EE and lower NSA developed simultaneously but did not precede PCM [24]. More research is needed to investigate whether the EE and NSA could be helpful in selecting high-risk subgroups and developing prevention strategies for PCM.

There are several strengths in this study. Firstly, this is the first longitudinal, prospective, population-based study with a large sample size to investigate PCM development in the general population. The second strength is the use of automatic AA measurements, which maintains consistency between baseline and follow-up assessments and reduces reader bias. Thirdly, the large sample size of females allows us to compare differences in associated factors of PCM development between males and females. Moreover, this multi-ethnic study design enables the examination of differences in PCM development across ethnicities. Lastly, this is the first study to explore potential modifiable risk factors of PCM such as weight category, type of sports and physical activity frequency in the general population, providing a first indication of preventive measures.

This study also had some limitations. Firstly, due to the inability to perform DXA imaging at baseline and follow-up in all participants, this study is subject to selection bias. Excluded participants were more often males (44% of included vs 56% of excluded participants) and had on average lower physical activity frequency compared to included participants. This may introduce bias in the estimated associations, as these factors influence PCM development. Secondly, our analysis of only right hip DXA images could underestimate the person-level prevalence, as individuals with unilateral PCM in left hips are missed. Thirdly, PCM is a three-dimensional structure, and AP view DXA images primarily capture the superior aspect of the femoral head-neck junction rather than the anterosuperior aspect where PCM most commonly occurs. This could result in an underestimation of the prevalence compared to three-dimensional imaging modalities. Lastly, while our study population was diverse, the number of Asian individuals was limited; therefore, the generalisability of our findings to the Asian population may be limited.

In conclusion, this prospective, population-based study provides novel insights into the aetiology and potential avenues for primary prevention of PCM in the general population. We identified several factors associated with PCM development within 5 years, including Asian ethnicity, underweight status, participation in cutting and impingement sports, and a lower NSA at age 13, in both the overall cohort and male subgroup. In the secondary analysis, male sex, predominantly being underweight from ages 9 to 18, and a higher lateral EE at age 9 were associated with PCM development within 8 years. These findings underscore the importance of creating risk subgroups for prevention and suggest that modifiable factors such as sport type and weight category may be relevant targets for early prevention strategies.

REFERENCES

1. Dijkstra HP, Ardern CL, Serner A, Mosler AB, Weir A, Roberts NW, et al. Primary cam morphology; bump, burden or bog-standard? A concept analysis. Br J Sports Med 2021; 55: 1212-1221.
2. Griffin DR, Dickenson EJ, O'Donnell J, Agricola R, Awan T, Beck M, et al. The Warwick Agreement on femoroacetabular impingement syndrome (FAI syndrome): an international consensus statement. Br J Sports Med 2016; 50: 1169-1176.
3. Claes PAM, Hanff DF, Weir A, Riedstra NS, Weinans H, Eygendaal D, et al. The Association Between the Development of Cam Morphology During Skeletal Growth in High-Impact Athletes and the Presence of Cartilage Loss and Labral Damage in Adulthood: A Prospective Cohort Study With a 12-Year Follow-up. Am J Sports Med 2024; 52: 2555-2564.
4. Heerey J, Kemp J, Agricola R, Srinivasan R, Smith A, Pizzari T, et al. Cam morphology is associated with MRI-defined cartilage defects and labral tears: a case-control study of 237 young adult football players with and without hip and groin pain. BMJ Open Sport Exerc Med 2021; 7: e001199.
5. Tang J, van Buuren MMA, Riedstra NS, Boel F, Runhaar J, Bierma-Zeinstra S, et al. Cam morphology is strongly and consistently associated with development of radiographic hip osteoarthritis throughout 4 follow-up visits within 10 years. Osteoarthritis Cartilage 2023; 31: 1650-1656.
6. Casartelli NC, Maffiuletti NA, Valenzuela PL, Grassi A, Ferrari E, van Buuren MMA, et al. Is hip morphology a risk factor for developing hip osteoarthritis? A systematic review with meta-analysis. Osteoarthritis Cartilage 2021; 29: 1252-1264.
7. van Klij P, Heerey J, Waarsing JH, Agricola R. The Prevalence of Cam and Pincer Morphology and Its Association With Development of Hip Osteoarthritis. J Orthop Sports Phys Ther 2018; 48: 230-238.
8. Agricola R, Heijboer MP, Ginai AZ, Roels P, Zadpoor AA, Verhaar JA, et al. A cam deformity is gradually acquired during skeletal maturation in adolescent and young male soccer players: a prospective study with minimum 2-year follow-up. Am J Sports Med 2014; 42: 798-806.
9. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Cam morphology in young male football players mostly develops before proximal femoral growth plate closure: a prospective study with 5-yearfollow-up. Br J Sports Med 2019; 53: 532-538.
10. Fernquest S, Palmer A, Gimpel M, Birchall R, Broomfield J, Wedatilake T, et al. A longitudinal cohort study of adolescent elite footballers and controls investigating the development of cam morphology. Sci Rep 2021; 11: 18567.
11. Agricola R, Weinans H. What causes cam deformity and femoroacetabular impingement: still too many questions to provide clear answers. Br J Sports Med 2016; 50: 263-264.
12. Tanner JM. Growth and maturation during adolescence. Nutr Rev 1981; 39: 43-55.
13. Agricola R, Bessems JH, Ginai AZ, Heijboer MP, van der Heijden RA, Verhaar JA, et al. The development of Cam-type deformity in adolescent and young male soccer players. Am J Sports Med 2012; 40: 1099-1106.
14. Palmer A, Fernquest S, Gimpel M, Birchall R, Judge A, Broomfield J, et al. Physical activity during adolescence and the development of cam morphology: a cross-sectional cohort study of 210 individuals. Br J Sports Med 2018; 52: 601-610.
15. Zadpoor AA. Etiology of Femoroacetabular Impingement in Athletes: A Review of Recent Findings. Sports Med 2015; 45: 1097-1106.
16. Mosler AB, Crossley KM, Waarsing JH, Jomaah N, Weir A, Holmich P, et al. Ethnic Differences in Bony Hip Morphology in a Cohort of 445 Professional Male Soccer Players. Am J Sports Med 2016; 44: 2967-2974.

17. Zheng J, Frysz M, Faber BG, Lin H, Ebsim R, Ge J, et al. Comparison between UK Biobank and Shanghai Changfeng suggests distinct hip morphology may contribute to ethnic differences in the prevalence of hip osteoarthritis. Osteoarthritis Cartilage 2023.
18. Doran C, Pettit M, Singh Y, Sunil Kumar KH, Khanduja V. Does the Type of Sport Influence Morphology of the Hip? A Systematic Review. Am J Sports Med 2022; 50: 1727-1741.
19. Pettit M, Doran C, Singh Y, Saito M, Sunil Kumar KH, Khanduja V. How does the cam morphology develop in athletes? A systematic review and meta-analysis. Osteoarthritis Cartilage 2021; 29: 1117-1129.
20. Philippon MJ, Ho CP, Briggs KK, Stull J, LaPrade RF. Prevalence of increased alpha angles as a measure of cam-type femoroacetabular impingement in youth ice hockey players. Am J Sports Med 2013; 41: 1357-1362.
21. Lerebours F, Robertson W, Neri B, Schulz B, Youm T, Limpisvasti O. Prevalence of Cam-Type Morphology in Elite Ice Hockey Players. Am J Sports Med 2016; 44: 1024-1030.
22. Gerhardt MB, Romero AA, Silvers HJ, Harris DJ, Watanabe D, Mandelbaum BR. The prevalence of radiographic hip abnormalities in elite soccer players. Am J Sports Med 2012; 40: 584-588.
23. Tak I, Weir A, Langhout R, Waarsing JH, Stubbe J, Kerkhoffs G, et al. The relationship between the frequency of football practice during skeletal growth and the presence of a cam deformity in adult elite football players. Br J Sports Med 2015; 49: 630-634.
24. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Clinical and radiological hip parameters do not precede, but develop simultaneously with cam morphology: a 5-year follow-up study. Knee Surg Sports Traumatol Arthrosc 2021; 29: 1401-1410.
25. Dijkstra HP, Mc Auliffe S, Ardern CL, Kemp JL, Mosler AB, Price A, et al. Oxford consensus on primary cam morphology and femoroacetabular impingement syndrome: part 2-research priorities on conditions affecting the young person's hip. Br J Sports Med 2022; 57: 342-358.
26. Kooijman MN, Kruithof CJ, van Duijn CM, Duijts L, Franco OH, van IMH, et al. The Generation R Study: design and cohort update 2017. Eur J Epidemiol 2016; 31: 1243-1264.
27. Boel F, Wortel J, van Buuren MMA, Rivadeneira F, van Meurs JBJ, Runhaar J, et al. DXA images vs. pelvic radiographs: Reliability of hip morphology measurements. Osteoarthritis Cartilage 2025; 33: 283-292.
28. Chen D, Boel F, van Klij P, van Buuren MMA, Bierma-Zeinstra SMA, Agricola R. The prevalence of primary cam morphology in early adolescents from the general population: A population-based study (Generation R). Osteoarthritis Cartilage 2025; 33: 633-637.
29. van Klij P, Reiman MP, Waarsing JH, Reijman M, Bramer WM, Verhaar JAN, et al. Classifying Cam Morphology by the Alpha Angle: A Systematic Review on Threshold Values. Orthop J Sports Med 2020; 8: 2325967120938312.
30. Agricola R, Waarsing JH, Thomas GE, Carr AJ, Reijman M, Bierma-Zeinstra SM, et al. Cam impingement: defining the presence of a cam deformity by the alpha angle: data from the CHECK cohort and Chingford cohort. Osteoarthritis Cartilage 2014; 22: 218-225.
31. Boel F, de Vos-Jakobs S, Riedstra NS, Lindner C, Runhaar J, Bierma-Zeinstra SMA, et al. Automated radiographic hip morphology measurements: An open-access method. Osteoarthr Imaging 2024; 4: 100181.
32. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med 2011; 30: 377-399.
33. van Buuren S G-OK. mice: Multivariate Imputation by Chained Equations in R. Journal of Statistical Software 2011; 45: 1-67.

34. Faber BG, Ebsim R, Saunders FR, Frysz M, Gregory JS, Aspden RM, et al. Cam morphology but neither acetabular dysplasia nor pincer morphology is associated with osteophytosis throughout the hip: findings from a cross-sectional study in UK Biobank. Osteoarthritis Cartilage 2021; 29: 1521-1529.
35. Raveendran R, Stiller JL, Alvarez C, Renner JB, Schwartz TA, Arden NK, et al. Population-based prevalence of multiple radiographically-defined hip morphologies: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2018; 26: 54-61.
36. Laborie LB, Lehmann TG, Engesaeter IO, Eastwood DM, Engesaeter LB, Rosendahl K. Prevalence of radiographic findings thought to be associated with femoroacetabular impingement in a population-based cohort of 2081 healthy young adults. Radiology 2011; 260: 494-502.
37. Gosvig KK, Jacobsen S, Sonne-Holm S, Palm H, Troelsen A. Prevalence of malformations of the hip joint and their relationship to sex, groin pain, and risk of osteoarthritis: a population-based survey. J Bone Joint Surg Am 2010; 92: 1162-1169.
38. Siebenrock KA, Ferner F, Noble PC, Santore RF, Werlen S, Mamisch TC. The cam-type deformity of the proximal femur arises in childhood in response to vigorous sporting activity. Clin Orthop Relat Res 2011; 469: 3229-3240.
39. Ross KA, Mojica ES, Lott A, Carter C, Gonzalez-Lomas G. Characterization of pincer-type Hip impingement in professional women's ice hockey players. Phys Sportsmed 2023; 51: 610-614.
40. Nawabi DH, Bedi A, Tibor LM, Magennis E, Kelly BT. The demographic characteristics of high-level and recreational athletes undergoing hip arthroscopy for femoroacetabular impingement: a sports-specific analysis. Arthroscopy 2014; 30: 398-405.
41. Roels P, Agricola R, Oei EH, Weinans H, Campoli G, Zadpoor AA. Mechanical factors explain development of cam-type deformity. Osteoarthritis Cartilage 2014; 22: 2074-2082.
42. Hanke MS, Schmaranzer F, Steppacher SD, Reichenbach S, Werlen SF, Siebenrock KA. A Cam Morphology Develops in the Early Phase of the Final Growth Spurt in Adolescent Ice Hockey Players: Results of a Prospective MRI-based Study. Clin Orthop Relat Res 2021; 479: 906-918.
43. Siebenrock KA, Behning A, Mamisch TC, Schwab JM. Growth plate alteration precedes cam-type deformity in elite basketball players. Clin Orthop Relat Res 2013; 471: 1084-1091.

SUPPLEMENTARY MATERIALS

Supplementary methods

Covariates

Sex assigned at birth was obtained from medical records. Child's ethnicity was categorised into four groups: Western (Dutch, Turkish, European, Oceanian, and American Western [including North American]), African (Cape Verdian, Moroccan, Dutch Antilles, Surinamese-Creole and other African), Asian (Indonesian, Surinamese-Hindustani, other Asian) and Other (Surinamese-Unspecified and American non-Western [including South American and Central American]). FHGP status (open or closed) around age 9, 13, and 18 years was evaluated by one investigator (DC) on the DXA images of the right hip. The growth plate was classified as closed if complete fusion was observed; otherwise, it was classified as open. The intraobserver reliability for this assessment was 0.90 (95% CI 0.85 – 0.94), and the interobserver reliability was 0.87 (95% CI 0.78 – 0.92) [1].

Body mass index (BMI, kilograms [kg]/meter $[m]^2$) was calculated using weight and height, both measured at the Generation R research centre during the visits. Weight categories (underweight, normal weight, overweight including obesity) were defined based on the International Obesity Task Force age- and sex-specific BMI cut-offs [2]. For the secondary analysis, weight patterns over time were created based on the weight categories as determined at ages 9, 13 and 18. Participants were assigned to one of three weight status groups (underweight, normal weight, or overweight including obesity) based on consistent classification at two or more timepoints.

Information on primary sport at ages 13 and 18, and physical activity frequency at age 13 was obtained through questionnaires completed by children. Primary sport at age 9 was reported by primary care givers in questionnaires due to the absence of this question in children's questionnaires. The sport in which children played the most at ages 9, 13, and 18 years was categorised based on the mechanical loading placed on the hip into: cutting, flexibility, asymmetric, impingement, endurance, contact and other [3]. Contact sports were grouped into cutting sports due to the small sample size (N = 12). For the primary analysis, physical activity frequency at 13 years was determined by the number of days per week with at least one hour of physical activity, and was categorised into two groups: < 4 days/week or ≥ 4 days/week [4]. For the secondary analysis, sport type patterns were derived from the types of sports participants engaged in at ages 9, 13, and 18. Participants were assigned to one of seven sport type categories (none, cutting, flexibility, asymmetric, impingement, endurance, or other) if they were consistently classified within the same category at two or more timepoints. Participants who engaged in three different sport types across the three timepoints were categorized as ‘other’.

Statistical analysis

Missing data

Missing data ranged from 1.4% (ethnicity) to 24.7% (physical activity frequency) in the primary analysis, and from 0.1% (weight category) to 27.8% (type of sport) in the secondary analysis. Missing data of covariates were assumed to be missing at random and were imputed using multivariate imputations by chained equations (MICE) with 35 imputations and 30 iterations for the primary analysis, and 50 imputations and 30 iterations for the secondary analysis [5]. MICE was performed based on all variables of interest, confounders, and auxiliary variables (for the primary analysis: maternal ethnicity, primary sport around ages 9 and 17, sporting activity frequency and outdoor activity frequency around age 9). The outcome was not imputed. We presented pooled results of all imputed datasets.

Supplementary references

1. Chen D, Boel F, van Klij P, van Buuren MMA, Bierma-Zeinstra SMA, Agricola R. The prevalence of primary cam morphology in early adolescents from the general population: A population-based study (Generation R). Osteoarthritis Cartilage 2025; 33: 633-637.
2. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes 2012; 7: 284-294.
3. Heerey JJ, Kemp JL, Mosler AB, Jones DM, Pizzari T, Scholes MJ, et al. What is the Prevalence of Hip Intra-Articular Pathologies and Osteoarthritis in Active Athletes with Hip and Groin Pain Compared with Those Without? A Systematic Review and Meta-Analysis. Sports Med 2019; 49: 951-972.
4. Tak I, Weir A, Langhout R, Waarsing JH, Stubbe J, Kerkhoffs G, et al. The relationship between the frequency of football practice during skeletal growth and the presence of a cam deformity in adult elite football players. Br J Sports Med 2015; 49: 630-634.
5. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med 2011; 30: 377-399.

Supplementary tables

Supplementary Table 1. Observed and imputed characteristics of included participants for the primary analysis in the sex-combined group (N = 2,572).

Characteristics	Data missing	Observed dataset	Imputed dataset
Ethnicity	36 (1.4)	-	-
Western	-	1,994 (77.5)	2,019 (78.5)
African	-	332 (13.1)	340 (13.2)
Asian	-	135 (5.2)	137 (5.3)
Other	-	75 (3.0)	76 (3.0)
Type of sport	509 (19.8)	-	-
None	-	333 (16.1)	431 (16.8)
Cutting	-	917 (44.4)	1,121 (43.6)
Flexibility	-	326 (15.8)	412 (16.0)
Asymmetric	-	163 (7.9)	201 (7.8)
Impingement	-	159 (7.7)	198 (7.7)
Endurance	-	142 (6.9)	176 (6.8)
Other	-	23 (1.1)	33 (1.3)
Physical activity frequency	636 (24.7)	-	-
< 4 days/week	-	638 (33.0)	881 (34.2)
≥ 4 days/week	-	1,298 (67.0)	1,691 (65.8)
NSA, degrees	26 (1.0)	131.9 (5.5)	131.9 (5.5)

Note: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables. NSA, neck shaft angle.

Supplementary Table 2. Observed and imputed characteristics of included participants for the secondary analysis in the sex-combined group (N = 399).

Characteristics	Age 9		Age 13		Age 18	
	Observed dataset	Imputed dataset	Observed dataset	Imputed dataset	Observed dataset	Imputed dataset
Weight category	-	-	-	-	-	-
Normal weight	309 (77.6)	310 (77.7)	288 (72.2)	-	276 (69.2)	-
Underweight	33 (8.3)	33 (8.3)	52 (13.0)	-	57 (14.3)	-
Overweight or Obesity	56 (14.1)	56 (14.0)	59 (14.8)	-	66 (16.5)	-
Missingness	1 (0.2)	-	-	-	-	-
Type of sport	-	-	-	-	-	-
None	32 (11.1)	51 (12.8)	52 (16.3)	71 (17.8)	95 (32.9)	123 (30.8)
Cutting	145 (50.3)	182 (45.6)	146 (45.6)	167 (41.9)	63 (21.8)	93 (23.3)
Flexibility	69 (24.0)	92 (23.1)	57 (17.8)	73 (18.3)	22 (7.6)	32 (8.0)
Asymmetric	13 (4.5)	23 (5.8)	26 (8.1)	35 (8.8)	24 (8.3)	32 (8.0)
Impingement	10 (3.5)	17 (4.3)	23 (7.2)	29 (7.3)	66 (22.8)	90 (22.6)
Endurance	11 (3.8)	20 (5.0)	13 (4.1)	18 (4.5)	10 (3.5)	14 (3.5)
Other	8 (2.8)	14 (3.5)	3 (0.9)	6 (1.5)	9 (3.1)	15 (3.8)
Missingness	111 (27.8)	-	79 (19.8)	-	110 (27.6)	-

Note: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables.

6

Supplementary Table 3. Baseline characteristics of included and excluded participants for the primary analysis.

Characteristics	Included			Excluded		
	Combined (N = 2,572)	Male (N = 1,133)	Female (N = 1,439)	Combined (N = 2,357)	Male (N = 1,287)	Female (N = 1,070)
Age, years	13.6 (0.3)	13.6 (0.4)	13.6 (0.3)	13.7 (0.4)	13.7 (0.4)	13.7 (0.4)
Ethnicity						
Western	1,994 (77.5)	884 (78.0)	1,110 (77.1)	1,630 (69.2)	886 (68.8)	744 (69.5)
African	332 (12.9)	135 (11.9)	197 (13.7)	438 (18.6)	244 (19.0)	194 (18.1)
Asian	135 (5.2)	62 (5.5)	73 (5.1)	146 (6.2)	79 (6.1)	67 (6.3)
Other	75 (2.9)	39 (1.5)	36 (2.5)	70 (3.0)	45 (3.5)	25 (2.3)
Weight category						
Normal weight	1,921 (74.7)	871 (76.9)	1,050 (73.0)	1679 (71.2)	916 (71.2)	763 (71.3)
Underweight	299 (11.6)	128 (11.3)	171 (11.9)	212 (9.0)	125 (9.7)	87 (8.1)
Overweight or Obesity	352 (13.7)	134 (11.8)	218 (15.1)	455 (19.3)	239 (18.6)	216 (20.2)
Type of sport						
None	333 (12.9)	107 (9.4)	226 (15.7)	327 (13.9)	153 (11.9)	174 (16.3)
Cutting	917 (35.7)	528 (46.6)	389 (27.0)	766 (32.5)	521 (40.5)	245 (22.9)
Flexibility	326 (12.7)	89 (7.9)	237 (16.5)	239 (10.1)	90 (7.0)	149 (13.9)
Asymmetric	163 (6.3)	74 (6.5)	89 (6.2)	109 (4.6)	61 (4.7)	48 (4.5)
Impingement	159 (6.2)	28 (2.5)	131 (9.1)	106 (4.5)	29 (2.3)	77 (7.2)
Endurance	142 (5.5)	57 (5.0)	85 (5.9)	131 (5.6)	62 (4.8)	69 (6.4)
Other	23 (0.9)	16 (1.4)	7 (0.5)	15 (0.6)	14 (1.1)	1 (0.1)
Physical activity frequency						
< 4 days/week	638 (24.8)	233 (20.6)	405 (28.1)	460 (19.5)	210 (16.3)	250 (23.4)
≥ 4 days/week	1,298 (50.5)	606 (53.5)	692 (48.1)	952 (40.4)	523 (40.6)	429 (40.1)
FHGP						
Open	1,487 (57.8)	1,048 (92.5)	439 (30.5)	1,139 (48.3)	923 (71.7)	216 (20.2)
Closed	1,085 (42.2)	85 (7.5)	1,000 (69.5)	766 (32.5)	110 (8.5)	656 (61.3)
Radiographic measurements						
NSA, degrees	131.9 (5.5)	131.6 (5.2)	132.1 (5.7)	132.0 (5.6)	131.9 (5.5)	132.1(5.7)
AA, degrees	43.4 (4.5)	44.5 (4.1)	42.4 (4.5)	46.2 (10.1)	47.4 (10.1)	44.8(10.1)

Note: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables, based on observed data. FHGP, femoral head growth plate; NSA, neck shaft angle; AA, alpha angle.

Supplementary Table 4. The prevalence of primary cam morphology at age 18 years by overall, sex-specific, and ethnicity-specific subgroups (N = 2,572).

	Prevalence N (%; 95%CI)
Overall	311/2,572 (12.1%; 10.8%-13.4%)
Birth-assigned sex	
Male	268/1,133 (23.7%; 21.2%-26.1%)
Female	43/1,439 (3.0%; 2.1%-3.9%)
Ethnicity*	
Western	257/1994 (12.9%; 11.4%-14.4%)
African	35/332 (10.5%; 7.2%-13.8%)
Asian	5/135 (3.7%; 0.5%-6.9%)
Other	11/75 (14.7%; 6.7%-22.7%)

Note: Data on ethnicity was missing in 36 participants.

6

Supplementary Table 5. Associated factors at age 13 and primary cam morphology development within 5 years in complete cases (N = 1,695).

Characteristics	Combined (N = 1,695)			Male (N = 734)			Female (N = 961)	
	PCM N = 207	No PCM N = 1,488	aOR (95% CI)	PCM N = 173	No PCM N = 561	aOR (95% CI)	PCM N = 34	Not PCM N = 927
Age	13.5 (0.3)	13.6 (0.3)	0.84 (0.46, 1.46)	13.5 (0.3)	13.6 (0.3)	0.81 (0.40, 1.55)	13.6 (0.5)	13.6 (0.3)
Sex								
Female	34 (16.4)	927 (62.3)	1 (Ref.)	-	-	-	-	-
Male	173 (83.6)	561 (37.7)	6.62 (4.13, 11.00) ***	-	-	-	-	-
Ethnicity								
Western	183 (88.4)	1,205 (81.0)	1 (Ref.)	154 (89.0)	450 (80.2)	1 (Ref.)	29 (85.3)	755 (81.4)
African	13 (6.3)	166 (11.2)	0.66 (0.34, 1.19)	10 (5.8)	58 (10.3)	0.60 (0.28, 1.18)	3 (8.8)	108 (11.7)
Asian	3 (1.4)	76 (5.1)	0.25 (0.06, 0.70) *	2 (1.2)	34 (6.1)	0.18 (0.03, 0.61) *	1 (2.9)	42 (4.5)
Other	8 (3.9)	41 (2.8)	1.14 (0.46, 2.54)	7 (4.0)	19 (3.4)	1.13 (0.42, 2.77)	1 (2.9)	22 (2.4)
Weight category								
Normal weight	154 (74.4)	1,143 (76.8)	1 (Ref.)	131 (75.7)	443 (79.0)	1 (Ref.)	23 (67.6)	700 (75.5)
Underweight	37 (17.9)	170 (11.4)	1.61 (1.03, 2.48) *	32 (18.5)	56 (10.0)	1.79 (1.08, 2.95) *	5 (14.7)	114 (12.3)
Overweight or Obesity	16 (7.7)	175 (11.8)	0.98 (0.53, 1.70)	10 (5.8)	62 (11.0)	0.70 (0.32, 1.39)	6 (17.6)	113 (12.2)
Type of sport								
None	12 (5.8)	244 (16.4)	1 (Ref.)	8 (4.6)	77 (13.7)	1 (Ref.)	4 (11.8)	167 (18.0)
Cutting	124 (59.9)	634 (42.6)	2.24 (1.20, 4.52) *	112 (64.7)	315 (56.1)	2.83 (1.35, 6.70) **	12 (35.3)	319 (34.4)
Flexibility	20 (9.7)	239 (16.1)	1.73 (0.80, 3.86)	14 (8.1)	60 (10.7)	2.00 (0.78, 5.40)	6 (17.6)	179 (19.3)
Asymmetric	18 (8.7)	126 (8.5)	2.22 (1.00, 5.08)	13 (7.5)	49 (8.7)	2.24 (0.86, 6.19)	5 (14.7)	77 (8.3)
Impingement	14 (6.8)	120 (8.1)	3.70 (1.55, 8.97) **	9 (5.2)	13 (2.3)	6.53 (2.06, 21.44) **	5 (14.7)	107 (11.5)
Endurance	15 (7.2)	110 (7.4)	2.12 (0.91, 5.03)	13 (7.5)	38 (6.8)	2.81 (1.05, 7.85) *	2 (5.9)	72 (7.8)
Other	4 (1.9)	15 (1.0)	2.76 (0.66, 9.86)	4 (2.3)	9 (1.6)	3.79 (0.84, 15.72)	0 (0)	6 (0.6)
Physical activity frequency								
< 4 days/week	45 (21.7)	511 (34.3)	1 (Ref.)	36 (20.8)	174 (31.0)	1 (Ref.)	9 (26.5)	337 (36.4)
≥ 4 days/week	162 (78.3)	977 (65.7)	1.35 (0.93, 2.00)	137 (79.2)	387 (69.0)	1.31 (0.85, 2.04)	25 (73.5)	590 (63.6)
Radiographic measurements								
NSA	130.5 (4.7)	132.1 (5.7)	0.95 (0.92, 9.79) ***	130.4 (4.8)	132.0 (5.6)	0.95 (0.92, 0.98) ***	131.1 (4.2)	132.1 (5.8)

Note: Values are expressed as mean (SD) for continuous variables or frequencies (percentages) for categorical variables based on observed data.
The effect estimates were derived from multivariable logistic regression in complete cases. This model included baseline age, sex, ethnicity, weight category, type of sport, physical activity frequency, NSA, and was adjusted for femoral head growth plate status. Due to the limited number of cases, no separate logistic regression analysis was performed in females. Abbreviation: PCM, primary cam morphology; aOR, adjusted odds ratios; CI, confidence interval; NSA, neck shaft angle. *P value < 0.05, ** P value < 0.01, *** P value < 0.001.

Chapter 7

General Discussion

This thesis represents the first large-scale population-based study investigating the prevalence and associated factors of primary cam morphology (PCM) and pincer morphology in the general adolescent population. In the first part, we estimated the prevalence of PCM and pincer morphology in early adolescents. In the second part, we investigated factors associated with PCM and pincer morphology in early adolescents. In the third part, we longitudinally assessed factors associated with the development of PCM in the general population. This chapter will discuss the definition of PCM and pincer morphology, imaging modalities, findings (including prevalence and associated factors), prevention strategies, strengths and limitations, clinical relevance and future perspectives.

1. DEFINING PRIMARY CAM MORPHOLOGY

PCM, characterized by an extra bone formation at the femoral-head neck junction, is recognized as a physiological response to mechanical loadings during skeletal maturation [1]. The alpha angle is one of the most common measures to define PCM in various imaging modalities, planes and views, quantifying the deviation of the femoral head from sphericity. Although alpha angle thresholds ranging from 50° to 83° have been proposed in various studies [1], the threshold of 60° was supported by a systematic review, the Lisbon agreement, and the Oxford consensus [2-4]. Additionally, epidemiological data from the CHECK cohort and Chingford cohort indicated that an alpha angle of 60° represented a minimum separating two distinct peaks in the bimodal distribution, supporting an alpha angle threshold of 60° to define PCM [5]. While an alpha angle threshold ≥ 60° is widely used for classifying PCM, it does not diagnose femoroacetabular impingement (FAI) syndrome on its own. Clinicians must integrate imaging findings with symptoms and clinical signs for diagnosis, as outlined in the Warwick agreement [6]. **Chapters 2, 4** and **6** used an alpha angle ≥ 60° to define PCM.

However, recent research from the CHECK cohort has revealed that not all PCM subtypes captured by an alpha angle ≥ 60° on the anteroposterior (AP) pelvic radiograph are associated with the development of hip osteoarthritis (OA) within 10-year follow-up [7]. Using statistical shape modeling, the CHECK study identified four distinct morphological subtypes of PCM, but only two specific subtypes (e.g. a flattened head-neck junction in males and females, a pistol-grip morphology in males) were associated with incident radiographic hip OA. This suggests that the classification of PCM by an alpha angle ≥ 60° alone could include too many shape variations irrelevant to the development of hip OA.

Chapter 4 used the alpha angle as a dichotomous outcome (alpha angle ≥ 60°) and a continuous outcome, which has advantages and disadvantages. Using a dichotomous outcome based on a validated alpha angle threshold of ≥ 60° allows for comparisons with other epidemiological studies on the prevalence or etiology of PCM and is helpful for clinical practice. The disadvantage of dichotomization is that individuals with alpha angles close to the threshold may be classified differently due to alpha angle measurement variability. Moreover, dichotomizing could obscure associations between factors and the extent of morphological change. For example, a dichotomized approach (i.e. ≥ 60° vs. < 60°) treats an alpha angle of 40° and 59° as equivalent, while separating an alpha angle of 59° from an alpha angle of 60°. The advantage of continuous outcome is that it preserves more information regarding changes in alpha angles than dichotomous classifications. Moreover, a continuous outcome increases statistical power to detect subtle associations. The recent Oxford Consensus also advised using continuous alpha angle measures for research on the etiology of PCM [2]. However, a notable disadvantage is that small increments of increase in low alpha angles may lack clinical relevance and could be challenging to interpret in a clinical context. Another disadvantage of a continuous outcome is that if the chosen statistical model does not correctly model the relationship between variables and the continuous outcome, the results may lead to incorrect inclusions.

In addition to the alpha angle, the triangular index ratio (TIR) is another radiographic measurement used to assess PCM on the AP view. Gosvig et al. defined PCM in adults by the presence of the triangular index (a pathologically increased radius ≥ natural radius + 2 mm) on the AP view [8]. **Chapter 2** converted the triangular index into a TIR threshold of ≥ 1.05 to define PCM due to differences in femoral head size between adolescents and adults. **Chapter 2** determined the prevalence of PCM in four groups: 1) an alpha angle ≥ 60°; 2) a TIR ≥ 1.05; 3) an alpha angle ≥ 60° or a TIR ≥ 1.05; and 4) both an alpha angle ≥ 60° and a TIR ≥ 1.05. Although the alpha angle is the most commonly used measurement to define PCM, we argue that by additionally including TIR, we provide a more complete assessment of the femoral head morphology compared to studies that only employ the alpha angle. The main difference between an alpha angle and a TIR is the point at which they are measured. An alpha angle measures the alpha point where the femoral head deviates from the best-fitting circle, while a TIR evaluates the lateral bone extension at the midpoint of the femoral head radius along the femoral neck axis. Therefore, they could identify different PCM at the femoral head-neck junction. Using an alpha angle ≥ 60° or a TIR ≥ 1.05 allows for the detection of PCM that might be missed by either measurement alone. For example, if a bony prominence is present at half of the femoral head radius (where a TIR is measured) but not at the alpha point (where an alpha angle is measured), a hip can be classified as PCM by a TIR ≥ 1.05 but not by an alpha angle ≥

60°, and vice versa. We are the first to propose a TIR threshold of ≥ 1.05 to define PCM; however, this threshold still needs to be validated in more cohort studies. In **Chapters 4** and **6**, we only used the alpha angle to define PCM, consistent with the recommendation from the Oxford Consensus [2].

In addition to these quantitative measures, PCM can also be assessed using femoral head-neck offset and offset ratio on lateral views. An offset < 8 mm and an offset ratio ≤ 0.15 are considered indicative of PCM [3]. Additionally, a visual scoring system provides a semi-quantitative approach to PCM assessment, categorizing femoral head-neck junction morphology as normal, flattening, or prominence on lateral and AP views [9, 10]. In this visual classification system, PCM is defined when either flattening or prominence is present. PCM is a complex, three-dimensional structure, and different measurements capture different aspects of PCM. In future studies, the quantification of PCM could combine different radiographic parameters in different views, which may provide a more comprehensive evaluation of PCM. An alpha angle and a TIR can be combined on the AP view, while an alpha angle and an offset ratio can be combined on the lateral view.

2. DEFINING PINCER MORPHOLOGY

Focal pincer morphology is characterized by localized acetabular overcoverage of the femoral head and is associated with acetabular retroversion. Global pincer morphology involves generalized acetabular overcoverage of the femoral head due to a deep hip socket. There is significant heterogeneity in the definition of focal and global pincer morphology. Various radiographic signs, like the crossover sign, posterior wall sign, and ischial spine sign, are used to define focal pincer morphology. At the same time, they have poor reliability and validity due to pelvic positioning variability [11, 12]. To date, the definition of global pincer morphology lacks a validated measure and accompanying thresholds. The most commonly used objective measure is the center edge angle, which includes the lateral center edge angle (LCEA) and the Wiberg center edge angle (WCEA). The LCEA assesses acetabular bony coverage at the most lateral bony edge of the acetabulum, while WCEA measures acetabular coverage at the most lateral weight-bearing part of the acetabular sourcil [3]. The LCEA and WCEA do not always coincide: the LCEA values can be equal to or higher than the WCEA values in the same hip. This thesis employs the LCEA for assessing global pincer morphology as it more accurately reflects the biomechanical mechanism of pincer-type FAI, where impingement occurs between the femoral head-neck junction and the most lateral bony edge of the acetabulum during hip movements.

In adults, the LCEA threshold to define pincer morphology varies across studies. A LCEA threshold of ≥ 40° [13-15] is the most commonly used threshold for defining global pincer morphology in adults, but thresholds of 39° [16, 17] and 45° [18, 19] were also reported in the literature, which makes comparing across studies difficult. **Chapters 3** and **5** used a LCEA threshold of ≥ 40° to define global pincer morphology in early adolescents. Given a lack of a clear consensus on a threshold of LCEA for pincer morphology in early adolescents, **Chapter 5** also used the LCEA as a continuous outcome. This approach preserves more information regarding changes in LCEA and avoids loss of statistical power to detect associations. Using a continuous outcome enables the assessment of relationships between factors and the magnitude of changes in acetabular coverage. However, similar to alpha angles, small increments of increase in low LCEA may not necessarily result in FAI or hip OA. Nevertheless, a dichotomized outcome remains valuable for comparing findings across epidemiological studies and for translating research findings into clinical practice. However, defining LCEA dichotomously (i.e. ≥ 40° vs < 40°) may misclassify hips with LCEA close to the threshold (e.g. 39° or 41°) due to measurement variability.

There are several alternative radiographic measurements for defining pincer morphology besides the LCEA and WCEA. The modified acetabular index quantifies the inclination of the acetabular roof on the AP view, with a threshold of ≤ 0° indicating pincer morphology [3, 20]. The anterior center edge angle (ACEA) assesses anterior acetabular coverage on the lateral view, which may be clinically relevant as anteriorly located pincer morphology (ACEA ≥ 40°) with hip pain was associated with incident radiographic hip OA [13].

3. IMAGING MODALITIES

PCM and pincer morphology can be assessed by different imaging modalities, such as dual-energy X-ray absorptiometry (DXA) scans, radiographs, computed tomography (CT) scans and magnetic resonance imaging (MRI), each with its own strengths and limitations. Conventional radiographs, including AP pelvic and lateral views (e.g. Dunn), are commonly used for initial assessment of hip morphologies due to their cost-effectiveness and accessibility. The AP pelvic view assesses lateral PCM and pincer morphology; however, it cannot fully capture the three-dimensional structure of PCM and pincer morphology. PCM is usually located anterolaterally at the femoral head-neck junction. Lateral views provide the visualization of the anterolateral aspect of the femoral head-neck junction, making them more suitable for identifying PCM. Moreover, lateral views can improve the detection of anterior pincer morphology. CT scans and MRI enable three-dimensional reconstructions, allowing for precise evaluation of cam and pincer morphology. Moreover, MRI can assess intra-articular damage associated with FAI syndrome, including labral and cartilage lesions. Despite their accuracy, high costs, facility requirements, and radiation exposure (in case of CT scans) hinder their use in large-scale epidemiological studies.

In this thesis, we used DXA scans of the right hip and full-body to assess PCM and pincer morphology. We acknowledge that the DXA scan is not traditionally considered the optimal imaging modality for evaluating PCM and pincer morphology. However, this thesis aimed to assess a large cohort of children and adolescents in a population-based setting. Hip DXA scans involve lower radiation exposure (4.6–13.2 μSv) than hip or pelvic radiographs (600–700 μSv) [21, 22], which is particularly important when imaging healthy and young populations. Previous studies have utilized DXA scans for assessing hip morphologies and their relationship to hip OA [18, 23, 24], demonstrating its utility in large-scale epidemiological studies. Although the differences in imaging methods between supine DXA scans and weight-bearing pelvic radiographs may lead to measurement differences when assessing PCM and pincer morphology, Boel et al. confirmed the reliability of measurements between these two imaging modalities in adults (the intermethod intraclass correlation coefficient (ICC) was 0.72 [95% CI 0.68 – 0.75] for alpha angle, 0.81 [95% CI 0.79 – 0.84] for TIR, and 0.93 [95% CI 0.91 – 0.94] for LCEA) [25].

4. PCM AND PINCER MORPHOLOGY: PREVALENCE IN EARLY ADOLESCENCE AND LONGITUDINAL CHANGES

Until now, the prevalence of PCM and pincer morphology is poorly understood in early adolescence – the period when these bony morphologies likely develop. **Chapter 2** found that the prevalence of PCM as defined by an alpha angle ≥ 60° or a TIR ≥ 1.05 was 3.5% (3.9% in males vs. 3.0% in females). **Chapter 3** revealed that the prevalence of pincer morphology as defined by a LCEA ≥ 40° was 3.1% (3.0% in males vs. 3.3% in females) in early adolescents on DXA images of the right hip. These prevalence numbers are lower than those reported in adults, where PCM ranges from 15% – 35% in males and 2% – 10% in females [18, 19, 26, 27], and global pincer morphology ranges from 7% – 15% in males and 8% – 19% in females in population-based studies [18, 19, 26], depending on different imaging modalities, definitions and study populations.

Several factors may contribute to the relatively low prevalence in early adolescents. First, analyzing only in the right hip can lead to an underestimation in the person-level prevalence of PCM or pincer morphology, as they can also be present in the contralateral hip. Secondly, the use of AP DXA hip images limits the detection of anterolateral PCM, so this may lead to an underestimation of the prevalence. Despite the limitations of the AP view, it is still used to assess PCM and its association with hip OA in large-scale epidemiological studies [14, 28]. Thirdly, PCM and pincer morphology may not yet have developed by the age of 13 years. As demonstrated in **Chapter 6**, there was a marked increase in the prevalence of PCM when following this cohort until young adulthood (age 18). The overall prevalence of PCM increased from 3.5% at age 13 to 12.1% at age 18 in the general population. This finding is consistent with prospective studies in male athletes, which have demonstrated that PCM gradually increases in size until the femoral head growth plate is closed [9, 10]. For example, a hip with an alpha angle of 55° may develop to 60° as the individual ages, thereby progressing from not having PCM to having PCM, and contributing to a higher prevalence. In contrast, if a hip already has an alpha angle ≥ 60°, further increases in age and PCM size do not influence the prevalence. Pincer morphology may also develop further during skeletal maturation of the hip, like PCM, although prospective studies are needed to confirm the development of pincer morphology over time.

Interestingly, the prevalence of PCM was similar between male and female early adolescents (3.9% in males vs. 3.0% in females) in **Chapter 2**. However, males will be more likely to develop PCM in the follow-up than females in this cohort. As shown in **Chapter 6**, there is a marked increase in PCM prevalence of 19.8% (from 3.9% to 23.7%) in males between ages 13 and 18, whereas in females, the prevalence remained stable at 3.0%. One of the reasons is that males are, on average, less skeletally mature (open femoral head growth plate: 91% in males vs. 28% in females), and therefore still have skeletal growth potential. In addition to skeletal maturation, sex-specific differences in PCM development may also be explained by variations in sports participation. **Chapter 6** showed that at age 13, females participated in sports less frequently than males (79.9% vs. 87.6% in males), and were less likely to engage in cutting sports (32.4% vs. 57.8% in males). Similarly, **Chapter 3** demonstrated the comparable prevalence of pincer morphology between male and female early adolescents (3.0% in males vs. 3.3% in females). It is important to note that the timing of triradiate cartilage closure differs by sex, with an open triradiate cartilage observed in 48% of males compared to 4% of females around the age of 13 years. Longitudinal follow-up of the current cohort can reveal whether sex-specific differences in pincer morphology become apparent after skeletal maturation.

5.ASSOCIATED FACTORS OF PCM AND PINCER MORPHOLOGY

PCM is more prevalent in males and is associated with ethnicity, high-impact sports and higher physical activity levels [24, 29-34]. However, these associations are mostly based on studies in male athletes with small sample sizes. Moreover, it is unclear whether these factors also hold for pincer morphology and in the general population. Currently, no studies investigate factors associated with PCM and pincer morphology in the general population.

5.1 Sex and ethnicity

Chapter 6 revealed that male sex was associated with higher odds of PCM development in the general population, while Asian ethnicity was associated with lower odds. This finding aligns with evidence from population-based adult studies, which consistently demonstrated higher PCM prevalence in males compared to females [18, 19, 26, 27]. Regarding ethnicity, cross-sectional studies have shown a lower prevalence of PCM in East Asian individuals compared to Western individuals [24], even among male soccer athletes with comparable athletic backgrounds [35]. These findings suggested that underlying genetic factors may influence the susceptibility to developing PCM during adolescence.

5.2 Sporting activities

In **Chapter 4**, we found that early adolescents who participated in cutting sports had, on average, 1.07° higher alpha angles than those who did not participate in sports. This was in line with a cross-sectional study showing that elite male soccer players had alpha angles 4.3° higher than male controls [30]. **Chapter 6** revealed that participating in cutting and impingement sports at age 13 was associated with PCM development within 5 years in the sex-combined and male groups. The prevalence of PCM is highly prevalent in male (60%-90%) and female (50%-84%) athletes involved in cutting (e.g. soccer, basketball) [35-38] and impingement (e.g. ice hockey) [39-41] sports. Cutting sports involve rapid hip directional changes that place high shear forces on the hip joint, while impingement sports require deep hip flexion with internal rotation. One possible explanation is that the mechanical loading patterns inherent to cutting and impingement sports may contribute to altered femoral head growth plate orientation on the growing hip. Finite element analysis has revealed that hip flexion and external rotation (common movements in cutting and impingement sports) generate large compressive stresses at the lateral side of the femoral head growth plate. These compressive stresses stimulate more bone formation at the medial side compared to the lateral side, leading to the asymmetric stress distribution. The femoral head growth plate extends toward the femoral neck, increasing shear stresses at the lateral femoral head growth plate. The shear stresses trigger extra bone formation at the femoral head-neck junction, where PCM typically develops [31, 42]. This could potentially explain how certain sporting activities influence the development of PCM; however, it remains a hypothesis rather than an established fact.

Compared to PCM, the relationship between pincer morphology and high-impact sporting activity is less defined. **Chapter 5** observed that participating in flexibility sports was associated with lower odds of pincer morphology in early adolescents. Although a high prevalence (74%) of pincer morphology was previously reported in elite male and female ballet (flexibility sport) players [43], the definition included both focal and global overcoverage. Given the cross-sectional design of the study, the observed association between flexibility sport type and pincer morphology should be interpreted with caution. It is possible that participating in flexibility sports may have a protective effect against pincer morphology in this age group. Alternatively, early adolescents with pincer morphology could be less likely to participate in flexibility sports due to movement limitations. Longitudinal studies are needed to determine the direction and causality of this association.

5.3 Body mass index

In **Chapter 5**, we found that being overweight and obese were associated with higher odds of pincer morphology and higher LCEA in early adolescents. This aligns with a cross-sectional Generation R study found that obesity was negatively associated with the presence of mild acetabular dysplasia (undercoverage of the femoral head by the acetabulum) in 1,188 children around age 9, suggesting that increased body weight may contribute to greater acetabular coverage [44]. A potential mechanism for this association involves increased mechanical loading on the hip joint due to excessive body weight, which may stimulate bone formation at the acetabular rim, leading to femoral head overcoverage. In addition to increased mechanical loading, altered metabolic and hormonal profiles may also contribute to this association [45]. Although our findings in **Chapter 4** indicated that being overweight and obese were associated with higher alpha angles in early adolescents, this association became non-significant in the sensitivity analysis of complete cases when the sample size decreased.

This suggests that the relationship between body mass index (BMI) and higher alpha angles might be weak. In **Chapter 6**, we are the first to demonstrate that being underweight was associated with the development of PCM in the general population. In contrast, a 3-year longitudinal study of 69 male soccer players and 71 male and female controls has not demonstrated an association between BMI and change in average alpha angles. However, due to the different study populations, variations in body composition may limit the comparability of these findings. More research is needed to confirm this relationship in the general population.

5.4 Femoral head growth plate and triradiate cartilage

Regarding the relationship between the femoral head growth plate and PCM, it was reported that PCM gradually increases in size until the femoral head growth plate closure [9, 10]. This observation is consistent with the findings presented in **Chapter 4**, where a closed femoral head growth plate was associated with higher odds of PCM and higher alpha angles. After femoral head growth plate closure, significant changes in the proximal femur become rare. These findings suggest that possible interventions aimed at preventing PCM might be only useful before femoral head growth plate closure. Currently, the relationship between triradiate cartilage status and pincer morphology remains unclear. Findings from **Chapter 5** indicated that a closed triradiate cartilage was associated with higher odds of pincer morphology and higher LCEA in early adolescents. This implies that early adolescents with open triradiate cartilage in this age group still have the potential to develop pincer morphology as their triradiate cartilage closes. After triradiate cartilage closure, the acetabulum rim continues to develop through a secondary ossification center known as the os acetabuli. The ossification and fusion of the os acetabuli may further increase acetabular coverage. Longitudinal follow-up of the current cohort can elucidate how pincer morphology develops throughout adolescence.

5.5 Radiographic factors

Our findings in **Chapter 6** demonstrated that higher lateral epiphyseal extension at age 9 and lower neck shaft angle at age 13 were associated with the development of PCM in the general population. Higher lateral epiphyseal extension represents that the lateral endpoint of the femoral head growth plate moves more toward the femoral neck. These findings are consistent with longitudinal studies of young male soccer and ice hockey athletes, which identified the association between lateral epiphyseal extension and alpha angle measurements [34, 46]. Lower neck shaft angle represents a more varus hip orientation, which may contribute to PCM development by altering the distribution of mechanical stress across the femoral head growth plate. Our findings in **Chapter 6** indicated that higher lateral epiphyseal extension and lower neck shaft angle could serve as radiographic predictors for PCM development in the general population. However, a 5-year longitudinal study of 49 male soccer players found that lateral epiphyseal extension and lower neck shaft angle developed simultaneously with PCM, rather than preceding it [47]. More population-based studies are needed to investigate the association of lateral epiphyseal extension and neck shaft angle with PCM development in the general population, and to determine whether these radiographic factors can be used to identify high-risk subgroups.

6. PREVENTION STRATEGIES

The findings presented in **Chapters 4** and **6** inform potential primary prevention of PCM in the general population. Primary prevention may include reducing cutting and impingement sport loads (e.g. soccer, basketball, field/ice hockey) before femoral head growth plate closure. However, adolescents aiming for high-level cutting or impingement sport performance often engage in intensive training during critical developmental windows. Reducing training volume could limit their skill development and chances of reaching elite levels. The U.S. Little League Baseball offers a practical precedent for load management in young players that could inform primary prevention strategies for PCM. For arm safety in youth, it provides harmonized age bands with daily pitch-count limits and required rest thresholds, and broader guidance [48, 49]. This baseball program demonstrates that sport-specific, age-adjusted workload caps with mandatory recovery windows can be implemented in youth, striking a balance between sports and musculoskeletal health during periods of physeal vulnerability.

In **Chapter 6**, we observed that young adults who developed PCM were less likely to have participated in flexibility sports or to have been inactive during adolescence, compared to those who did not develop PCM. The finding suggests that incorporating flexibility sports as an alternating activity with cutting or impingement sports during adolescence could serve as a potential preventive strategy by mitigating the mechanical stress from cutting or impingement sports. However, given that around 10% of adolescents engaged in flexibility sports still developed PCM, this potential preventive strategy warrants further evaluation.

Our findings in **Chapter 6** revealed a marked sex-specific difference in PCM development between ages 13 and 18. During this period, prevalence increased from 3.9% to 23.7% in males, while it remained stable at approximately 3% in females. This suggests that the timing and necessity of primary prevention strategies should differ by sex in the general population. For males, the timing for primary prevention might be around or before age 13. For females from the general population, primary prevention might not be necessary due to the low prevalence at age 18, and should be prioritized for males. It is worth noting that female athletes participating in cutting and impingement sports have a high prevalence of PCM (50%-84%) [38, 41]; the timing and strategies of primary prevention need further exploration in female athletes.

Secondary prevention strategies for individuals with existing PCM focus on reducing symptoms or future hip OA through targeted interventions. These approaches aim to preserve joint function, minimize further intra-articular damage as well as delay hip OA development and progression, and may include several aspects. First, educating patients and adjusting activities to avoid motions that exacerbate impingement between the femoral head-neck junction and the acetabulum rim, which may reduce intra-articular damage [50]. Secondly, physiotherapy-led rehabilitation to improve hip strength, balance, and functional movement patterns could help optimize hip joint mechanics and reduce symptoms [50-55]. Thirdly, arthroscopic hip surgery could be used to remove the bony prominence to reduce the mechanical conflict and repair co-existing damaged tissues when conservative treatment fails. While it is effective for symptom relief and short-term function [56, 57], long-term hip OA prevention remains unproven.

7. STRENGTHS AND LIMITATIONS

This thesis has several strengths. This thesis is the first longitudinal, prospective, population-based study to investigate the prevalence and associated factors of PCM and pincer morphology in the general population. Its large sample size increases the statistical power of the study and allows for exploring multiple modifiable factors, including type of sports, the frequency of physical activity and body weight throughout adolescence. This thesis included a substantial proportion of females, allowing for robust sex-based analyses that are scarce in the literature on the etiology of hip morphologies. The multi-ethnic population in this thesis enhances generalizability and allows the assessment of potential differences across ethnic backgrounds. The use of automated measurement to define PCM and pincer morphology is another strength. These precise and reproducible measurements reduce the potential reader bias of manual measurements.

This thesis also has several limitations that should be considered. First, **Chapters 2-6** reported hip-level rather than person-level prevalence of PCM and pincer morphology. Analyzing only the right hip can lead to an underestimation in the person-level prevalence as PCM and pincer morphology can also be present unilaterally in the left hip. Secondly, the presence of PCM and pincer morphology is most likely underestimated due to the use of AP views of the right hip in **Chapters 2-6**, as we can only identify lateral PCM and pincer morphology. Thirdly, **Chapters 4-6** only involved sport types and the frequency of physical activity, without considering the intensity and volume of physical activity. Future research could employ objective measurement tools to quantify levels of physical activity more comprehensively. Fourthly, alpha angle and LCEA were analyzed as continuous outcomes in **Chapters 4** and **5**. Small increments of increase in low alpha angle and LCEA may not be clinically meaningful or associated with FAI syndrome and hip OA. Fifthly, other potential factors — such as acetabular morphology, femur torsion, and factors contributing to hip instability – were not included but may influence the findings in **Chapters 4** and **6**. Lastly, potential selection bias was introduced in this thesis since some participants did not undergo DXA scans, or in some cases, the automated measurements could not be performed.

8. CLINICAL RELEVANCE

Hip OA is a common and debilitating disorder that has a considerable burden on individuals, healthcare systems and society [58-60]. Prospective cohort studies have shown that cam and pincer morphology are associated with the development of hip OA [28, 61, 62]. Therefore, investigating associated factors of PCM and pincer morphology development allows for primary prevention, potentially reducing the future burden of FAI syndrome and subsequent hip OA.

Primary prevention strategies may include reducing cutting and impingement sport loads for PCM, as well as controlling overweight and obesity for pincer morphology during early adolescence in the general population. From a clinical perspective, caution should be taken in labeling individuals with asymptomatic PCM or pincer morphology as having a disease, as this may lead to unnecessary anxiety and potentially harmful interventions. Most individuals with PCM or pincer morphology remain asymptomatic. There may be a continuum from PCM to intraarticular damage and eventual hip OA later in life [63]. However, the onset of symptoms along this continuum may vary between individuals, and the specific factors driving progression from asymptomatic PCM to FAI syndrome or future hip OA remain unclear. Given that not all individuals with PCM will develop hip OA (the 10-year absolute risk for incident radiographic hip OA is 69.2% [28]), secondary prevention should be tailored to target those at higher risk of developing cam-type FAI syndrome or hip OA. The developmental process from pincer morphology to intraarticular damage and eventual hip OA might be similar to PCM; however, longitudinal studies need to confirm this notion.

9.FUTURE PERSPECTIVES

In this thesis, DXA scans were employed to assess the prevalence of PCM and pincer morphology in adolescents. Although DXA scans offer advantages for large-scale epidemiological studies due to the accessibility and low radiation exposure, the intrinsic two-dimensional limitations hinder the detection of three-dimensional hip morphologies. Future Generation R studies could use hip MRI to quantify three-dimensional hip morphologies. For the next step, one could compare the differences in the definition of PCM and pincer morphology as defined by DXA versus MRI in the same participants. Moreover, the volume of PCM and pincer morphology can be quantified by hip MRI. This would not only allow for more accurate measurement of the size and extent of PCM and pincer morphology but also enable a more nuanced analysis of their etiology and clinical significance.

Future research could develop multivariable predictive models for FAI syndrome that integrate demographic characteristics, lifestyle factors, radiographic parameters, kinetic and kinematic factors, biomechanical factors, and other relevant variables. Applying machine learning algorithms (e.g. neural networks) to longitudinal cohorts could enable the early identification of high-risk individuals before FAI syndrome develops. These developed and validated predictive models would facilitate risk stratification, allowing for personalized primary prevention strategies.

Another direction for research is to understand the natural history of PCM and pincer morphology. While this thesis examined associated factors of PCM and pincer morphology in the general adolescent population, it did not address how these morphologies progress to FAI syndrome or hip OA in young adults. Following up this cohort may help identify which factors are predictive of developing symptoms or early hip OA, thereby refining risk stratification and targeted prevention strategies.

This thesis did not identify factors associated with PCM development in females from the general population. Given that the femoral head growth plate is mainly closed around age 13 in females, future investigations into the etiology of PCM in females should be conducted before age 13, ideally between ages 9 and 10. Another challenge is the inherently lower prevalence of PCM in females compared to males, which reduces statistical power and the ability to detect associations. Future research is needed to explore the etiology of PCM development in females with sufficient PCM cases, and to determine whether the etiology differs between females and males.

Lastly, future research should prioritize the development of a validated measure and its corresponding threshold for pincer morphology. The lack of consensus in quantifying pincer morphology remains a significant barrier to research comparability. Although **Chapter 5** found that overweight and obesity were associated with higher odds of pincer morphology in early adolescents, whether they are associated factors for the development of pincer morphology throughout adolescence warrants further investigation.

10. CONCLUSIONS

In this Dutch population-based cohort study, **Chapter 2** found that the prevalence of PCM as defined by an alpha angle ≥ 60° or a TIR ≥ 1.05 was 3.5% (3.9% in males vs. 3.0% in females) in early adolescents. The prevalence of pincer morphology as defined by a LCEA ≥ 40° was 3.1% (3.0% in males vs. 3.3% in females) in early adolescents based on DXA images of the right hip (**Chapter 3**). Male sex and closed femoral head growth plate were associated with higher odds of PCM and higher alpha angles in early adolescents. Additional factors associated with higher alpha angles included being overweight or obese, and participating in cutting sports (**Chapter 4**). Being overweight or obese and closed triradiate cartilage were associated with higher odds of pincer morphology and higher LCEA in early adolescents, while participating in flexibility sports was associated with lower odds of pincer morphology and lower LCEA (**Chapter 5**).

Chapter 6 revealed that being underweight, participating in cutting and impingement sports, and a lower neck shaft angle at age 13 were associated with higher odds, while Asian ethnicity was associated with lower odds of PCM development at age 18 in both the sex-combined and male groups. In a subset of participants with DXA images available at ages 9, 13 and 18 years, male sex, mostly being underweight from ages 9 to 18, as well as a higher lateral epiphyseal extension at age 9 were associated with higher odds of PCM development within 8 years (**Chapter 6**). These findings could inform the etiology of PCM and pincer morphology in the general population, providing insights into the development of potential primary prevention strategies for FAI syndrome and subsequent hip OA later in life.

REFERENCES

1. Dijkstra HP, Ardern CL, terminology, taxonomy and imaging outcomes. Br J Sports Med 2022; 57: 325-341.Serner A, Mosler AB, Weir A, Roberts NW, et al. Primary cam morphology; bump, burden or bog-standard? A concept analysis. Br J Sports Med 2021; 55: 1212-1221.
2. Dijkstra HP, Mc Auliffe S, Ardern CL, Kemp JL, Mosler AB, Price A, et al. Oxford consensus on primary cam morphology and femoroacetabular impingement syndrome: part 1-definitions,
3. Mascarenhas VV, Castro MO, Afonso PD, Rego P, Dienst M, Sutter R, et al. The Lisbon Agreement on femoroacetabular impingement imaging-part 2: general issues, parameters, and reporting. Eur Radiol 2021; 31: 4634-4651.
4. van Klij P, Reiman MP, Waarsing JH, Reijman M, Bramer WM, Verhaar JAN, et al. Classifying Cam Morphology by the Alpha Angle: A Systematic Review on Threshold Values. Orthop J Sports Med 2020; 8: 2325967120938312.
5. Agricola R, Waarsing JH, Thomas GE, Carr AJ, Reijman M, Bierma-Zeinstra SM, et al. Cam impingement: defining the presence of a cam deformity by the alpha angle: data from the CHECK cohort and Chingford cohort. Osteoarthritis Cartilage 2014; 22: 218-225.
6. Griffin DR, Dickenson EJ, O'Donnell J, Agricola R, Awan T, Beck M, et al. The Warwick Agreement on femoroacetabular impingement syndrome (FAI syndrome): an international consensus statement. Br J Sports Med 2016; 50: 1169-1176.
7. Tang J, Boel F, van Buuren MMA, Riedstra NS, Runhaar J, Bierma-Zeinstra S, et al. The different subtypes of cam morphology as defined by statistical shape modeling and their relationship with the development of hip osteoarthritis: A nationwide prospective cohort study (CHECK) with 10 years follow-up. Osteoarthritis Cartilage 2024; 32: 1647-1654.
8. Gosvig KK, Jacobsen S, Palm H, Sonne-Holm S, Magnusson E. A new radiological index for assessing asphericity of the femoral head in cam impingement. J Bone Joint Surg Br 2007; 89: 1309-1316.
9. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Cam morphology in young male football players mostly develops before proximal femoral growth plate closure: a prospective study with 5-yearfollow-up. Br J Sports Med 2019; 53: 532-538.
10. Agricola R, Heijboer MP, Ginai AZ, Roels P, Zadpoor AA, Verhaar JA, et al. A cam deformity is gradually acquired during skeletal maturation in adolescent and young male soccer players: a prospective study with minimum 2-year follow-up. Am J Sports Med 2014; 42: 798-806.
11. Larson CM, Moreau-Gaudry A, Kelly BT, Byrd JW, Tonetti J, Lavallee S, et al. Are normal hips being labeled as pathologic? A CT-based method for defining normal acetabular coverage. Clin Orthop Relat Res 2015; 473: 1247-1254.
12. Zaltz I, Kelly BT, Hetsroni I, Bedi A. The crossover sign overestimates acetabular retroversion. Clin Orthop Relat Res 2013; 471: 2463-2470.
13. Riedstra NS, Boel F, van Buuren M, Eygendaal D, Bierma-Zeinstra S, Runhaar J, et al. Pincer Morphology Is Not Associated With Hip Osteoarthritis Unless Hip Pain Is Present: Follow-Up Data From a Prospective Cohort Study. Arthritis Care Res (Hoboken) 2024; 76: 644-651.
14. Saberi Hosnijeh F, Zuiderwijk ME, Versteeg M, Smeele HT, Hofman A, Uitterlinden AG, et al. Cam Deformity and Acetabular Dysplasia as Risk Factors for Hip Osteoarthritis. Arthritis Rheumatol 2017; 69: 86-93.
15. Agricola R, Heijboer MP, Roze RH, Reijman M, Bierma-Zeinstra SM, Verhaar JA, et al. Pincer deformity does not lead to osteoarthritis of the hip whereas acetabular dysplasia does: acetabular

coverage and development of osteoarthritis in a nationwide prospective cohort study (CHECK). Osteoarthritis Cartilage 2013; 21: 1514-1521.
16. Polat G, Arzu U, Dinc E, Bayraktar B. Prevalence of femoroacetabular impingement and effect of training frequency on aetiology in paediatric football players. Hip Int 2019; 29: 204-208.
17. Larson CM, Sikka RS, Sardelli MC, Byrd JW, Kelly BT, Jain RK, et al. Increasing alpha angle is predictive of athletic-related "hip" and "groin" pain in collegiate National Football League prospects. Arthroscopy 2013; 29: 405-410.
18. Faber BG, Ebsim R, Saunders FR, Frysz M, Gregory JS, Aspden RM, et al. Cam morphology but neither acetabular dysplasia nor pincer morphology is associated with osteophytosis throughout the hip: findings from a cross-sectional study in UK Biobank. Osteoarthritis Cartilage 2021; 29: 1521-1529.
19. Gosvig KK, Jacobsen S, Sonne-Holm S, Palm H, Troelsen A. Prevalence of malformations of the hip joint and their relationship to sex, groin pain, and risk of osteoarthritis: a population-based survey. J Bone Joint Surg Am 2010; 92: 1162-1169.
20. Kapron AL, Peters CL, Aoki SK, Beckmann JT, Erickson JA, Anderson MB, et al. The prevalence of radiographic findings of structural hip deformities in female collegiate athletes. Am J Sports Med 2015; 43: 1324-1330.
21. Mettler FA, Jr., Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic nuclear medicine: a catalog. Radiology 2008; 248: 254-263.
22. Thomas SR, Kalkwarf HJ, Buckley DD, Heubi JE. Effective dose of dual-energy X-ray absorptiometry scans in children as a function of age. J Clin Densitom 2005; 8: 415-422.
23. Faber BG, Baird D, Gregson CL, Gregory JS, Barr RJ, Aspden RM, et al. DXA-derived hip shape is related to osteoarthritis: findings from in the MrOS cohort. Osteoarthritis Cartilage 2017; 25: 2031-2038.
24. Zheng J, Frysz M, Faber BG, Lin H, Ebsim R, Ge J, et al. Comparison between UK Biobank and Shanghai Changfeng suggests distinct hip morphology may contribute to ethnic differences in the prevalence of hip osteoarthritis. Osteoarthritis Cartilage 2025; 33: 473-481.
25. Boel F, Wortel J, van Buuren MMA, Rivadeneira F, van Meurs JBJ, Runhaar J, et al. DXA images vs. pelvic radiographs: Reliability of hip morphology measurements. Osteoarthritis Cartilage 2025; 33: 283-292.
26. Raveendran R, Stiller JL, Alvarez C, Renner JB, Schwartz TA, Arden NK, et al. Population-based prevalence of multiple radiographically-defined hip morphologies: the Johnston County Osteoarthritis Project. Osteoarthritis Cartilage 2018; 26: 54-61.
27. Laborie LB, Lehmann TG, Engesaeter IO, Eastwood DM, Engesaeter LB, Rosendahl K. Prevalence of radiographic findings thought to be associated with femoroacetabular impingement in a population-based cohort of 2081 healthy young adults. Radiology 2011; 260: 494-502.
28. Tang J, van Buuren MMA, Riedstra NS, Boel F, Runhaar J, Bierma-Zeinstra S, et al. Cam morphology is strongly and consistently associated with development of radiographic hip osteoarthritis throughout 4 follow-up visits within 10 years. Osteoarthritis Cartilage 2023; 31: 1650-1656.
29. Westermann RW, Scott EJ, Schaver AL, Schneider A, Glass NA, Levy SM, et al. Activity Level and Sport Type in Adolescents Correlate with the Development of Cam Morphology. JB JS Open Access 2021; 6.
30. Palmer A, Fernquest S, Gimpel M, Birchall R, Judge A, Broomfield J, et al. Physical activity during adolescence and the development of cam morphology: a cross-sectional cohort study of 210 individuals. Br J Sports Med 2018; 52: 601-610.

31. Agricola R, Weinans H. What causes cam deformity and femoroacetabular impingement: still too many questions to provide clear answers. Br J Sports Med 2016; 50: 263-264.
32. Zadpoor AA. Etiology of Femoroacetabular Impingement in Athletes: A Review of Recent Findings. Sports Med 2015; 45: 1097-1106.
33. Tak I, Weir A, Langhout R, Waarsing JH, Stubbe J, Kerkhoffs G, et al. The relationship between the frequency of football practice during skeletal growth and the presence of a cam deformity in adult elite football players. Br J Sports Med 2015; 49: 630-634.
34. Fernquest S, Palmer A, Gimpel M, Birchall R, Broomfield J, Wedatilake T, et al. A longitudinal cohort study of adolescent elite footballers and controls investigating the development of cam morphology. Sci Rep 2021; 11: 18567.
35. Mosler AB, Crossley KM, Waarsing JH, Jomaah N, Weir A, Holmich P, et al. Ethnic Differences in Bony Hip Morphology in a Cohort of 445 Professional Male Soccer Players. Am J Sports Med 2016; 44: 2967-2974.
36. Johnson AC, Shaman MA, Ryan TG. Femoroacetabular impingement in former high-level youth soccer players. Am J Sports Med 2012; 40: 1342-1346.
37. Siebenrock KA, Ferner F, Noble PC, Santore RF, Werlen S, Mamisch TC. The cam-type deformity of the proximal femur arises in childhood in response to vigorous sporting activity. Clin Orthop Relat Res 2011; 469: 3229-3240.
38. Gerhardt MB, Romero AA, Silvers HJ, Harris DJ, Watanabe D, Mandelbaum BR. The prevalence of radiographic hip abnormalities in elite soccer players. Am J Sports Med 2012; 40: 584-588.
39. Philippon MJ, Ho CP, Briggs KK, Stull J, LaPrade RF. Prevalence of increased alpha angles as a measure of cam-type femoroacetabular impingement in youth ice hockey players. Am J Sports Med 2013; 41: 1357-1362.
40. Lerebours F, Robertson W, Neri B, Schulz B, Youm T, Limpisvasti O. Prevalence of Cam-Type Morphology in Elite Ice Hockey Players. Am J Sports Med 2016; 44: 1024-1030.
41. Ross KA, Mojica ES, Lott A, Carter C, Gonzalez-Lomas G. Characterization of pincer-type Hip impingement in professional women's ice hockey players. Phys Sportsmed 2023; 51: 610-614.
42. Roels P, Agricola R, Oei EH, Weinans H, Campoli G, Zadpoor AA. Mechanical factors explain development of cam-type deformity. Osteoarthritis Cartilage 2014; 22: 2074-2082.
43. Harris JD, Gerrie BJ, Varner KE, Lintner DM, McCulloch PC. Radiographic Prevalence of Dysplasia, Cam, and Pincer Deformities in Elite Ballet. Am J Sports Med 2016; 44: 20-27.
44. Chung WK, De Vos-Jakobs S, Rivadeneira F, Bierma-Zeinstra SM, Waarsing JH. The association of BMI and physical activity on acetabular dysplasia in children. Osteoarthritis Cartilage 2021; 29: 50-58.
45. Shapses SA, Sukumar D. Bone metabolism in obesity and weight loss. Annu Rev Nutr 2012; 32: 287-309.
46. Hanke MS, Schmaranzer F, Steppacher SD, Reichenbach S, Werlen SF, Siebenrock KA. A Cam Morphology Develops in the Early Phase of the Final Growth Spurt in Adolescent Ice Hockey Players: Results of a Prospective MRI-based Study. Clin Orthop Relat Res 2021; 479: 906-918.
47. van Klij P, Heijboer MP, Ginai AZ, Verhaar JAN, Waarsing JH, Agricola R. Clinical and radiological hip parameters do not precede, but develop simultaneously with cam morphology: a 5-year follow-up study. Knee Surg Sports Traumatol Arthrosc 2021; 29: 1401-1410.
48. Dowling B, McNally MP, Chaudhari AMW, Onate JA. A Review of Workload-Monitoring Considerations for Baseball Pitchers. J Athl Train 2020; 55: 911-917.
49. Feeley BT, Schisel J, Agel J. Pitch Counts in Youth Baseball and Softball: A Historical Review. Clin J Sport Med 2018; 28: 401-405.

50. Wall PD, Dickenson EJ, Robinson D, Hughes I, Realpe A, Hobson R, et al. Personalised Hip Therapy: development of a non-operative protocol to treat femoroacetabular impingement syndrome in the FASHIoN randomised controlled trial. Br J Sports Med 2016; 50: 1217-1223.
51. Hoit G, Whelan DB, Dwyer T, Ajrawat P, Chahal J. Physiotherapy as an Initial Treatment Option for Femoroacetabular Impingement: A Systematic Review of the Literature and Meta-analysis of 5 Randomized Controlled Trials. Am J Sports Med 2020; 48: 2042-2050.
52. Casartelli NC, Bizzini M, Maffiuletti NA, Sutter R, Pfirrmann CW, Leunig M, et al. Exercise Therapy for the Management of Femoroacetabular Impingement Syndrome: Preliminary Results of Clinical Responsiveness. Arthritis Care Res (Hoboken) 2019; 71: 1074-1083.
53. Kemp JL, Risberg MA, Schache AG, Makdissi M, Pritchard MG, Crossley KM. Patients With Chondrolabral Pathology Have Bilateral Functional Impairments 12 to 24 Months After Unilateral Hip Arthroscopy: A Cross-sectional Study. J Orthop Sports Phys Ther 2016; 46: 947-956.
54. Freke MD, Kemp J, Svege I, Risberg MA, Semciw A, Crossley KM. Physical impairments in symptomatic femoroacetabular impingement: a systematic review of the evidence. Br J Sports Med 2016; 50: 1180.
55. Hatton AL, Kemp JL, Brauer SG, Clark RA, Crossley KM. Impairment of dynamic single-leg balance performance in individuals with hip chondropathy. Arthritis Care Res (Hoboken) 2014; 66: 709-716.
56. Palmer AJR, Ayyar Gupta V, Fernquest S, Rombach I, Dutton SJ, Mansour R, et al. Arthroscopic hip surgery compared with physiotherapy and activity modification for the treatment of symptomatic femoroacetabular impingement: multicentre randomised controlled trial. BMJ 2019; 364: l185.
57. Griffin DR, Dickenson EJ, Wall PDH, Achana F, Donovan JL, Griffin J, et al. Hip arthroscopy versus best conservative care for the treatment of femoroacetabular impingement syndrome (UK FASHIoN): a multicentre randomised controlled trial. Lancet 2018; 391: 2225-2235.
58. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019; 393: 1745-1759.
59. Glyn-Jones S, Palmer AJ, Agricola R, Price AJ, Vincent TL, Weinans H, et al. Osteoarthritis. Lancet 2015; 386: 376-387.
60. Hunter DJ, Schofield D, Callander E. The individual and socioeconomic impact of osteoarthritis. Nat Rev Rheumatol 2014; 10: 437-441.
61. Casartelli NC, Maffiuletti NA, Valenzuela PL, Grassi A, Ferrari E, van Buuren MMA, et al. Is hip morphology a risk factor for developing hip osteoarthritis? A systematic review with meta-analysis. Osteoarthritis Cartilage 2021; 29: 1252-1264.
62. van Klij P, Heerey J, Waarsing JH, Agricola R. The Prevalence of Cam and Pincer Morphology and Its Association With Development of Hip Osteoarthritis. J Orthop Sports Phys Ther 2018; 48: 230-238.
63. Heerey JJ, van Klij P, Agricola R, Dijkstra HP, Plass L, Crossley KM, et al. Preventing hip osteoarthritis in athletes: is it really a mission impossible? Br J Sports Med 2024; 58: 465-467.

Chapter 8

Summary/Samenvatting

SUMMARY

Osteoarthritis (OA) is a chronic and disabling joint disease that affects 7.6% of the global population and imposes a substantial burden on individuals, healthcare systems, and society. Currently, there is no cure for OA, and treatments primarily focus on symptom relief and improving joint function. By the time symptoms appear, irreversible damage to joint structures has often already occurred. Although joint replacement remains an effective intervention for late-stage disease, it is costly and not universally accessible. Therefore, preventive measures targeting modifiable risk factors are of importance to reduce the burden of OA. Femoroacetabular impingement (FAI) syndrome, a strong risk factor for hip OA development, is a clinical disorder characterized by abnormal contact between the proximal femur and the acetabulum during hip movements. Two types of morphological variants of FAI syndrome include cam and pincer morphology. Both morphologies can lead to FAI, which can induce shear forces on the acetabular labrum and articular cartilage, resulting in intra-articular damage and hip OA in future. However, the etiology of primary cam morphology (PCM) and pincer morphology in the general population remains largely unexplored at present.

This thesis consists of three parts. The first part described the overall and sex-specific prevalence of PCM and pincer morphology in early adolescents from the general population. The second part determined associated factors of the presence of PCM and pincer morphology in early adolescents from the general population. The third part determined factors associated with the development of PCM in the general population.

Although some studies have investigated the prevalence of PCM in the general adult population, the prevalence in early adolescence remains unclear. Chapter 2 included 4,477 Dutch early adolescents with a mean age of 13.5 years, of whom 48.4% were male. PCM was defined as an alpha angle ≥ 60° and/or a triangular index ratio (TIR) ≥ 1.05, measured automatically using validated, in-house developed methods. The overall prevalence of PCM was 3.5% (95% confidence interval [CI] 2.9 – 4.0%) as defined by an alpha angle ≥ 60° or a TIR ≥ 1.05, and the prevalence was similar in males (3.9% [95% CI 3.1 – 4.7%]) and females (3.0% [95% CI 2.3 – 3.7%]). The overall prevalence of PCM was 1.0% (95% CI 0.7 – 1.3%) as defined by an alpha angle ≥ 60° and a TIR ≥ 1.05, and the prevalence was also similar between sexes: 1.2% (95% CI 0.7 – 1.6%) in males vs. 0.9% (95% CI 0.5 – 1.2%) in females.

Until now, the exact age at which pincer morphology starts to develop has not yet been elucidated. No studies have investigated the prevalence of pincer morphology in early adolescence – the period when this bony shape likely develops. A total of 3,986 Dutch

early adolescents (median age 13.5 years; 46.8% males) were included in Chapter 3. Pincer morphology was defined as a lateral center edge angle (LCEA) ≥ 40°. The overall prevalence of pincer morphology was 3.1% (95% CI 2.6% – 3.6%) and that it was similar in males (3.0%, [95% CI 2.2% – 3.7%]) and females (3.3%, [95% CI 2.5% – 4.0%]).

In Chapter 4, we investigated factors associated with PCM (an alpha angle ≥ 60°) in 4,477 early adolescents from the general population. We found that male sex (adjusted odds ratio [aOR] 2.56, 95% CI 1.62 – 4.04) and closed femoral head growth plate (aOR 3.28, 95% CI 2.05 – 5.24) were associated with higher odds of PCM, whereas underweight (aOR 0.42, 95% CI 0.18 – 0.97) was associated with lower odds of PCM. We also investigated factors associated with higher alpha angles in early adolescents in Chapter 4. We observed that male sex (β coefficient 2.99, 95% CI 2.40 – 3.58), closed femoral head growth plate (β coefficient 1.22, 95% CI 0.61 – 1.82), cutting sport type (β coefficient 1.07, 95% CI 0.30 – 1.85), overweight (β coefficient 0.89, 95% CI 0.22 – 1.55) and obesity (β coefficient 1.81, 95% CI 0.57 – 3.04) were associated with higher alpha angles. Ethnicity and physical activity frequency were not associated with PCM or higher alpha angles.

In Chapter 5, we investigated factors associated with pincer morphology (an LCEA ≥ 40°) in 3,986 early adolescents from the general population. We observed that overweight (aOR 2.26, 95% CI 1.45 – 3.51), obesity (aOR 4.49, 95% CI 2.41 – 8.34), and closed triradiate cartilage (aOR 5.04, 95% CI 2.45 – 10.39) were associated with higher odds of pincer morphology, while flexibility sport type (aOR 0.35, 95% CI 0.13 – 0.92) was associated with lower odds of pincer morphology. Given a lack of a clear consensus on a threshold of LCEA for pincer morphology in early adolescents, we also used the LCEA as a continuous outcome in Chapter 5. We found that overweight (β coefficient 1.00, 95% CI 0.47 – 1.53), obesity (β coefficient 2.20, 95% CI 1.23 – 3.17) and closed triradiate cartilage (β coefficient 3.31, 95% CI 2.83 – 3.80) were associated with higher LCEA, while flexibility sport type (β coefficient 0.72, 95% CI -1.43 – -0.01) was associated with lower LCEA. Sex, ethnicity and physical activity frequency were not associated with pincer morphology or higher LCEA.

In Chapter 6, we longitudinally assessed demographic, anthropometric, lifestyle, and radiographic factors at age 13 that are associated with the development of PCM within 5 years in the general population. We found that being underweight, participating in cutting and impingement sports, and a lower neck shaft angle at age 13 were associated with higher odds, while Asian ethnicity was associated with lower odds of PCM development at age 18 in both the sex-combined and male groups. Additionally, we evaluated factors associated with the development of PCM within 8 years (ages 9, 13, and 18 years). We found that male sex, mostly being underweight from ages 9 to 18, and a higher lateral epiphyseal extension at age 9 were associated with PCM development within 8 years.

Finally, Chapter 7 discussed the definitions and imaging modalities of PCM and pincer morphology, and interpreted the findings from the previous chapters. Moreover, this chapter acknowledged methodological strengths and limitations, and explored clinical implications and future research directions. The main findings of this thesis enhance our understanding of the etiology of PCM and pincer morphology in the general population and offer valuable insights for developing potential primary prevention strategies for FAI syndrome and subsequent hip OA later in life.

SAMENVATTING

Artrose is een chronische en invaliderende gewrichtsaandoening die bij 7.6% van de wereldbevolking voorkomt en brengt een aanzienlijke last met zich mee voor individuen, de gezondheidszorg en de maatschappij. Momenteel bestaat er geen genezende behandeling voor artrose; de behandelingen richten zich voornamelijk op symptoombestrijding en het verbeteren van de gewrichtsfunctie. Tegen de tijd dat de symptomen zich presenteren, is er vaak al onherstelbare schade aan het gewricht opgetreden. Hoewel gewrichtsvervanging een effectieve interventie blijft bij artrose in een vergevorderd stadium, is het een kostbare, en niet voor iedereen toegankelijke, behandeling. Dit is waarom preventieve maatregelen die gericht zijn op beïnvloedbare risicofactoren van belang zijn, om zo de last van artrose te verminderen. Femoroacetabulair impingement (FAI)-syndroom, een sterke risicofactor voor de ontwikkeling van heupartrose, is een klinische aandoening die wordt gekenmerkt door abnormaal contact tussen het acetabulum en het proximale femur tijdens beweging. Cam- en pincermorfologie zijn de twee afwijkende morfologieën betrokken bij FAI syndroom. FAI oefent schuifkrachten uit op het acetabulair labrum en het gewrichtskraakbeen, resulterend in intra-articulair letsel en het ontstaan van heupartrose in de toekomst. De etiologie van primaire cammorfologie (PCM) en pincermorfologie in de algemene bevolking is echter tot op heden nog grotendeels onbekend.

Dit proefschrift bestaat uit drie delen. Het eerste deel beschrijft de algehele en geslachtsspecifieke prevalentie van PCM en pincermorfologie bij jonge adolescenten in de algemene bevolking. Het tweede deel bestudeert de factoren die geassocieerd zijn met de aanwezigheid van PCM en pincermorfologie bij jonge adolescenten in de algemene bevolking. Het derde deel bestudeerd de factoren die geassocieerd zijn met de ontwikkeling van PCM in de algemene bevolking.

Hoewel sommige studies de prevalentie van PCM in de algemene volwassen bevolking hebben onderzocht, blijft de prevalentie in de vroege adolescentie onduidelijk. Hoofdstuk 2 onderzocht 4,477 Nederlandse vroege adolescenten met een gemiddelde leeftijd van 13.5 jaar, van wie 48.4% man was. PCM werd gedefinieerd als een alfahoek ≥ 60° en/of een triangulaire indexratio (TIR) ≥ 1.05. Beiden werden automatisch gemeten met behulp van gevalideerde, intern ontwikkelde methoden. De prevalentie van PCM was 3.5% (95% CI 2.9 – 4.0%), zoals gedefinieerd door een alfahoek ≥ 60° of een TIR ≥ 1,05. De prevalentie was vergelijkbaar bij mannen (3.9% [95% CI 3.1 – 4.7%]) en vrouwen (3.0% [95% CI 2.3 – 3.7%]). De algehele prevalentie van PCM was 1.0% (95% CI 0.7 –1.3%), zoals gedefinieerd door een alfahoek ≥ 60° en een TIR ≥ 1,05. De prevalentie was ook

vergelijkbaar tussen de geslachten: 1.2% (95% CI 0.7 – 1.6%) bij mannen versus 0.9% (95% CI 0.5 – 1.2%) bij vrouwen.

Tot nu toe is de exacte leeftijd waarop pincermorfologie zich begint te ontwikkelen nog onbekend. Er zijn geen studies die de prevalentie van pincermorfologie in de vroege adolescentie onderzoeken – de periode waarin deze botvorm zich waarschijnlijk ontwikkelt. In totaal werden 3,986 Nederlandse vroege adolescenten (mediane leeftijd 13.5 jaar; 46,8% mannen) geïncludeerd in Hoofdstuk 3. Pincermorfologie werd gedefinieerd als een laterale center edge angle (LCEA) ≥ 40°. De prevalentie van pincermorfologie was 3.1% (95% CI 2.6% – 3.6%) en dat deze vergelijkbaar was bij mannen (3.0% [95% CI 2.2% – 3.7%]) en vrouwen (3.3% [95% CI 2.5% – 4.0%]).

In Hoofdstuk 4 onderzochten we factoren die verband houden met de PCM (een alfahoek ≥ 60°) bij 4,477 vroege adolescenten uit de algemene bevolking. We ontdekten dat mannelijk geslacht (gecorrigeerde odds ratio [aOR] 2.56, 95% CI 1.62 – 4.04) en een gesloten groeischijf van de femurkop (aOR 3.28, 95% CI 2.05 – 5.24) geassocieerd waren met een hogere kans op PCM, terwijl ondergewicht (aOR 0.42, 95% CI 0.18 – 0.97) geassocieerd was met een lagere kans op PCM. In Hoofdstuk 4 onderzochten we ook factoren die verband houden met hogere alfahoeken bij vroege adolescenten. We observeerden dat mannelijk geslacht (β coefficient 2.99, 95% CI 2.40 – 3.58), gesloten groeischijf van de femurkop (β coefficient 1.22, 95% CI 0.61 – 1.82), cutting sport type (β coefficient 1.07, 95% CI 0.30 – 1.85), overgewicht (β coefficient 0.89, 95% CI 0.22 – 1.55) en obesitas (β coefficient 1.81, 95% CI 0.57 – 3.04) geassocieerd waren met een hogere alfahoek. Etniciteit en frequentie van fysieke activiteit waren niet geassocieerd met PCM of een hogere alfahoek.

In Hoofdstuk 5 onderzochten we factoren die geassocieerd zijn met pincermorfologie (een LCEA ≥ 40°) bij 3,986 vroege adolescenten uit de algemene bevolking. We observeerden dat overgewicht (aOR 2.26, 95% CI 1.45 – 3.51), obesitas (aOR 4.49, 95% CI 2.41 – 8.34) en gesloten triradiële groeischijf (aOR 5.04, 95% CI 2.45 – 10.39) geassocieerd waren met een hogere kans op pincermorfologie, terwijl lenigheidssporten (aOR 0.35, 95% CI 0,13 – 0,92) geassocieerd was met een lagere kans op pincermorfologie. Gezien het ontbreken van een duidelijke consensus over de drempelwaarde van de LCEA voor pincermorfologie bij vroege adolescenten, gebruikten we in Hoofdstuk 5 ook de LCEA als continue uitkomstmaat. We vonden dat overgewicht (β coefficient 1.00, 95% CI 0.47 – 1.53), obesitas (β coefficient 2.20, 95% CI 1.23 – 3.17) en gesloten triradiaat kraakbeen (β coefficient 3.31, 95% CI 2.83 – 3.80) geassocieerd waren met een hogere LCEA, terwijl lenigheidssporten (β coefficient -0.72, 95% CI -1.43 – -0.01) geassocieerd was met een lagere LCEA. Geslacht, etniciteit en frequentie van fysieke activiteit waren niet geassocieerd met pincermorfologie of een hogere LCEA.

In hoofdstuk 6 hebben wij longitudinaal onderzocht of demografische, antropometrische, leefstijl- en radiografische factoren op de leeftijd van 13 jaar onderzocht = geassocieerd zijn met de ontwikkeling van PCM binnen 5 jaar in de algemene populatie. Wij vonden dat ondergewicht, deelname aan cutting en impingementsporten, en een kleinere collum-diafysaire hoek op de leeftijd van 13 jaar geassocieerd waren met hogere kansen, terwijl Aziatische etniciteit geassocieerd was met lagere kansen op de ontwikkeling van PCM op 18-jarige leeftijd in zowel de gecombineerde groep als de mannelijke groep. Daarnaast hebben wij factoren geëvalueerd die geassocieerd zijn met de ontwikkeling van PCM binnen 8 jaar (leeftijden 9, 13 en 18 jaar). Wij vonden dat mannelijk geslacht, voornamelijk ondergewicht tussen 9 en 18 jaar, en een grotere laterale epifysaire extensie op de leeftijd van 9 jaar geassocieerd waren met de ontwikkeling van PCM binnen 8 jaar.

Tot slot besprak Hoofdstuk 7 de definities en beeldvormingsmodaliteiten van PCM en pincermorfologie, en interpreteerde het de bevindingen uit de voorgaande hoofdstukken. Daarnaast belichtte dit hoofdstuk methodologische sterktes en beperkingen, en werden de klinische implicaties en richtingen voor toekomstig onderzoek verkend. De bevindingen van dit proefschrift dragen bij aan een beter begrip van de etiologie van PCM en pincermorfologie in de algemene bevolking en bieden waardevolle inzichten voor het ontwikkelen van mogelijke primaire preventiestrategieën voor het FAI-syndroom en daaropvolgende heupartrose later in het leven.

Appendics

PHD PORTFOLIO

PhD student	Delong Chen
Department	Orthopaedics and Sports Medicine
PhD Period	October 2021-October 2025
Promotor	Prof. Dr. S.M.A. Bierma-Zeinstra
Co-promotor	Dr. R. Agricola
	Dr. F.D.E.M. Boel

	Year	ETCS*
Courses		
Research master's degree Health Sciences, specialization Clinical Epidemiology, NIHES, Erasmus University Rotterdam, the Netherlands	2022-2024	70
Scientific Integrity	2022	0.3
Seminars and Meetings		
Generation R research meetings	2022-2025	1
Department research meetings	2021-2025	1
Science Day Orthopaedics and Sports Medicine	2022-2025	1
Soup and Science meeting	2022-2025	1
Presentations		
Oral presentation Combined 61st NOF Congress and NOV Jaarcongres 2024	2024	1
Oral presentation Young Athlete's Hip Conference and Workshops 2024	2024	2
Elevator pitch presentation Science Day Orthopaedics and Sports Medicine 2025	2025	1
Conferences		
2023 European Sports Orthopedic Congress	2023	0.5
Other activities		
Light WMO/GCP training – start onderzoek	2022	
MRI safety training (Generation R)	2022	
General tasks (data collection Generation R)	2022-2024	
Total		78.8

*One ETCS (European Credit Transfer and Accumulation System) credit corresponds to a workload of 28 hours.

ACKNOWLEDGMENTS

Looking back on my time as a PhD student, I realize that this dissertation would not have been possible without the help of many remarkable people. The past four years have been an unforgettable chapter, filled with both challenges and triumphs. I would like to take this opportunity to express my sincere appreciation to everyone who has been part of this journey.

I would like to express my deepest gratitude to my promoter, **Prof. dr. Sita Bierma-Zeinstra**, for recruiting me into this research group and providing me with the opportunity to work on this exciting project. Your profound insights into the field of osteoarthritis have greatly inspired and guided my research. Thank you for helping me grow as a researcher.

I would also like to extend my deepest gratitude to my co-promoter, **Dr. Rintje Agricola**, for fostering a collaborative environment in the research group and creating a relaxed, supportive academic atmosphere that made my projects productive. I also appreciated the opportunity to observe Zimmer Rosa robot-assisted total knee replacement, which was an invaluable clinical learning experience. I look forward to continuing to learn from your extensive clinical expertise and knowledge in the future.

My sincere thanks go to my co-promoter, **Dr. Fleur Boel.** Whenever I faced obstacles in my project, you were available for timely discussions; without your immediate guidance, moving these projects forward would have been far more difficult. Beyond the projects, I will always remember the enjoyable moments we shared during department activities.

I am also deeply grateful to the members of my assessment committee—**Prof. dr. J. Harlaar**, **Prof. dr. J.B.J. Van Meurs**, and **Prof. dr. J.L. Tol**—for generously dedicating their time and expertise to evaluating my work. I equally appreciate the opponents who took part in the defense of this dissertation, and I thank them sincerely for their insightful engagement and valuable contributions.

To my paranymphs, **Nadine and Zhongcan**: thank you for your encouragement and for being by my side. Having you stand with me during this important milestone gives me great confidence and makes the occasion even more meaningful.

I would like to express my sincere gratitude to the HIPSTAR PIs (**Jos, Jaap, Nazli and Jukka**) and my co-authors (**Fernando, Pim, Suzzane and Michiel**) for their valuable advice and contributions to my projects. I also extend my thanks to the HIPSTAR mem-

bers (**Edwin, Mirthe, Mohammad, Morteza, Nadine, and Zhongcan**) as I have learned a great deal from your insightful presentations during our meetings.

Thank you to my amazing colleagues—**Abi, Annika, Brechtje, Britt, Derek, Eline, Erin, Floris, Irene, Jinchi, Joshua, Laura, Lichelle, Mariska, Mark, Maud, Max, Merel, Michiel, Myrthe, Niels, Noortje, Sree, Tjerk, Tom and Veerle**—for all the support you've given me both at work and in daily life. I'm also truly grateful for the department activities that made me feel included and connected. Working at NC-424 was a truly pleasant experience because of the warm and friendly environment you all created, making me feel relaxed and at home.

Thank you, **Alan, Enping, Jie Deng, Jinchi, Peng Wang, Tom, Yifan, Zhiming and Zuoluo**, for all the wonderful travel memories we made together. I truly treasured our trips to Dolomites, Ireland, London, Naples, Oxford, Paris, Prague and Rome. Every trip was filled with laughter, great company, and unforgettable moments. I'm truly grateful for your friendship and for making those journeys so special.

I would like to express my appreciation to **Chunsheng, Fang Zhu, Fangxiang, Frank, Freddie, Hai, Haojie, Heng Liu, Hong Su, Hongzhen, Jiawei, Jie Gao, Junting, Kai, Letao, Liang Wu, Linfeng, Min Xia, Qiaolin, Shan Jiang, Siyu, Tian Xiao, Tong Wu, Wenchao, Wei Zhang, Wunan, Xiangjun, Xinran, Yahong, Yanyan, Yanlin, Yiqian, Yin Di, Ying Liu, Yisha, Yu Cai, Yu Shuai, Yubo, Yueyue, Yunxi, Yujie, Ze, Zhaochen, Zhenwei, Zheng Cao, Zhong Ren, Zijian and Zhangzan**. Whether we met at EMC, EUR, or elsewhere, I am so grateful for the friendships we formed during my time in the Netherlands. I will always cherish our memories of playing badmintons, sharing dinners, playing card games, cycling, traveling around the Netherlands, and so many other moments together. Thank you for making my life here so much richer and more colorful.

Last but not least, I would like to thank my girlfriend, **Weiping**, for supporting me throughout the past four years as I pursued my Ph.D. abroad. Even though you're in China, we've stayed closely connected, and your constant encouragement has meant the world to me. I look forward to experiencing many more exciting moments together in the future. I would also like to thank my parents for their unwavering love and support throughout this journey. Without you, I could not have completed my Ph.D. I am deeply grateful for everything you have done for me.

ABOUT THE AUTHOR

Delong Chen was born on December 14, 1991, in Huizhou City, Guangdong Province, China. In 2010, he began studying medicine at Guangzhou University of Chinese Medicine, where he obtained his Bachelor's degree in 2015. The same year, he pursued a master's degree at the same University. From 2015 to 2018, he completed his residency training at the First Affiliated Hospital of Guangzhou University of Chinese Medicine. In 2018, he received a scholarship to spend a year as a visiting researcher in the molecular laboratory at the University of Western Australia. Delong obtained his Master's degree in Orthopedics of Chinese medicine in 2019. Following his graduation, he worked as an orthopedic surgeon at the Clifford Hospital of Guangzhou University of Chinese Medicine for two years.

In October 2021, Delong was awarded a Doctoral Scholarship by the China Scholarship Council and began his PhD at the Generation R Study Group and the Department of Orthopedics and Sports Medicine at Erasmus MC University Medical Center Rotterdam. His PhD project focused on the prevalence and associated factors of primary cam and pincer morphology in the general adolescent population under the supervision of Prof. dr. Sita Bierma-Zeinstra, Dr. Rintje Agricola and Dr. Fleur Boel. During this project Delong obtained his second Master's degree in Clinical Epidemiology at the Netherlands Institute of Health Sciences in 2024. After completing his PhD, Delong plans to return to China to work as an orthopedic surgeon.

A

LIST OF PUBLICATIONS

In this thesis

Delong Chen, Fleur Boel, Pim van Klij, Michiel M. A. van Buuren, Sita M. A. Bierma-Zeinstra, Rintje Agricola. The prevalence of primary cam morphology in early adolescents from the general population: A population-based study (Generation R). Osteoarthritis Cartilage. 2025;33(5):633-637.

Delong Chen, Fleur Boel, Suzanne de Vos-Jakobs, Pim van Klij, Michiel M.A. van Buuren, Sita M.A. Bierma-Zeinstra, Rintje Agricola. The prevalence of pincer morphology in early adolescents from the general population: a population-based study (Generation R). Arthritis Care & Research. 2025. 77(12):1436-1442.

Delong Chen, Fleur Boel, Pim van Klij, Jos Runhaar, Fernando Rivadeneira, Sita M.A. Bierma-Zeinstra, Rintje Agricola. Associated factors of primary cam morphology in 4,477 early adolescents: a multi-ethnic, population-based, cross-sectional study (Generation R). The Orthopaedic Journal of Sports Medicine. 2025; 13(12): 23259671251394027.

Delong Chen, Fleur Boel, Suzanne de Vos-Jakobs, Pim van Klij, Jos Runhaar, Fernando Rivadeneira, Sita M.A. Bierma-Zeinstra, Rintje Agricola. Associated factors of pincer morphology in 3,986 early adolescents: a multi-ethnic population-based study in the Netherlands (Generation R). Under review.

Delong Chen, Fleur Boel, Pim van Klij, Jos Runhaar, Fernando Rivadeneira, Sita M.A. Bierma-Zeinstra, Rintje Agricola. Development of primary cam morphology and associated factors: a longitudinal population-based study (Generation R). Submitted.

Not in this thesis

Suzanne de Vos-Jakobs, Fleur Boel, **Delong Chen**, Jolien C.M. van Haasteren, Jaap J Tolk, Sita M.A. Bierma-Zeinstra, Rintje Agricola. Prevalence of acetabular dysplasia in early adolescents in a general population: a Generation R study. Under review.

Fleur Boel, Suzanne de Vos-Jakobs, **Delong Chen**, Jos Runhaar, Sita M.A. Bierma-Zeinstra, Rintje Agricola. Acetabular dysplasia at adolescence and developmental dysplasia of the hip might be a different disease: findings from a prospective population-based cohort study. Submitted.

Fleur Boel, Suzanne de Vos-Jakobs, **Delong Chen**, Fernando Rivadeneira, Sita M.A. Bierma-Zeinstra, Jos Runhaar, Rintje Agricola. Hip shape and the change in acetabular coverage in early adolescence: a longitudinal study. Submitted.