



# Multiple risk factors related to familial predisposition to anterior cruciate ligament injury: fraternal twin sisters with anterior cruciate ligament ruptures

T E Hewett,<sup>1,2,3</sup> T R Lynch,<sup>4</sup> G D Myer,<sup>1,5</sup> K R Ford,<sup>1,3</sup> R C Gwin,<sup>4</sup> R S Heidt Jr<sup>4</sup>

► Additional data (supplementary video 1) are published online only at <http://bjsm.bmj.com>

<sup>1</sup>Cincinnati Children's Hospital Medical Center and Research Foundation, Sports Medicine Biodynamics Center and Human Performance Laboratory, Cincinnati, Ohio, USA

<sup>2</sup>University of Cincinnati, College of Allied Health Sciences, Rehabilitation Sciences, Cincinnati, Ohio, USA

<sup>3</sup>University of Cincinnati Department of Pediatrics and Orthopaedic Surgery, College of Medicine, Rehabilitation Sciences and Department of Biomedical Engineering, College of Engineering, Cincinnati, Ohio, USA

<sup>4</sup>Wellington Orthopaedic and Sports Medicine, Cincinnati, Ohio, USA

<sup>5</sup>Rocky Mountain University of Health Professions, Provo, Utah, USA

## Correspondence to

T E Hewett, Cincinnati Children's Hospital, 3333 Burnet Avenue; MLC 10001, Cincinnati, Ohio 45229, USA; [tim.hewett@cchmc.org](mailto:tim.hewett@cchmc.org)

Accepted 13 December 2008

Published Online First  
21 January 2009

## ABSTRACT

**Objective** A multifactorial combination of predictors may increase anterior cruciate ligament (ACL) injury risk in athletes. The objective of this twin study was to examine these risk factors to identify commonalities in risk factors that predisposed female fraternal twins to ACL injury.

**Methods** Female twins in high-risk sports were prospectively measured prior to an injury for neuromuscular control using three-dimensional motion analysis during landing, hamstrings and quadriceps muscular strength on a dynamometer and joint laxity using a modified Beighton–Horan index and a Compu-KT arthrometer. Intraoperative measures of femoral intercondylar notch width were recorded during ACL reconstruction.

**Results** Abduction angles were increased at one knee in both of the twin sister athletes relative to uninjured controls at initial contact and at maximum displacement during landing. The twin female athletes that went on to ACL injury also demonstrated decreased peak knee flexion motion at both knees than uninjured females during landing. The twin athletes also had increased joint laxity and decreased hamstrings to quadriceps (H/Q) torque ratios compared to controls. Femoral intercondylar notch widths were also below the control mean in the twin siblings.

**Conclusions** Prescreened mature female twins that subsequently experienced ACL injury demonstrated multiple potential risk factors including: increased knee abduction angles, decreased knee flexion angles, increased general joint laxity, decreased H/Q ratios and femoral intercondylar notch width.

Anterior cruciate ligament (ACL) rupture is a severe ligamentous knee injury, leading to functional instability in the short term and to degenerative joint disease in the long term. Although ACL reconstructive procedures are available, they are costly and may have high morbidity. Between 100 000 and 250 000 ACL reconstructions are performed each year at a cost of US\$17 000 to US\$25 000 per procedure.<sup>8–12</sup> Hence, the direct medical cost for reconstructive surgeries alone are over a billion US dollars per year. This figure does not include the initial costs of conservative treatment and rehabilitation of those injuries that are not repaired.<sup>13</sup>

The high physical, mental, emotional and economic costs of ACL injury have prompted analyses of predictive risk factors for this devastating injury.<sup>11–15</sup> Anderson *et al* did not observe a difference in the prevalence of ACL injuries among family members of ACL injured and non-injured subjects.<sup>2</sup> However, two case-control studies have

reported familial history as a factor related to increased risk of ACL injury.<sup>5,20</sup> Athletes that experience an ACL tear may be more likely to have a relative with an ACL tear compared with controls matched for age, sex and sport.<sup>5</sup> First, Lambert *et al*, and more recently Flynn *et al*, reported a familial predisposition for ACL rupture. A third study, that of Harner *et al*, reported an increased prevalence of ACL rupture among family members of ACL injured subjects compared to controls. They reported that 11 of 31 patients (35%) with ACL injury had a family history of ACL tear.<sup>9</sup> In comparison, only 1 subject out of 23 (4%) from the uninjured control group had a family history of ACL injury.<sup>9</sup> Flynn *et al* reported that subjects with a history of ACL injury were twice as likely to have a first-degree relative with a history of ACL injury as a matched control group without a history of ACL injury.<sup>5</sup> Similar, Lambert *et al* reported a higher prevalence of family members with a history of ACL rupture among ACL injured subjects.

Potential risk factors for an ACL injury can be classified as intrinsic (within the body) or extrinsic (outside the body).<sup>11–15</sup> Specific intrinsic factors that have been investigated include anthropometric, biomechanical, neuromuscular, anatomic, developmental and hormonal, genetic, ligament integrity, activity level and prior injury. For example, knee abduction torque and motion during landing is a potentially strong predictor of ACL injury risk in female athletes.<sup>16</sup> Hewett *et al* reported that external knee abduction torque at the knee predicted ACL injury risk with 78% sensitivity and 73% specificity in young female athletes.<sup>16</sup>

Comparison of twin siblings may provide initial delineation of genetic traits and predisposition to disease or injury. In general, neuromuscular control, osseous anatomy, ligament integrity and body type or body mass index (BMI) theories have all been proposed as potential factors or contributors in the increased risk of ACL injury.<sup>11–15</sup> Specifically, knee abduction (valgus), knee laxity, increased quadriceps strength and relative hamstrings to quadriceps strength ratios, and intercondylar notch width have all been reported to be associated with increased risk of ACL injury in female athletes.<sup>11–15,19,23,29</sup> However, the genetic underpinnings of these potentially important risk factors remain unreported. The potential for genetic transmittal of the biomechanics of high-risk sports movements and of neuromuscular control of these movements remains an intriguing, but unstudied phenomenon.

Bony anatomic and ligamentous integrity traits, on the contrary to biomechanics of movement and neuromuscular control, are more understandable and testable potentially genetic characteristics. For example, femoral intercondylar notch width may be an inheritable trait that may predict ACL injury risk in women.<sup>34–36</sup> Knee laxity (hyperextension) may also be predictive of increased ACL injury risk.<sup>29–32</sup> Women, on average, may have narrower femoral intercondylar notch widths than men, which may be indicative of either notch impingement on the ACL or lead to a smaller ACL within the narrower intercondylar notches.<sup>34</sup> Athletes with stenosis of the intercondylar notch have been reported to be significantly more likely to injure the ACL during a non-contact sports injury.<sup>36</sup> Other reports have found no sex difference in intercondylar notch width, but these studies used the notch width index as a measure.<sup>1–4, 21</sup> The notch width index is a ratio of intercondylar notch width divided by the femoral condyle width but may not give an accurate indication of actual ACL size, especially when normalised to body/femur size.<sup>21</sup>

The objective of this study was to compare risk factors that may have predisposed two female twins and their older sister to subsequent ACL injuries playing soccer and basketball. This study examined the concept that injury risk is increased among athletes with ACL injured first-degree family members. The first theory examined was that female sibling athletes would demonstrate biomechanical differences, such as greater knee abduction and decreased knee flexion, than uninjured athletes during landing (table 1). A second theory examined was that female sibling athletes would demonstrate different neuromuscular strength measures than the mean female athlete values. The third theory examined was that these twins would demonstrate increased generalised ligamentous and knee laxity measures than the average uninjured female athlete. The final theory examined was that female sibling athletes would demonstrate narrower intercondylar notch widths than the average woman.

## METHODS

### Subjects

Two fraternal twin sibling female high school soccer and basketball players volunteered to participate in a large cohort study of soccer and basketball athletes. Parents and participants read and signed the informed consent and assent, respectively. Height and mass were measured and leg dominance was determined by which leg the athlete stated that they would use to kick a ball the greatest distance.

**Table 1** Multifactorial assessment approach for potential future anterior cruciate ligament (ACL) injury risk

Category	Factor
Genetic	Number of first-degree relatives with ACL injury
History of prior injury	Prior knee injury, lower extremity injury, low back or other injury
Developmental and hormonal	Sex, pubertal stage (Tanner or PMOS), menstrual status
Biomechanical	Knee abduction, knee flexion, side to side asymmetries in these biomechanical parameters
Anatomic and anthropometric	Femoral notch width height, weight, BMI
Neuromuscular	Hamstrings (H), quadriceps (Q) strength, H/Q ratios, side to side asymmetries, vertical jump height
Ligamentous integrity	Knee recurvatum, joint laxity index score, KT-2000 measure, side to side asymmetries

BMI, body mass index; PMOS, Pubertal Maturational Observational Scale.

## Procedures

### Laxity assessment

Generalised joint laxity tests consisted of: fifth-finger hyperextension greater than 90°, elbow hyperextension greater than 0°, wrist and thumb to forearm opposition, knee hyperextension greater than 0°.<sup>29–31</sup> Anterior–posterior tibiofemoral translation was quantified using the Compu-KT knee arthrometer (Medmetric, San Diego, California, USA) to measure total anterior–posterior displacement of the tibia relative to the secured femur. During the measurement, each leg was placed on the adjustable thigh support with knee stabilised at 20° to 35° of knee flexion. The arthrometer was secured to the shank such that the patellar sensor pad was rested on the patella with the knee joint line reference mark on the Compu-KT aligned with the subject's joint line. The ankle and foot were stabilised to limit leg rotation. The tester provided a posterior and anterior ( $\pm 134$  N) pressure on an axis perpendicular to the tibia. Total displacement (mm) was plotted on the computer and recorded.<sup>29</sup> Hamstring flexibility was measured at the time of neuromuscular and biomechanical testing by knee angle (degrees from full extension, with full extension designated as 0° and knee flexion angles greater than 0° designated as negative) and the hip at 90 degrees flexion using a goniometer as per the method of Knapik *et al.*<sup>19</sup>

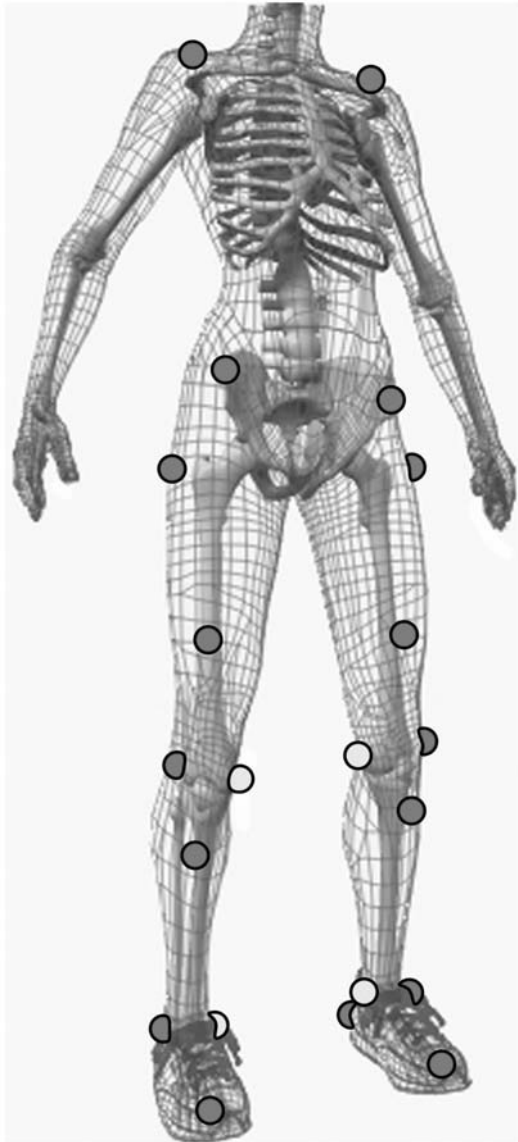
### Maximal jump height

A maximum vertical height was determined using a MX-1 vertical jump trainer (MXP Sports, Reading, Pennsylvania, USA) with a basketball as a target to encourage maximum jump height.<sup>7</sup> The athlete was instructed to grab the ball with both hands as they jump as high as possible. The height of the ball was adjusted until the athlete failed to grab the ball in three consecutive trials. The greatest vertical jump height was recorded.<sup>7</sup> This target height was then set for all drop vertical jump trials.

### Three-dimensional biomechanical analysis of drop vertical jump testing

Each subject was instrumented with 19 retroreflective markers placed bilaterally on the greater trochanter, mid-thigh, medial and lateral knee (joint line), mid-shank, medial and lateral ankle (malleolus), posteriorly on the calcaneus and superiorly on the dorsal aspect of the foot (between second and third metatarsals). An additional marker on the left posterior superior iliac spine was also applied to offset the right and left side to aid the real-time identification of markers during data collection (fig 1). The motion analysis system consisted of eight digital cameras (Eagle cameras, Motion Analysis, Santa Rosa, California, USA) connected through an Ethernet hub to the data collection computer (Dell, Round Rock, Texas, USA) and sampled at 240 Hz. Two force platforms (Advanced Mechanical Technology, Watertown, Massachusetts, USA) were sampled at 1200 Hz and time was synchronised to the motion analysis system.

A static trial was collected with the subjects standing as positioned in fig 1. Kinematic measures were in relation to the static position. Each athlete was shown the drop vertical jump (DVJ) manoeuvre and was given adequate practice to be able to successfully complete the task (fig 2). The drop vertical jump consisted of dropping off the box and jumping immediately to grab the target.<sup>6</sup> Three drop vertical jumps were performed from a box height of 31 cm (fig 2). The data were collected with EVaRT software (V. 4, Motion Analysis). The motion analysis system was calibrated to recommended specification prior to each data collection session.



**Figure 1** Locations of reflective markers during data collection. Medial knee and ankle markers (white) were removed after collection of the static trial. Sacrum, left posterior superior iliac spine, left mid-tibia and right heel markers are not visible in this view.

Three-dimensional marker trajectories were calculated in EVaRT and exported to MATLAB (version 7.5, The Mathworks, Natick, Massachusetts, USA) for analysis. Marker trajectories were smoothed with a low pass Butterworth filter at a cut-off frequency of 12 Hz. Knee joint flexion–extension and abduction–adduction cardan angles were calculated within MATLAB with modified versions from the KineMat Toolbox.<sup>33</sup>

### NOTCH WIDTH MEASUREMENT

Notch width was measured intraoperatively and arthroscopically per the method of Shelbourne and Kerr.<sup>35</sup> Measurements included femoral condylar width, femoral notch width and the widest point of notch opening. (fig 3)

### CLINICAL FINDINGS AND RESULTS

#### Injury details and anthropometric measures

Sibling 1 ruptured the ACL of her non-dominant left knee, whereas sibling 2 ruptured the ACL of her dominant right knee.

Video images were obtained of the left ACL injury of sibling 1 (fig 4). Sibling 2 reported a prior knee injury, torn cartilage, at the time of testing. Sibling 1 reported prior ankle injury, but no prior knee injury, at the time of testing. The twins had a family history of ACL Injury, as their older sister experienced an ACL rupture previous to their injuries. Both of these twin siblings were physically and developmentally mature, at the time of testing. They reported beginning regular menstrual periods at ages 12 and 13, respectively. Their data were compared to 72 school-sponsored soccer and basketball players, who were teammates of the twin siblings. Age, height, mass and BMI for each twin sibling were similar to each other and to control values for the 72 non-injured female soccer and subjects (table 2, anthropometric data).

#### Biomechanical measures

Table 3 and figs 5 and 6 show measured knee kinematic variables in the frontal and sagittal planes in the twin siblings and the means (SDs) of a large (72 female athletes) control cohort. The biomechanical assessment of landing demonstrated that peak knee abduction motion was increased compared to uninjured controls in one knee of both of these twin siblings (fig 5 and table 3). Knee abduction range of motion was observed to be higher than uninjured controls (fig 5 and table 3).

Kinematic variables at the knee in the sagittal plane were observed to be different than controls at peak motion (table 3 and fig 6). The twin female athletes demonstrated decreased maximum knee flexion motion compared with the uninjured athletes. The sibling athletes demonstrated lesser peak knee flexion than other athletes. Hence, differences in knee motion were also observed in the sagittal plane. These female athletes demonstrated lesser knee flexion range of motion than uninjured athletes. In addition, fig 6 illustrates that sibling 1 demonstrated lesser peak knee flexion than uninjured athletes. However, sibling 2 did not. Hence, differences in knee motion were observed in the coronal and sagittal planes.

#### Neuromuscular: strength and power

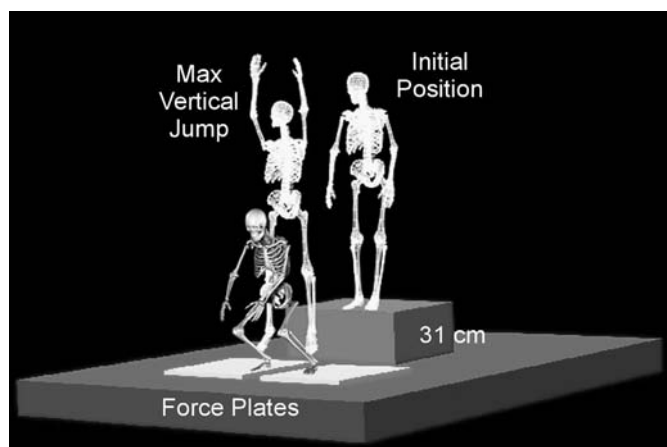
The neuromuscular findings of the twin siblings followed trends similar to the neuromuscular variables of control subjects. Table 4 shows the neuromuscular variables in the sagittal plane. The hamstrings/quadriceps ratio peak torque values are shown in table 4. Sibling 1 showed decreased hamstrings to quadriceps peak torque ratios compared to controls and large side to side differences in these relative peak torques. In addition, maximal vertical jump was evaluated as a performance measure of whole body power. The twin athletes demonstrated vertical jumps that were in the control range of female athletes of similar age and sport (table 4).

#### Joint and ligament laxity and hamstring flexibility

Generalised joint laxity measurements were similar between the sibling female athletes and greater than the controls (table 5). In addition, sibling 1 had hamstring flexibility that was similar to injured subjects, while sibling 2 had greater hamstring flexibility (–5) on her later injured right dominant side that was more than 1 SD greater than the control mean (table 5). Arthrometer-measured ligament laxity at the knee in the sagittal plane was similar between twins and controls.

#### Notch width

Notch width was observed to be relatively low for these twin siblings relative to comparable control values from the literature



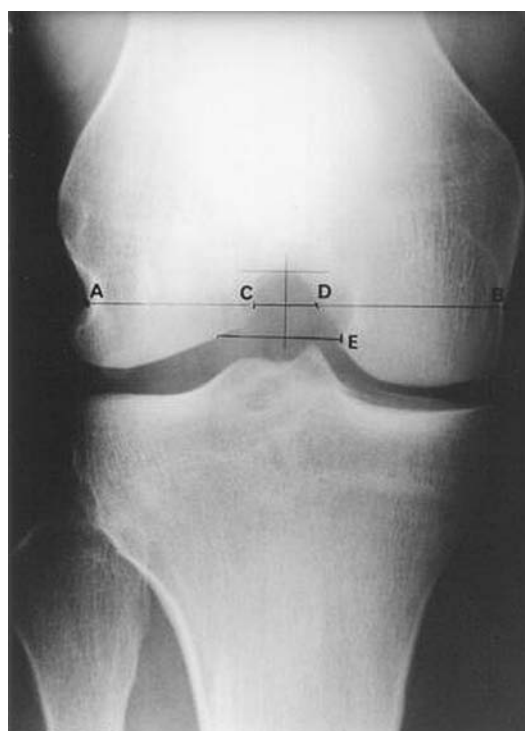
**Figure 2** Reflective marker locations collected simultaneously with two force platforms. Skeletal segments created using external marker locations. Drop vertical jump task and accompanying body models are shown.

(table 2).<sup>35</sup> Femoral intercondylar notch widths were 12 and 13 mm, respectively, approximately 1 SD below the mean in the twins relative to uninjured, weight-matched women.<sup>35</sup> Published data in the literature from the same doctor that measured the notch width of the siblings (KDS) reported a mean (SD) notch of 15 (2.7) mm in a similar weight-matched (61 to 75 kg) athletic population. Hence, twin siblings 1 and 2 had intercondylar notch widths 3 to 2 mm lower than controls, respectively, with sibling 1 greater than 1 SD lower than the mean.<sup>35</sup>

## DISCUSSION

The theoretical basis of this sibling study was to determine if there are specific potential risk factors that underlie a familial tendency toward ACL rupture.<sup>1</sup> The purpose of this twin sibling study was to identify potential factors, including anthropometrics, injury history, biomechanics of high-risk movement, neuromuscular performance measures, ligament integrity and notch width in twin sibling athletes with ACL injuries would differ from a large control population of similar athletes. A corollary objective was to spur further investigation into these important areas of research. Limited studies have addressed the familial tendency toward ACL rupture, with varying results. Anderson *et al* found no greater prevalence of ACL injuries among family members or ethnic groups.<sup>1</sup> While Lambert *et al*, Harner *et al*, and more recently Flynn *et al*, concluded that there was a familial predisposition toward rupture of the ACL.<sup>5, 20</sup> In addition, in a recent 4-year cohort study, it was found that white European American athletes were 6.6 times more likely to experience an ACL tear compared with other ethnic groups, which was indicative of genetic underpinnings for ACL injury risk.

The first theory examined was that female sibling players would demonstrate differences in knee abduction and knee flexion measures compared to control athletes during a vertical drop manoeuvre. Increased knee abduction angles, knee abduction angular range of motion and decreased knee flexion were observed in the twin female siblings relative to a large control cohort from the same sports teams. In addition, side to side differences in knee abduction motion were observed. These differences have been reported to be significant predictors of future injury risk.<sup>16</sup> A second theory examined was that female sibling athletes would demonstrate different neuromuscular strength measures than the mean female athlete values. This

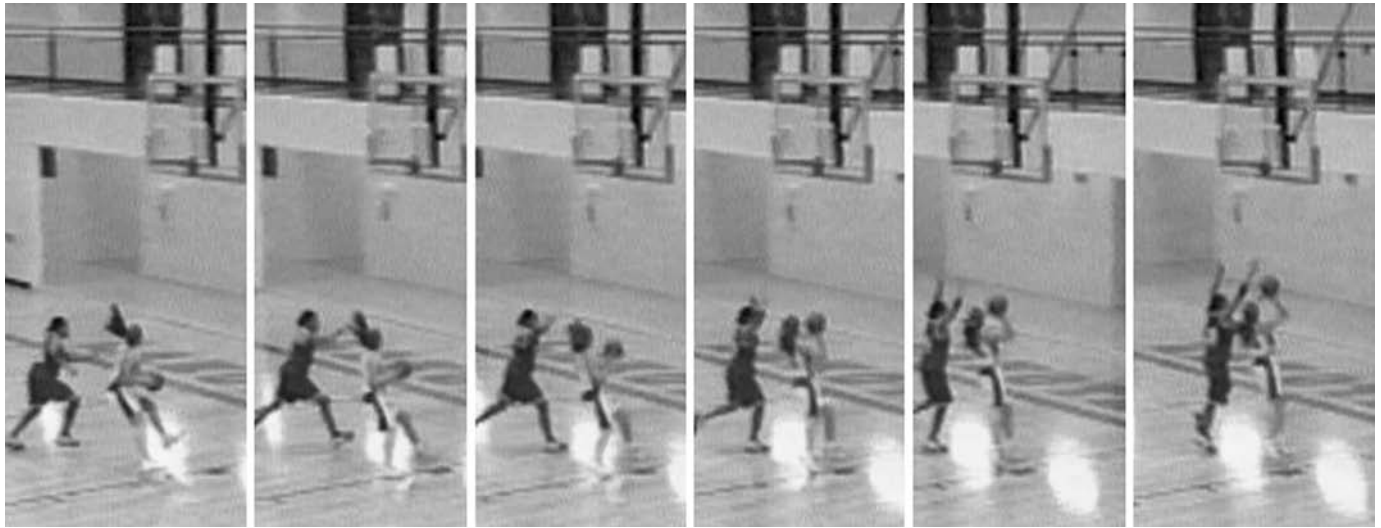


**Figure 3** Notch width measure as per Shelbourne and Kerr.<sup>35</sup> A to B is a measure of femoral condylar width, C to D is a measure of femoral notch width and E represents the widest point of notch opening.

was observed in one of the twin athletes. Low hamstrings to quadriceps peak torque values were observed in sibling 1. The third theory examined was that these twins would demonstrate increased generalised ligamentous and knee laxity measures than the average uninjured female athlete. Increased generalised joint laxity was observed in both siblings. The final theory examined was that female sibling athletes would demonstrate a lower intercondylar notch width than the average woman. Both twins were on the low end of control values.

Uhorchak *et al* studied non-contact ACL injuries and associated risk factors over 4 years in 859 US military recruits.<sup>36</sup> A predictive model was developed based on 24 non-contact ACL injuries that included the following factors: narrowed femoral notch width, increased body mass index (BMI), generalised joint laxity and increased KT-2000 scores (anterior/posterior tibiofemoral translation was quantified using the knee arthrometer (Medimetric, San Diego, California, USA)). These factors accounted for 28% of the variance in the occurrence of non-contact ACL injuries in all subjects, while it predicted 75% of the non-contact ACL injuries in women.<sup>36</sup> Women with a BMI just 1 SD or more above average had a relative risk for non-contact ACL injury 3.5 times greater than women with a lower BMI, while high BMI men did not.<sup>36</sup>

Increased risk of ACL rupture in athletes is likely multifactorial and if genetic, is likely pleiotropic in nature. The sex disparity in ACL injury risk is clearly evident in the literature.<sup>3</sup> However, it is unknown whether this is a sex-linked (X chromosome) trait. The risk factors of increased valgus joint loading, decreased intercondylar notch width, decreased hamstrings relative to quadriceps muscle strength and/or increased ligament laxity, especially about the knee joint, may lead to increased risk of ACL injury. These factors in combination may contribute to the final injury mechanism.



**Figure 4** Injury sequence of sibling 1. See also supplementary material.

Non-contact ACL injuries typically occur with a combined mechanism of knee abduction, lower extremity valgus positioning, extension, rotation of the tibia and the foot planted away from the centre of mass, with the foot flat on the ground.<sup>30</sup> The sports manoeuvres primarily associated with ACL injury are rapid deceleration during landing a jump or a change in direction during a pivot or cutting motion. Hewett and colleagues reported a high sensitivity and specificity for measures of dynamic valgus during landing to predict ACL injury risk,<sup>16</sup> and adolescent women are at greater risk of a non-contact ACL injury because they land a jump with greater knee valgus than prepubertal women and men.<sup>6 10 14 18</sup>

It is difficult to address the prevention and treatment of ACL injuries in young athletes based on findings from a twin sibling study. However, what is currently known is that neuromuscular training conducted during adolescence appears to increase dynamic knee stability and to decrease knee and ACL injury risk.<sup>15 17 24–28</sup> What is unknown is how to determine the high-risk population that can most benefit from neuromuscular training. Once isolated, those subjects at increased risk of ACL injury could undergo preventative neuromuscular training programs designed to reduce the risk of injury to the ACL. Questionnaires could be utilised to assess the presence of familial predisposition in a retrospective and prospective fashion. Screening tests could be used to identify athletes at high risk and target timing of intervention for injury prevention. With this information obtained, investigators may be able to determine when a subject may be at increased risk of knee injury, and additionally,

**Table 2** Characteristics for siblings 1 and 2 and controls

Characteristic	Sibling 1	Sibling 2	Controls (n = 72)
Height, cm	171	168	170 (7)
Mass, kg	64	65	64.2 (9.2)
Age, years	16	16	15 (1)
BMI, kg/m <sup>2</sup>	21.9	22.8	22.1 (2.7)
Notch width, mm	12	13	15 (2.7)*

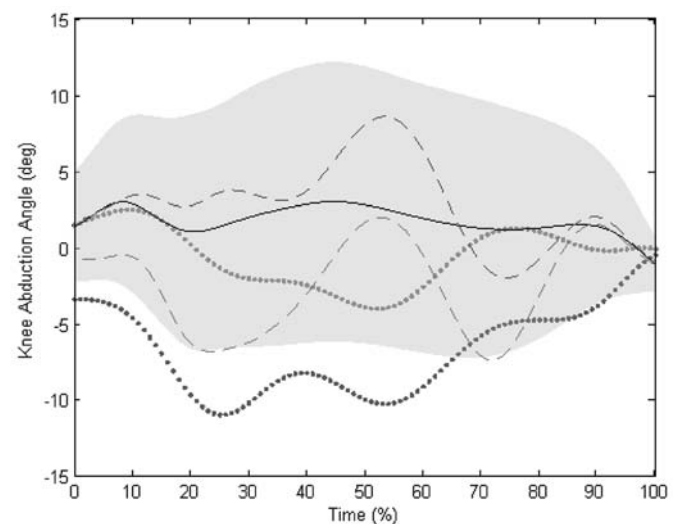
Control values (mean (SD)) were taken from 72 female soccer and basketball players from the same team as the sisters. Notch width is also included (in mm) for the twin siblings.

\*Control values reported from the literature.<sup>35</sup>

BMI, body mass index.

if a subject's first-degree relative (ie, mother, father or sibling) may be at increased risk of knee injury.

Certain risk factors, including increased valgus joint loading and decreased intercondylar notch width, may occur in a family and may lead to the predisposition for ACL injury. There may be familial predisposition toward tearing of the ACL and therefore, there may be familial inheritance of neuromuscular and biomechanical risk factors for ACL injury. If risk factors such as increased valgus joint loading, decreased flexion, decreased intercondylar notch width and/or increased ligament laxity are present within a family, this would likely increase the likelihood of ACL injury among relatives. Clinicians may use greater information on the genetic basis of this important problem to develop methods to identify subjects with risk factors for ACL injury, including a family history, and institute appropriate interventions, or a neuromuscular training program or perhaps even notchplasty. The risk of ACL injury can be decreased in high-risk subjects with neuromuscular training.



**Figure 5** Knee abduction angle during stance phase of the drop vertical jump (DVJ). The dotted line is sibling 1 (S1) and the dashed line is sibling 2 (S2). The red line is the injured side and the blue line is uninjured side. The solid black line and grey shading represent population mean  $\pm$  1 SD.

**Table 3** Knee flexion and abduction kinematics during landing from a drop vertical jump (DVJ) manoeuvre

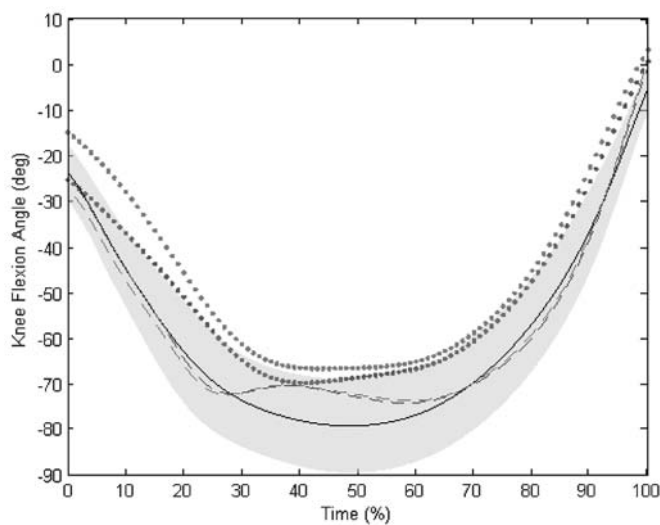
	Sibling 1		Sibling 2		Controls (n = 72)
	Involved	Uninvolved	Involved	Uninvolved	Uninvolved
Knee abduction, degrees:					
Initial contact	1.5	-3.4	-0.8	1.8	0.7 (3.2)
Peak	-4.3	-11.3	-7.7	-2.1	-4.6 (5.6)
ROM	5.8	7.9	6.9	3.9	5.3
Knee flexion, degrees:					
Initial contact	-15.0	-25.4	-27.4	-24.7	-24.5 (6.1)
Peak	-67.5	-69.9	-74.0	-74.2	-79.9 (10.2)
ROM	52.5	44.5	46.6	49.5	55.4

Control values (mean (SD)) were taken from 72 female soccer and basketball players from the same team as the sisters. Negative (-) values indicate knee abduction (valgus) and flexion angular knee motion. ROM, range of motion.

### Potential limitations

This study has numerous potential limitations. The biomechanical patterns demonstrated by sibling female athletes may not be able to be generalised to other athletes. We also examined biomechanical and neuromuscular control characteristics during landing. Though the majority of ACL injuries occur during landing, many result from cutting or pivoting manoeuvres, particularly in the sports of soccer and basketball.

Social, cultural, financial and environmental factors may account for or influence the predisposition of an athlete and their first-degree relatives to ACL injury. These influences should be studied before the relationship between the genetics of the athlete and ACL injury risk can be better understood. In addition, there is the question of how neuromuscular traits would be genetically transmitted. There would be potential environmentally inputs, for example, growth, development and prior training. Though there is some evidence for a genetic connection to ACL injury risk, other confounding and contributing factors must be considered. However, the two siblings and the uninjured controls played the same two sports on the same teams, which does control for some potentially confounding variables.<sup>5</sup> In addition, our studies of the genetic underpinnings of ACL injury risk continue in large longitudinal cohort studies.



**Figure 6** Knee flexion angle during stance phase of the drop vertical jump (DVJ). The dotted line is sibling 1 (S1) and the dashed line is sibling 2 (S2). The red line is the injured side and the blue line the uninjured side. The solid black line and grey shading represent population mean  $\pm$  1 SD.

This study focused on the potential multifactorial nature of this important clinical problem, including the anthropometric, anatomic, biomechanical, neuromuscular, ligament integrity theories, with the assumption that other intrinsic and extrinsic factors are involved. Neuromuscular and biomechanical imbalances, intercondylar notch width and joint laxity may not be the only factors underlying the differences in knee injury rate, but they may be the greatest contributors to increased injury risk in women. However, the preponderance of data shows that neuromuscular differences affect injury rates and offer the greatest potential for intervention. The current observations support the hypothesis that there is a familial predisposition to ACL injury. In addition, it could be hypothesised from these findings that the familial predisposition is at least in part due to neuromuscular imbalance and decrease dynamic knee stability. It has been previously demonstrated that the neuromuscular imbalances can largely be altered with training, resulting in a decreased risk of ACL injury.<sup>15</sup>

### Summary and conclusions

A relative paucity of literature has been published on the potential familial predisposition toward ACL injury. The purpose of this study was to determine if a familial predisposition to injury of the ACL of the knee occurs in twin siblings and what multiple, potentially heritable, factors may be related to this predisposition. Increased knee abduction angle, decreased intercondylar notch widths, increased general joint laxity and low H/Q ratios are potential traits related to the multifactorial familial predisposition to ACL injury. Quantification of these potential traits may lead to identification of athletes at increased risk of ACL injury, including those that possess a familial predisposition. The long-term objectives are to determine if a familial predisposition to ACL injury exists, and if so, to optimise the effectiveness of neuromuscular training designed to prevent knee ligament injuries in high-risk families. Determination of such a correlation may allow the investigators to achieve the long-term goal of reducing the rates of knee ligament injury in identified high-risk populations. Previous literature has elucidated several risk factors for tearing of the ACL. A number of risk factors including joint laxity, femoral intercondylar notch size and shape, hormonal influences, and ligament size which are considered to be intrinsic, or not changeable, in nature. Potentially controllable, or changeable, risk factors include knee abduction torque, neuromuscular firing patterns and proprioception. It is highly probable that many of the identified risk factors for an ACL tear are passed through families. Prevention would allow many thousands of athletes to continue the health benefits of sports participation while avoiding the long-term complications of osteoarthritis.<sup>22</sup>

**Table 4** Neuromuscular factors

	Sibling 1		Sibling 2		Controls (n = 72)
	Involved	Uninvolved	Involved	Uninvolved	Uninvolved
Isokinetic peak torque					
Knee extension, Nm	111.3	88.1	75.2	83.5	92.1 (14.7)
Knee flexion, Nm	49.0	54.4	43.3	43.3	45.0 (11.0)
H/Q ratio	0.43	0.62	0.57	0.52	0.49 (0.1)
Jump distance:					
Single leg hop, cm	179	185	165	164	176 (15)
Vertical jump, cm	47		39.4		43.3 (5.7)

Isokinetic peak flexion and extension peak torque and maximum horizontal and vertical jump distances are shown. Control values (mean (SD)) were taken from 72 female soccer and basketball players from the same team as the sisters. H, hamstrings; Nm, Newton metres; Q, quadriceps.

**Table 5** Joint and ligament integrity measures: general joint laxity indications and anterior–posterior knee laxity measures measured with a knee arthrometer of twins compared with large cohort of uninjured women

Side:	Sibling 1		Sibling 2	
	Dominant	*Non-dominant	*Dominant	Non-dominant
Little finger extension.	Yes	N/A	Yes	N/A
Elbow hyperextension	No	N/A	Yes	N/A
Knee hyperextension	No	N/A	Yes	N/A
Thumb opposition	Yes	N/A	Yes	N/A
Hamstring flexibility	−19	*−16	*−5	−14
KT arthrometer (30 N)	8.2	8.9	8.7	9.7

\*Injured side.

N/A, not applicable.

### What is already known on this topic

Three published studies have reported familial history as a factor related to increased risk of anterior cruciate ligament (ACL) injury, while one study reported no such association. Athletes that experience an ACL tear demonstrate multiple factors that may predispose them to an ACL tear compared with controls matched for age, sex and sport.

### What this study adds

This study supports earlier reports that family history of ACL injury may be a factor related to increased risk of ACL injury. In addition, multiple factors, including neuromuscular, biomechanical, anatomic, anthropometric and joint laxity characteristics, that may predispose athletes to an ACL tear, may be heritable in nature.

Future investigations must incorporate combinations of these potential predictive variables in order to maximise the predictive potential of preparticipation assessment and the effectiveness of future interventions.

**Acknowledgements** We would like to acknowledge team doctors Drs Angelo Colosimo and Jon Divine, and Donald Shelbourne for their patient records and contributions. We would also like to acknowledge Tinker Gray for her assistance with a critical reading of the manuscript.

**Funding** The authors would like to acknowledge funding support from National Institutes of Health Grant R01-AR049735 and R01-AR055563.

**Competing interests** None.

**Ethics approval** Ethics approval was granted by the Cincinnati Children's Hospital Medical Center.

### REFERENCES

1. **Anderson AF**, Dome DC, Gautam S, *et al.* Correlation of anthropometric measurements, strength, anterior cruciate ligament size, and intercondylar notch characteristics to sex differences in anterior cruciate ligament tear rates. *Am J Sports Med* 2001;**29**:58–66.
2. **Anderson AF**, Lipscomb AB, Liudahl KJ, *et al.* Analysis of the intercondylar notch by computed tomography. *Am J Sports Med* 1987;**15**:547–52.
3. **Arendt E**, Dick R. Knee injury patterns among men and women in collegiate basketball and soccer. NCAA data and review of literature. *Am J Sports Med* 1995;**23**:694–701.
4. **Charlton WP**, St John TA, Ciccotti MG, *et al.* Differences in femoral notch anatomy between men and women: a magnetic resonance imaging study. *Am J Sports Med* 2002;**30**:329–33.
5. **Flynn RK**, Pedersen CL, Birmingham TB, *et al.* The familial predisposition toward tearing the anterior cruciate ligament: a case control study. *Am J Sports Med* 2005;**33**:23–8.
6. **Ford KR**, Myer GD, Hewett TE. Valgus knee motion during landing in high school female and male basketball players. *Med Sci Sports Exerc* 2003;**35**:1745–50.
7. **Ford KR**, Myer GD, Smith RL, *et al.* Use of an overhead goal alters vertical jump performance and biomechanics. *J Strength Cond Res* 2005;**19**:394–9.
8. **Frank CB**, Jackson DW. Current concepts review. The science of reconstruction of the anterior cruciate ligament. *J Bone Joint Surg* 1997;**79A**:1556–76.
9. **Harner CD**, Paulos LE, Greenwald AE, *et al.* Detailed analysis of patients with bilateral anterior cruciate ligament injuries. *Am J Sports Med* 1994;**22**:37–43.
10. **Hass CJ**, Schick EA, Tillman MD, *et al.* Knee biomechanics during landings: comparison of pre- and postpubescent females. *Med Sci Sports Exerc* 2005;**37**:100–7.
11. **Hewett TE**. Neuromuscular and hormonal factors associated with knee injuries in female athletes: strategies for intervention. *Sports Med* 2000;**29**:313–27.
12. **Hewett TE**. Preventing knee injuries in female athletes. *Mayo Clin Symp Sports Med* 2000;**10**:45–55.
13. **Hewett TE**, Lindenfeld TN, Riccobene JV, *et al.* The effect of neuromuscular training on the incidence of knee injury in female athletes. A prospective study. *Am J Sports Med* 1999;**27**:699–706.
14. **Hewett TE**, Myer GD, Ford KR. Decrease in neuromuscular control about the knee with maturation in female athletes. *J Bone Joint Surg Am* 2004;**86-A**:1601–8.
15. **Hewett TE**, Myer GD, Ford KR. Anterior cruciate ligament injuries in female athletes: part 1, mechanisms and risk factors. *Am J Sports Med* 2006;**34**:299–311.
16. **Hewett TE**, Myer GD, Ford KR, *et al.* Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. *Am J Sports Med* 2005;**33**:492–501.
17. **Hewett TE**, Stroupe AL, Nance TA, *et al.* Plyometric training in female athletes. Decreased impact forces and increased hamstring torques. *Am J Sports Med* 1996;**24**:765–73.
18. **Kernozek TW**, Torry MR, VH H, *et al.* Gender differences in frontal and sagittal plane biomechanics during drop landings. *Med Sci Sports Exerc* 2005;**37**:1003–12.

19. **Knapik JJ**, Bauman CL, Jones BH, *et al*. Preseason strength and flexibility imbalances associated with athletic injuries in female collegiate athletes. *Am J Sports Med* 1991;**19**:76–81.
20. **Lambert KL**. The syndrome of the torn anterior cruciate ligament. *Adv Orthop Surg* 1984;**7**:304–14.
21. **LaPrade RF**, Burnett QM 2nd. Femoral intercondylar notch stenosis and correlation to anterior cruciate ligament injuries. A prospective study. *Am J Sports Med* 1994;**22**:198–202.
22. **Lohmander LS**, Englund PM, Dahl LL, *et al*. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med* 2007;**35**:1756–69.
23. **Myer GD**, Ford KR, Barber-Foss K, *et al*. The relationship of hamstrings and quadriceps strength to anterior cruciate ligament injury in female athletes. *Clin J Sport Med* 2009;**19**:3–8.
24. **Myer GD**, Ford KR, Brent JL, *et al*. The effects of plyometric versus dynamic balance training on landing force and center of pressure stabilization in female athletes. *Br J Sports Med* 2005;**39**:397.
25. **Myer GD**, Ford KR, Brent JL, *et al*. Differential neuromuscular training effects on ACL injury risk factors in “high-risk” versus “low-risk” athletes. *BMC Musculoskelet Disord* 2007;**8**:1–7.
26. **Myer GD**, Ford KR, Divine JG, *et al*. Specialized dynamic neuromuscular training can be utilized to induce neuromuscular spurt in female athletes. *Med Sci Sports Exerc* 2004;**36**:343–4.
27. **Myer GD**, Ford KR, McLean SG, *et al*. The effects of plyometric versus dynamic stabilization and balance training on lower extremity biomechanics. *Am J Sports Med* 2006;**34**:490–8.
28. **Myer GD**, Ford KR, Palumbo JP, *et al*. Neuromuscular training improves performance and lower-extremity biomechanics in female athletes. *J Strength Cond Res* 2005;**19**:51–60.
29. **Myer GD**, Ford KR, Paterno MV, *et al*. The effects of generalized joint laxity on risk of anterior cruciate ligament injury in young female athletes. *Am J Sports Med* 2008;**36**:1073–80.
30. **Olsen OE**, Myklebust G, Engebretsen L, *et al*. Injury mechanisms for anterior cruciate ligament injuries in team handball: a systematic video analysis. *Am J Sports Med* 2004;**32**:1002–12.
31. **Pasque CB**, Hewett TE. A prospective study of high school wrestling injuries. *Am J Sports Med* 2000;**28**:509–15.
32. **Ramesh R**, Von Arx O, Azzopardi T, *et al*. The risk of anterior cruciate ligament rupture with generalised joint laxity. *J Bone Joint Surg Br* 2005;**87**:800–3.
33. **Reinschmidt C**, van den Bogert AJ, Nigg BM, *et al*. Effect of skin movement on the analysis of skeletal knee joint motion during running. *J Biomech* 1997;**30**:729–32.
34. **Shelbourne K**, Davis T, Klootwyk T. The relationship between intercondylar notch width of the femur and the incidence of anterior cruciate ligament tears. *Am J Sport Med* 1998;**26**:402–8.
35. **Shelbourne KD**, Kerr B. The relationship of femoral intercondylar notch width to height, weight, and sex in patients with intact anterior cruciate ligaments. *Am J Knee Surg* 2001;**14**:92–6.
36. **Uhorchak JM**, Scoville CR, Williams GN, *et al*. Risk factors associated with noncontact injury of the anterior cruciate ligament: a prospective four-year evaluation of 859 West Point cadets. *Am J Sports Med* 2003;**31**:831–42.