Sveriges lantbruksuniversitet
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Department of Animal Breeding and Genetics

Patellar Luxation
- A Genetic Study

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Genetisk studie av patellaluxation

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Abstract

Patellar luxation is one of the most common orthopaedic diseases found in dogs today, and is also frequently found in other species such as cattle, horses and humans. Data was acquired from the Swedish Kennel Club for 14 dog breeds. These were selected on basic criteria such as high number of diagnosed dogs and a relatively high frequency of patellar luxation. Additional data were received for one of the breeds from the Finnish Kennel Club. After sorting and analysis of the data was completed, 4 breeds were selected from the original 14, upon which heritability estimations were made. Several environmental factors involved in the variation of patellar luxation were found, namely breed of the dog, sex of the dog, age at examination and examining veterinarian. Also birth month of the dog and birth year of the dog seemed to have an effect on the variation of patellar luxation. A heritability of 0.24-0.25 was found for the Chihuahua breed, and a heritability of 0.18-0.20 was found for the Bichon frise breed.

Sammanfattning

Patellaluxation är en av de vanligaste ortopediska sjukdomarna som drabbar hundar idag, och upptäcks dessutom ofta inom andra arter såsom nötkreatur, ponnyhästar och människor. Data för 14 hundraser erhölls från Svenska Kennelklubben. Dessa valdes ut baserat på vissa grundkriterier såsom att rasen har ett högt antal undersökta hundar och en relativt hög frekvens av patellaluxation. Ytterligare data hämtades från Finska kennelklubben för en av raserna. Efter att ha sorterat och analyserat dessa data valdes 4 raser ut från de första 14 för att arvbarhetsskattningar skulle kunna utföras. Ett flertal miljöfaktorer involverade i variationen för patellaluxation identifierades, nämligen ras, kön, ålder vid undersökning samt undersökande veterinär. Även hundens födelsemånad samt hundens födelseår verkar påverka variationen för patellaluxation. En arvbarhet på 0,24-0,25 skattades för rasen Chihuahua, och en arvbarhet på 0,18-0,20 skattades för rasen Bichon frise.

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Introduction

What is patellar luxation?

Patellar luxation is a condition where the patella, also called the knee cap, slips out of the throchlear groove, mainly during locomotion (Roush, 1993). This can happen easily and often, or rarely and with more force needed, depending on the severity of the condition. Patellar luxation (PL) is one of the most common developmental orthopedic diseases found in dogs (Priester, 1972; Roush, 1993; Ferguson, 1997; Alam et al, 2007; Bound et al., 2009; Campbell et al., 2010) along with, amongst others, hip dysplasia and elbow dysplasia. Despite this fact, most information that can be found on patellar luxation today relate to pathogenesis and treatment. Studies of inheritance of patellar luxation are still, to our knowledge, for the large part absent. The few studies found in literature that do consider the inheritance of patellar luxation indicate that the disease is under genetic control to varying degrees (Hayes et al., 1994; Vidoni, 2005; Chase et al., 2009).

Definition and description

Two types of patellar luxation have been described, one called lateral patellar luxation, where the knee cap slips out of the groove towards the outside of the leg, and the other is medial patellar luxation, where the knee cap slips out of the groove towards the inside of the leg. Medial patellar luxation is by far the most common, making up a total of about 90 % (Robins, 1990; Hayes et al., 1994; Arthurs & Langley-Hobbs, 2006; Bound et al., 2009; Nganvongpanit & Yano, 2013) of all cases of luxation seen in dogs. It is unclear how these two types interact, if they are in fact two different types of luxation, or if they are the results of the same genetic background. Patellar luxation is further divided into the categories bilateral patellar luxation and unilateral patellar luxation. Bilateral patellar luxation means that both hind limbs of the dog are affected, while a dog with unilateral patellar luxation only has one affected limb. Bilateral patellar luxation is about twice as common as unilateral patellar luxation according to some studies (Roush, 1993; Hayes et al., 1994; Ferguson, 1997; Campbell et al., 2010), but others have found the two types of luxation to be equally common (Gibbons et al., 2006; Alam et al., 2006; Linney et al, 2011; Kalff et al., 2014). Patellar luxation can be *inherited*, meaning the condition has developed without preceding trauma or being exposed to any evident external factors that could explain the luxation, or *acquired*, meaning that the patellar luxation of the dog was developed due to external factors such as an injury. The inherited form of patellar luxation is by far the most common (Hayes et al, 1994).

Clinical Signs

The most common clinical sign of patellar luxation is lameness, which can vary in severity, from the dog occasionally skipping a step when moving, to the dog being unable to use one or both hind limbs at all (Ferguson, 1997). Dogs with patellar luxation are usually not born with deformed knees, but instead, the condition develops over time as the dog grows. There are many contributing factors, such as laxity of the patellar ligament, a shallow trochlear groove, or if the angle of the femoral neck shaft is incorrect (so called *coxa vara* or *coxa valga*)

(Roush, 1993; Hayes et al, 1994; Ferguson, 1997; Beale, 2010). Because the effective movement of the patella is dependent on a perfect alignment of all the hind limb structures, any one of all previous mentioned conditions will result in the patella putting force in the wrong place of the trochlear groove, leading to incorrectly placed pressure within the groove, which in turn leads to increased risk of developing patellar luxation (Ferguson, 1997). The patella will then either slip out medially or laterally, depending on which deformities are present in the limb and in which way the knee joint has been worn.

Several studies show that female dogs are about 1.5 times as likely to develop the condition (Priester, 1972; Roush, 1993; Nganvongpanit & Yano, 2013) compared to males. Many dogs of smaller breeds do not require surgery for mild to medium severity of patellar luxation, but for most dogs with severe patellar luxation surgical treatment is necessary (Hayes et al.,1994; Gibbons et al., 2006; Alam et al., 2007; Kalff et al., 2014). In fact, a study made by Vidoni et al. (2005) showed that as many as 40 % of all dogs with patellar luxation were asymptomatic, and the luxation is often discovered by accident during a visit to the veterinarian for other reasons. The study made by Vidoni et al., (2005) also suggested that there could be a difference in the incidence of patellar luxation between neutered and intact dogs.

Treatment of patellar luxation

The treatment of patellar luxation will depend on the clinical signs of the dog, and also on which deformities of the hind limb is causing the development of the luxation. If the dog is mainly symptom free, and the joint is fairly normal, the dog could possibly live a good and long life without any treatment or surgery. If the knee joint and/or leg are severely affected however, for example with developed arthritis, high degree of luxation and/or showing severe bow leggedness (*genu vara*), surgery could be necessary. Surgery will aim to correct whichever structure is affected, so that as normal limb movement as possible can be obtained (Roush, 1993). Willauer (1987) and Matis & Fritz (1990) described that about half of all dogs that go through surgery to correct luxation of the patella, still have luxation remaining also after the operation. Kalff et al. (2014) also found similar results. A study performed on Pomeranians showed that about one in ten dogs still have luxation in the knee after surgery, and the recurrence becomes more frequent with higher severity of luxation prior to surgery (Wangdee et al., 2013). There is an increased risk of complications after surgery for dogs with more severe luxation and/or larger body size (Arthurs & Langley-Hobbs, 2006). Also dogs with mild PL have increased risk of developing arthritis and also of getting more severe patellar luxation later on due to wear and tear caused by the initial luxation (Roush, 1993; Ferguson, 1997).

Patellar luxation occurs in many species

Patellar luxation is also found in many species other than dogs, such as cats (Ferguson, 1997, Düzgün 2009), horses (Hermans et al., 1987), sheep (Shettko & Trostle, 2000), camelids (Whitehead, 2009), rabbits (Riggs & Langley-Hobs, 2013), cattle & buffalo (Naveen et al., 2014) and also humans (Eilert, 2001). It is fairly uncommon in most species, with the exception of dogs, horses and cattle (Düzgün 2009; Naveen et al., 2014). In most species, patellar luxation is more common in certain breeds, and certain lines within breeds, suggesting genetic predisposition (Düzgün 2009). The pathogenesis, clinical signs, management and treatment is similar for most species. Godgil et al. (1972) described the condition as being common enough in the draft cattle of India to have an effect of the production economy.

Patellar luxation is common in many different dog breeds, in particular breeds with small body size such as Chihuahuas, Pomeranians, small Poodles, Yorkshire terriers, Maltese, Bichon frises and Pugs (Roush, 1993; Soparat et al., 2012; LIDA, 2014). The condition is estimated to be about 10 times as common in small breeds compared to larger dog breeds (Roush, 1993). However, studies suggest that the incidence of patellar luxation is increasing also in large breed dogs (Beale, 2010), further increasing the need to understand the genetic background of the disease.

Problems with Patellar Luxation diagnostics

Today, there is a concern among breeders and scientists with regard to how patellar luxation is diagnosed. It is mainly diagnosed through palpation, which is a subjective evaluation that may differ among veterinarians (Campbell et al., 2010). When looking at the Swedish Kennel club registration database, also known as "Avelsdata", it can be seen that the same dog can get different results if examined at different occasions and/or by different veterinarians. Ongoing studies are trying to find ways to more accurately measure a dog's degree of luxation. One suggested method is through radiographic imaging, although this method is not sufficient to determine the grade of luxation. Dogs with mild to medium severity of luxation usually have the knee in correct position most of the time, and the force needed to dislocate the knee is not visualized in the image. One can use radiographic imaging to determine the depth of the femoral throchlear groove and also to determine if there has been any degenerative joint disease occurring as a result of the patellar luxation (Roush, 1993). Some studies have been made to attempt to correlate patellar luxation to different abnormalities of the stifles, such as *coxa valga* and *genu vara*. So far no clear significant results have been found, with the exceptions that in smaller breeds there seems to be an association between patellar luxation and a reduced angle between the head and shaft of the femur (*coxa vara*) (Bound et al., 2009). It also seems to be a significant difference in inclination angle of the femoral varus angle for dogs with severe patellar luxation compared with dog with milder degrees of luxation (Soparat et al., 2012).

Genetic background and heritabilities

A breeding study in Shetland ponies was carried out by Hermans et al. (1987), with the aim of concluding the mode of inheritance of the lateral patellar luxation. The study was conducted during a 20 year period, and during that time, both affected and unaffected animals were mated, and clinical findings in the foals examined. The authors concluded that patellar luxation was inherited in a monogenetic autosomal recessive manner, since unaffected animals could produce affected foals, and foals born from two affected parents were always themselves affected (Hermans et al., 1987). Similar findings were made by Gadgil et al. (1972), during a study of cattle. A study was recently conducted where the outcome of different matings be-

tween dogs with different results for patellar luxation were investigated based on kennel club data and veterinary records by Lavrijsen et a. (2013). This study indicated that there is a higher risk of having puppies born with patellar luxation if at least one parent is affected.
Studies are currently investigating potential DNA markers for patellar luxation, and a possible marker on chromosome 36 of the dog has been identified (Chomdej et al., 2014), as well as involvement of chromosome 7 and 31 (Lavrijsen, 2014). Some breeds tend to have a very high incidence of PL, such as the Chihuahua (LaFond et al., 2002), the Flat-coated retriever (Lavrijsen et al., 2013) and the Pomeranian (Soontornvipart et al., 2013). These breeds would be of particular interest in future studies, as they would benefit the most from the development of breeding value estimation based on patellar luxation and from genetic markers being identified. Lavrijsen et al. (2013) has previously found a significant heritability result for the Netherlands population of Flat-coated retrievers, upon which breeding values could be estimated.

Aim of study

This study aims to identify environmental factors possibly influencing the variation of patellar luxation within breeds. Some of the factors studied will be examining veterinarian, age at examination and sex of the dog. Furthermore, one goal is to estimate heritabilities for the trait patellar luxation for a number of breeds.

Material and methods

Data

Because patellar luxation is recognized as one of the most common disorders in dogs, it is part of the Swedish Kennel Club (SKK) central registration of disorders. Only observations made by approved veterinarians, specializing in dog and cat veterinary medicine, are allowed to submit their findings to the SKK registry. This is done in a standardized fashion, where the knee is graded from 0 to 3. A few breeds, such as the Chihuahua, has mandatory requirement for breeding animals to be screened for patellar luxation before mating in order to be approved for having puppies registered (SKK, 2014). This means there is a large amount of data available through the Swedish Kennel Club, making the dog a good model for studying the genetic background of patellar luxation. Fourteen breeds were chosen (Table 1) based on the following criteria:

- At least 300 recorded examinations in total for patellar luxation in the breed.
- A high incidence of patellar luxation, i.e. at least 5 % of all examined dogs within the breed diagnosed with patellar luxation
- Breeds having official breeding programs for patellar luxation were all included. Here, the SKK requires that the parents of a litter are both examined for patellar luxation before a litter can be registered. This should result in less biased data because all parent dogs are examined before mating.

Table 1. Registration data for the selected 14 breeds

	No of registered dogs/year 2002-2012	No (and %) of PL examined dogs/year 2002-2012	Total no of examined dogs
All 14 breeds	-	-	21749
Bichon Havanais	517	95 (18%)	1194
Bichon frise **	416	70 (17%)	1136
Cavalier King Charles Spaniel	1138	202 (18%)	2499
Chihuahua **	1580	560 (35%)	7225
Chinese Crested Dog	784	92 (12%)	1165
Finnish Spitz	270	74 (27%)	1333
French bulldog	344	110 (32%)	1675
Jack Russel Terrier	770	74 (10%)	895
Miniature Pinscher	400	92 (23%)	1194
Nederlandse Kooikerhondje **	76	27 (36%)	368
Papillon	530	134 (25%)	1661
Pomeranian (Swedish and Finnish)	300	27 (9%)	1059
Russkiy Toy* **	59	23 (39%)	345

*First registered dogs in the Swedish database was 2005
** Breed has mandatory breeding program for patellar luxation

Short-haired and long-haired Chihuahua were lumped together, since they are the same breed but simply have different types of coat. Data from the Swedish Kennel Club included breed code, registration number of the dog, pedigree name, sex, date of birth, breeder, degree of luxation, diagnosis, date of examination and examining veterinarian. “Degree of luxation” only contains a number between 0 and 3, specifying the severity of luxation, and “diagnosis” also includes information about if the luxation was medial or lateral.

The original dataset included 21,042 observations for patellar luxation for all breeds. Data was edited to remove records where the degree of luxation could not be determined by the veterinarian (one observation) and where the dog was younger than 12 months of age at examination (14 observations). The remaining 21,027 observations were related to 20,474 unique dogs where 532 dogs had been examined more than one time (2-5 times). For these 532 dogs, the result differed between examinations for 229 dogs. For dogs with more than one record, only the first record (according to date at examination) was kept for further analyses.

Four breeds were chosen for the genetic analyses: the Chihuahua, the Bichon frise, the Pomeranian and the French bulldog. The first two breeds were chosen because they have the largest number of records for patellar luxation, and both breeds are under breeding restriction regarding patellar luxation and consequently all animals used in breeding are required to have official examinations for patellar luxation for the litters to be registered within the kennel club. This should reduce bias in the data. The French bulldog was chosen because it was one of the heaviest breeds and the Pomeranian was chosen because it had the highest incidence of patellar luxation in the data set.

When looking at the data for Pomeranians, the number of examined dogs available was fairly small compared to many of the other breeds, especially for making statistical analysis. We knew that the Finnish and Swedish populations of Pomeranians frequently exchange breeding material, and so it was decided that information from the Finnish Pomeranians could be used as well. The Finnish kennel club was therefore contacted, and the same information for the Finnish Pomeranians was requested and received. Some basic conditions needed to be met before these observations could be used in the statistical analysis. One was to make sure that the two populations, the Swedish and the Finnish, were not isolated populations, but in fact had common ancestry. This analysis was performed using the SAS software (SAS user’s guide, 2010) and the results showed that 1,274 of the individual dogs, when searched on name and birth date, appeared in both data sets pedigree information. When looking closer at these duplicates, it was clear that most of the dogs were indeed the same dog, however not all. The Swedish breed registry contained a total of 15,181 Pomeranians and the Finnish data set contained a total of 6,817 Pomeranians. This means that over 18 % of the Pomeranians in the Finnish dataset, and over 8 % of the Pomeranians in the Swedish data set, are part of the common lineage of the two population. This confirms that these two populations do indeed share ancestry and can be used as one and the same population. The Swedish and Finnish data set were therefore merged together for the following analyses. When removing duplicates and dogs too young to be included in the study, the data set then had a total of 1,059 observations for Pomeranians. Some of these dogs appear in both data sets and so were merged so not to result in duplicates. This gave the data set a new total of 21,201 observations.

Trait definition

Several criteria have to be met before patella status of a dog can be officially registered by the Swedish Kennel Club. Generally dogs are examined between 1 and 2 years of age, but they cannot be younger than 12 months for an official record. The veterinarian will palpate the knee joints of the dog, and record the results using a standardized form, with a scale ranging from 0, which is unaffected, to 3, being the most severely affected:

0 The knee joint is considered normal
1 The patella can be luxated manually, but will spontaneously retract back into the femoral trochlear groove
2 The patella is fairly easily manually manipulated out of the femoral throchlear groove and will sometimes spontaneously retract, but also sometimes it will need manual retraction to its normal position
3 The patella is permanently luxated out of the femoral throchlear groove

A copy of the form is given to the owner of the dog, one is saved by the veterinarian, and a third is sent to the SKK for registration. There, the patella status is linked to the correct dog, through the information provided by the veterinarian, usually via the microchip number.

For this study, four traits were defined, with two different groupings of the scores for patellar luxation, to establish which one was most useful for genetic analysis:

PL02, using three categories:
0 normal
1 corresponding to score 1 in the veterinary protocol
2 corresponding to score 2 and 3 in the protocol, grouped together, owing to very few dogs scored as 3

PL01, using two categories:
0 normal
1 corresponding to scores 1, 2 and 3 in the protocol, grouped together.

PL02M: corresponding to PL02 but only including records of medial patellar luxation, excluding records of lateral luxation.

PL01M: corresponding to PL01 but only including records of medial patellar luxation, excluding records of lateral luxation.

In the Finnish data, a scale from 0 to 4 was used, as opposed to the Swedish scale of 0 to 3. The grading criteria for grades 0 and 1 were almost identical to the corresponding Swedish grades. For dogs scored in the Finnish system, score 4 was included in category 2 and 1 for PL02 and PL01 respectively.

Statistical Analysis

Statistical Analysis Software (SAS) was used to edit the data and prepare it for genetic analysis (SAS user's guide, 2010). The following factors were initially included in the model: sex, birth year, birth month, examination year, examination month, age in half years at the time of examination, and veterinarian. A large part of the veterinarians, 390 in total, had only examined very few dogs. Veterinarians that had examined fewer than 10 dogs (1-9), 136 in total, were excluded. This left the data set with 19,793 observations for the complete data set, and 19,693 observations after lateral observations for luxation were excluded.

In the genetic model, data for each breed were analyzed separately. In these analyses, two models were used, where the effect of veterinarian was included either as a fixed or as a random effect. In the models including fixed effect of veterinarian, the data was edited to keep only veterinarians that had examined 5 dogs or more (veterinarians who had examined 1-4 dogs were excluded). We had a less strict exclusion criterion for number of examined dogs per veterinarian within breed so not to risk that our data would be too small for each of the breeds. Including the effect as fixed or random had very little effect on the genetic parameters and in the following only the results from the models with random effect of veterinarian are presented. Proc GLM was used to study the influence of environmental factors on patellar luxation. The same data were also analysed using the GLIMMIX procedure with similar results. Birth year and examination year were run separately in the models because of confounding between these effects, and the same was done for birth month and examination month. P-values for all factors are shown in Table 2, when analyzing data from all breeds together, and for the four selected breeds. All effects included in the model showed low p-values on an all 14 breeds level except four: birth year, birth month, examination year, and examination month. The p-values for birth month and birth year were not very low on an all breed level, but had fairly low p-values for the Chihuahua and the Bichon frise (breeds with official breeding programs for patellar luxation), so these effects were included in the model.

Table 2. Effects tested in the model and their p-values (lowest to highest), both when looking at models using veterinarians as a random effect, and models using veterinarians as a fixed effect, and also with or without lateral results.

	Effect							
	Breed	Sex	Birth year	Birth month	Examination year	Examination month	Age in years	Examining Veterinarian
All 14 breeds	<0.0001	<0.0001	0.3169-0.4202	0.1116-0.3033	0.0634-0.2121	0.2275-0.4940	<0.0001	<0.0001
Chihuahua	-	0.0001-0.0021	0.0097-0.0719	0.0746-0.1033	0.3092-0.4086	0.0275-0.1086	<0.0001	<0.0001
Bichon frise	-	<0.0001	0.0698-0.1342	0.0643-0.1760	0.2736-0.3762	0.4933-0.9557	0.0262-0.0465	<0.0001-0.0048
Pomeranian	-	0.0002-0.0067	0.5582-0.6503	0.2824-0.7695	0.2818-0.4954	0.5114-0.8536	0.0025-0.0284	<0.0001
French bulldog	-	0.0006-0.0075	0.4748-0.7133	0.2592-0.7276	0.2595-0.4692	0.7445-0.8210	0.4491-0.5993	<0.0001

Variance components were estimated using an average information (AI) restricted maximum likelihood (REML) algorithm (Jensen et al., 1997) in the DMU package (Madsen and Jensen, 2013). The following model was used for estimation of variance components for the four breeds:

$$y_{ijklmno} = \mu + sex_i + bmonth_j + byear_k + ageyr_l + vet_m + a_o + e_{ijklmno}$$

where:

y_{ijklmn} is the score for patellar luxation, according to trait definition PL02, PL02M, PL01 or PL01M
μ is the overall mean
sex is the fixed effect of sex *i* (*i*=male, female)
bmonth is the fixed effect of birth month *j* (*j*=January,…, December)
byear is the fixed effect of birth year *k* (*k*=1995, 1996,…, 2013)
ageyr is the fixed effect of age at examination in half years *l* (*l*=1, 1.5,…6)
vet is the random effect of examining veterinarian *m* ~ND(0, σ^2_v), where σ^2_v is the veterinarian variance
a is the random additive genetic effect of animal *o* ~ND(0, Aσ^2_a), where σ^2_a is the additive genetic variance and A is the relationship matrix.
e is the random residual effect related to observation y_{ijklmn} ~ND(0, σ^2_e), where σ^2_e is the residual variance

The effect of years was limited to the age of 6 years of age at the time of exmaination. This is due to the very low number of examined dogs older than 6 years at the time of examination. Dogs older than 6 years at examination were grouped together with the dogs that were examined at 6 years of age.
Heritabilities were defined as $h^2 = \sigma^2_a / (\sigma^2_a + \sigma^2_e)$.

Results

Patellar luxation distribution

The percentage of affected dogs and the proportion of lateral vs. medial patellar luxation are shown in Table 3. Lateral luxations makes up a comparably large proportion of the found luxations in the Bichon frise breed, being 15.6%. This is quite high if one compares to for example Chihuahua, where the corresponding proportions were 2.6 %, and for all 14 breeds it is about 3.5 %.

Table 3. Frequency and distribution of patellar luxation (PL) overall and divided into lateral vs medial patellar luxation.

		Degree of luxation (%)				Diagnosis		
Breed	Number of dogs	0	1	2	3	Lateral PL (%)	Medial PL (%)	% Lateral PL of all PL
All 14 breeds	21 201	85.9	8.8	5.0	0.3	0.5	13.6	3.5
Chihuahua	7023	77.0	12.9	9.6	0.5	0.6	22.4	2.6
Bichon frise	1133	87.9	8.8	3.3	0	1.9	10.3	15.6
Pomeranian	1059	67.9	20.3	9.4	2.4	1.0	31.0	3.0
French bulldog	1631	89.9	8.0	2.0	0	0.4	9.7	4.0

Table 4. Frequency and relative frequency of patellar luxation (PL) considering sex of the dog

			Degree of luxation				Frequency by grading (%)				Total PL freq. (%)
Breed	No of dogs	Sex	0	1	2	3	0	1	2	3	
All breeds	21 201	M	6917	583	293	16	88.6	7.5	3.7	0.2	11.4
		F	11288	1278	772	54	84.3	9.5	5.8	0.4	15.7
Chihuahua	7023	M	2028	317	202	10	79.3	12.4	7.9	0.4	20.7
		F	3380	588	472	26	75.7	13.1	10.6	0.6	24.3
Bichon frise	1133	M	376	19	4	0	94.2	4.8	1.00	0	5.8
		F	620	81	33	0	84.5	11.0	4.5	0	15.5
Pomeranian	1059	M	287	62	21	4	76.7	16.6	5.6	1.1	23.3
		F	432	153	79	21	63.1	22.3	11.5	3.1	36.9
French bulldog	1631	M	577	31	5	0	94.1	5.1	0.8	0	5.9
		F	890	100	28	0	87.4	9.8	2.8	0	12.6

Table 4 shows frequency of patellar luxation by sex of the dog. Of all female dogs examined for PL, 15.7 % were considered affected. In comparison, only 11.4 % of all males were considered affected. This would suggest a 1:1.5 ratio between the sexes, where females are more likely to be affected with patellar luxation than males. The corresponding ratio of affected males to females for Chihuahuas, Bichon frises, Pomeranians and French bulldogs are 1:1.2, 1:3, 1:1.6 and 1:2 respectively. Overall, about twice as many females, compared to males, have been examined for patella luxation in the data.

Patellar luxation over time

SKK started recording patellar luxation in 1996. Birth year of the oldest dog that has a record of patellar luxation results in the SKK database was 1989. The number of examined dogs remained low for the following years until it started to increase for dogs born in 2000 and after (Figure 1). The number of patellar luxation examined dogs exceeded a thousand examined dogs per year first for dogs born in 2002 and later. After this, the percentage of patellar luxation free dogs started to level out at around 85% for the 14 breeds included in this study.

Figure 2 shows the proportion of patellar luxation free dogs per age group, along with the number of dogs examined per age group.

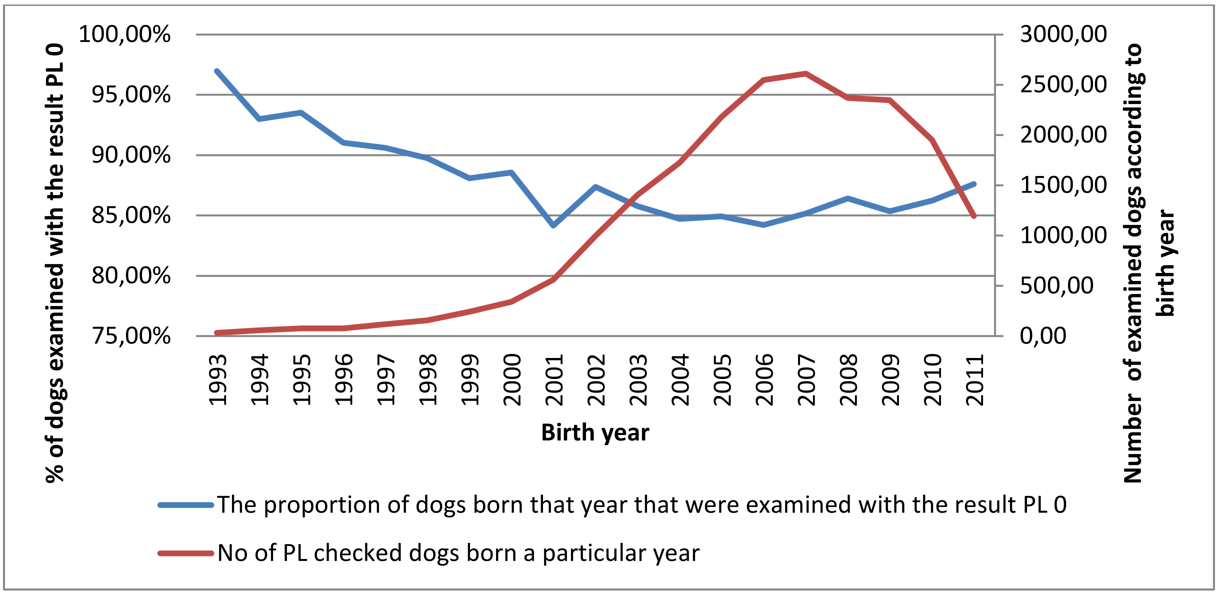

Figure 1. Comparison of number of patellar luxation (PL) examined dogs born each year to the proportion of PL 0 dogs born that year

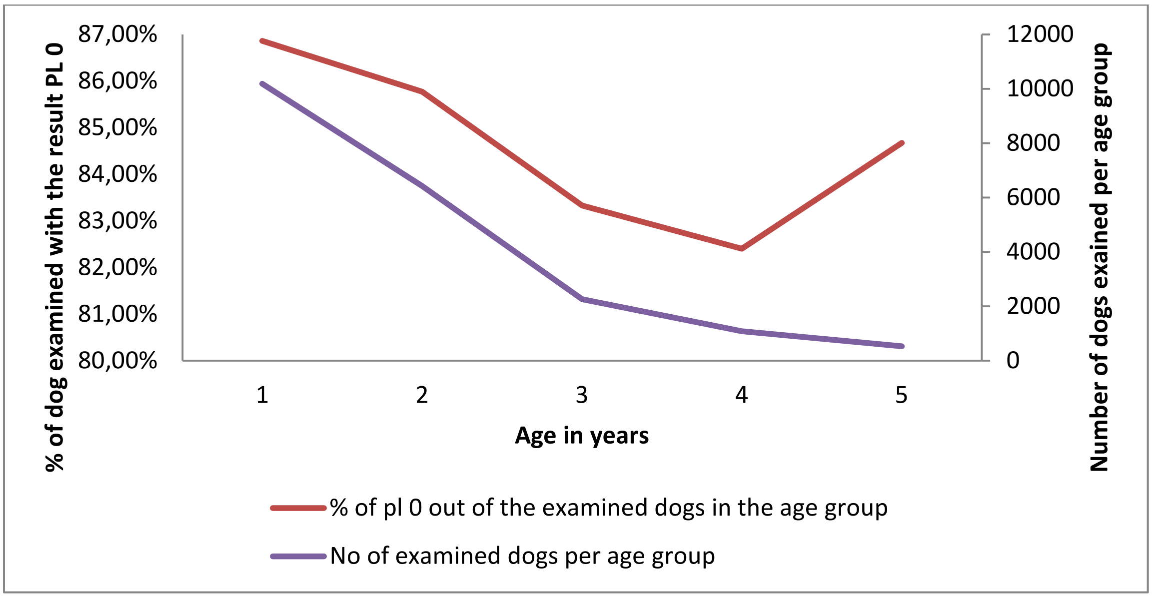

Figure 2. Number of dogs examined for patellar luxation (PL) in each age group, compared to the number of PL 0 dogs found in each age group

The majority of all dogs are examined between the age of 1 and 2, and most of them close after their first birthday. About half as many are examined between the ages 2 and 3. After the age of 4, the total number of examined dogs drops well under a 1000, making the data from age 5 and up unreliable. The same pattern illustrated in Figure 2 can also be seen at a breed level for the four breeds included in the genetic study. The proportion of patellar luxation free dogs is at its highest at 1 years of age at almost 87 %, and at its lowest at 4 year of age at just over 82 %, a difference of almost 5 %.

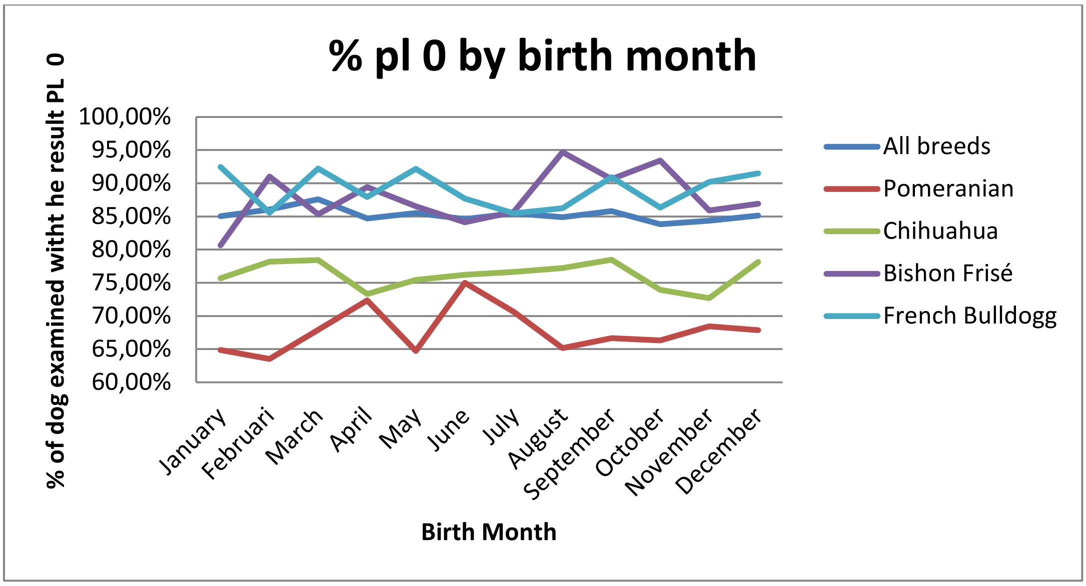

Figure 3. Percentage of PL 0 dogs out of examined dogs when looking at birth month

There was a difference in the results when looking at the birth month of the dog, where there was a difference of 3.8 % between the months with the highest and lowest proportion patellar luxation free dogs. Dogs born in October had the lowest frequency of dogs examined with the result PL 0 and dogs born in March had the highest frequency of PL 0 dogs (Figure 3). However, since the results on an all breed level was not significant, it is hard to determine if this is in fact the true seasonal fluctuation of PL. It could be that the results for the breeds without official breeding programs for PL are, in fact, distorting the statistics into a false fluctuation. When only looking at the two breeds where the results were close to significant, Bichon frise and the Chihuahua, a different picture is given. In the Chihuahua breed, the proportion of PL 0 dogs seem to be at its lowest for dogs born both in April and in November, and at its highest for dogs born in March and September. For the Bichon Frise, a clearer seasonal variation can be seen, with the results for dogs born January having the lowest proportion of PL 0 dogs, and the results for dogs born in August having the highest proportion of PL 0 dogs.

Patellar luxation heritabilities and variation estimates

The estimated heritabilities for the four selected breeds can be seen in Table 5.

Table 5 – Heritability estimates and their standard errors for patellar luxation traits, and number of observations included in the analyses

Breed	Trait	h^2	SE (h^2)	Number of observations
Chihuahua	PL01	0.24	0.023	7023
	PL02	0.25	0.023	7023
	PL01M	0.24	0.023	6982
	PL02M	0.25	0.024	6982
Bichon frise	PL01	0.22	0.061	1133
	PL02	0.21	0.062	1133
	PL01M	0.19	0.059	1112
	PL02M	0.20	0.061	1112
Pomeranian	PL01	0.11	0.061	1050
	PL02	0.08	0.058	1050
	PL01M	0.12	0.062	1040
	PL02M	0.09	0.059	1040
French bulldog	PL01	0.03	0.032	1631
	PL02	0.03	0.033	1631
	PL01M	0.03	0.032	1625
	PL02M	0.02	0.032	1625

For all four breeds, there was a small to no difference (0.00-0.002) in heritability estimates between the trait definitions including two or three categories, or the models including or excluding lateral patellar luxation.

The variation represented by each of the factors included in the model is described in Table 6 below. The model used to illustrate this variation is applying veterinarian as a random effect.

Table 6. Variance estimates of the model components for each breed for the trait PL02

	Effect			
	σ^2_{vet}	σ^2_a	σ^2_e	h^2
Chihuahua	0.013	0.100	0.307	0.25
Bichon frise	0.007	0.039	0.144	0.21
Pomeranian	0.075	0.032	0.373	0.08
French bulldog	0.012	0.004	0.130	0.03

Discussion

Most studies to date investigating patellar luxation are studies based on data from dogs that have visited veterinary clinics for different reasons. Furthermore, many studies are based on a small number of animals. These data have limited value for genetic studies for two reasons; data are not selected randomly from the general population, which is a necessary requirement for an unbiased statistical analysis, and in many cases the number of dogs in some of the breeds was lower than 20, which is too low to draw statistical conclusions about differences between breeds (Priester, 1972; Hayes et al., 1994; LaFond et al., 2002; Vidoni, 2005; Alam et al., 2007; Nganvongpanit, K., & Yano, T., 2013).

Based on previous scientific studies found and described in this project, combined with the findings of this study, the author feels that it can now be concluded that there is a clear genetic predisposition when it comes to developing patellar luxation, with an equally clear environmental influence. This genetic effect is especially evident when considering the continued over representation of some breeds in all previous studies, and also when looking at the breeding study of Flat-coated retrievers (Lavrijsen et al., 2013), where the incidence of patellar luxation was initially reduced thanks to breeding programs against PL. The current study is based on a larger number of animals screened for patellar luxation than in any other study found in the literature. Many of these observations are derived from breeds where it is mandatory to check breeding animals for PL, and this gives the data of this study high credibility and robustness when comes to being used in statistical calculations and a minimal amount of bias. It is therefore likely that the findings of this study relating to factors influencing patellar luxation are valid.

Possible genetic influences

The results found by Herman et al. (1987) in regards to the potential monogenetic inheritance of patellar luxation in Shetland ponies appears different from what is usually seen in the dog. When investigating the SKK database Avelsdata, one can find unaffected offspring produced despite both parents being affected. In the other end of the spectrum you can also find affected dogs where both parents were considered to be unaffected (results not shown). The same pattern was found by Soontornvipart et al. (2013), where unaffected as well as affected parent dogs, would give both affected and unaffected offspring.

There could be many reasons for this. One being that there is another type of mutation (or several) responsible for the patellar luxation seen in dogs compared to that seen in the Shetland pony. Another explanation could be that dogs are examined for patellar luxation at a young age, and dogs considered luxation free at that age may still develop patellar luxation later on. A third reason could be the uncertainty of the method used today to diagnose patellar luxation. In Avelsdata you can find dogs that have been tested by several veterinarians, and obtaining different clinical findings by each veterinarian (results not shown). Sometimes the different examinations have occurred during a very short period of time, even during the same day. This would not only vary in regards to degree of luxation, but also from being considered to not have patellar luxation at all, to being considered to have patellar luxation. It would be valuable to find a more objective method of evaluating patellar luxation.

It seems likely that that patellar luxation is not inherited in a monogenic fashion. Possibly, the mode of inheritance could be similar to that found in for example hip dysplasia, where so far as many as 9 different traits of the hip have been found to influence the development of the disorder (Wilson et al., 2012). It would seem plausible that many genes also influence the development of PL, given that many genes are involved in developing the complex structure of the patella and the hind limb as a whole. The literature suggest that several defects of the hind limb are involved in the pathogenesis of patellar luxation.

Difference between sexes

This study found a significant effect of sex where patellar luxation was more common in females, having a ratio of about 1:1.5 (Table 4), which is the same ratio found by Priester (1972) and also by Hayes et al (1994). A similar ratio of 1:1.95 towards females was also found by Soontornvipart et al (2013) and Lavrijsen et al. (2013), and a ratio of 1:1.8 was found by Alam et al. (2007) and also by Linney et al. (2011). This suggests that the genetic predisposition of patellar luxation could, at least partly, be (partially) sex-linked, or sex-influenced – that there could be other combinations of genetic and environmental factors unique to the females, such as hormonal influence or the extra strain of carrying puppies, which lead to a higher incidence of PL. These are usually referred to as secondary gender effects.

Overall about twice as many females as males have been examined for patellar luxation in the data (11 194 examined females and 6 846 examined males) (Table 4). This is to be expected, since there is a tendency towards a 2:1 ratio of females vs males being used in breeding (Avelsdata, 2014). It is less clear in the breeds with small population size, but evident in the breeds with a large number of litters born each year. Females also seem to be affected with more severe degree of patellar luxation compared with males. The proportion of female dogs with grading 2 or higher was 6.23 %, compared with 4.18 % for males.

Differences between breeds/sizes of dogs

A small size of the dog is often described as a risk factor for patellar luxation (Priester, 1972; Vidoni et al., 2005). Some of the breeds most affected with patellar luxation are of miniature breed type. However, several medium and large sized breeds also have a high incidence of patellar luxation, and many other miniature breeds have a very low proportion of patellar luxation. Lavrijsen et al. (2013), found an incidence of patellar luxation of 24 % in Flat-coated retrievers, a larger breed according to the classification set out by Priester (1972). Unfortunately there were very few Flat-coated retrievers examined for patellar luxation in the Swedish database, only 59 of which only 2 were diagnosed with patellar luxation, and so the breed could not be included in this study. In the Swedish Avelsdata, it is seen that there are many screened dogs in the breeds Jack Russel Terrier (n= 864) and the Chinese Crested Dog (n= 1129), both small breeds as classified by Priester (1972), with a much lower patellar luxation percentage than the average 15% for all the 14 breeds included in this study (5.79 % and 5.49 % respectively).

It is reasonable to think that large dogs with patellar luxation are more likely to have severe clinical issues, and perhaps even earlier in life, resulting in early exclusion from the breeding population. This could lead to them not having their PL results being part of the statistics. Because of the large variation in frequency of patellar luxation even among breeds of small size, the condition seems to be more heavily related to breed as a factor rather than size. One of the reasons why the prevalence is so much higher in some of the smaller breeds could simply be that larger dogs more often show clinical signs of patellar luxation and can more easily be identified and excluded from breeding.

Medial vs lateral patellar luxation

Priester (1972) attempted to compare different risk factors for patellar luxation in dogs, such as sex, size and breed. He found that medial patellar luxation was much more common than lateral patellar luxation in all breeds, including large breeds, and also that patellar luxation was more common if the dog belonged to a small sized breed and if the dog was a female. Also these results coincide with the findings in this study. The study could not identify much of a difference in heritability between data that included all examinations for PL, and data where lateral luxations were excluded. This could suggest that the genetic background for the two types are the same, but that environmental factors influence development, and that those factors have a tendency to lean increase the chance of the luxation being medial. This should be further investigated. However, some interesting numbers are worth mentioning. For example one of the breeds, the Bichon frise, had an unusual large proportion of lateral luxations (over 15 %). It would be interesting to examine what differs in this breed's physiology, that could explain this difference from the other breeds.

Differences between age groups

It seems as if the proportion of PL-free dogs decreases with age during the first 4 years of life. It could therefore be valuable to change the recommendations for patellar luxation examination that exist today. It could be of more value to breeders to have their dogs patellar luxation examined at 2 years of age rather than 1, and also to have the dog re-examined at 4 years of age. This is not unlike the procedure for examination of for example PRA (Progressive Retinal Atrophy), which can turn up at a later age. PRA is a inherited eye disorder, in which the retina deteriorates and the dog eventually becomes blind. This disorder can first be observed at varying ages of the dog, and therefore it is continuously tested for throughout the breeding dog's life, if a genetic test is not available (SKK, 2014). While some of the cases of patellar luxation later in life might be due to trauma or wear and tear, it seems likely that it is too early to determine a dog's true patellar luxation status at only 1 year of age.

Difference between birth months

This study shows indication, on an all 14 breed level, of a slight seasonal difference of 3.76 % (Figure 3) in the development of patellar luxation, where dogs born in the spring, have a lower prevalence of patellar luxation, and dogs born in the fall a higher prevalence. However, when looking at breed levels, this variation is much more unclear, and at times evens the opposite, as for example with the Bichon frise. It seems as if there is in fact a seasonal influence in the development of patellar luxation, but that it could be differing between breeds. Difference in birth month is indicating that there are other environmental factors related to the environment to which the dog is exposed during development, that is influencing the development of patellar luxation. Many similar studies have been done in dogs when considering hip dysplasia, and a large recent study made by Worth et al. (2012) showed a similar tendency to seasonal fluctuation in the prevalence of hip dysplasia, only reversed. Here dogs born in the fall had lower prevalence of hip dysplasia. It is reasonable to think that dogs born in the fall would experience less availability of exercise compared to dogs born in the spring, and perhaps this has a reversed effect on patellar luxation, than it has on hip dysplasia. Whereas dogs with hip dysplasia could benefit from milder exercise during their developmental stage as puppies, and dogs with patellar luxation could benefit from more exercise at this same stage. This possibility should be further investigated through studies where the dogs' exercise regimen are more closely monitored during development, and then compared.

Heritabilities

When deciding on the factors included in our model the decisions were mostly based on the results from the two breeds included with official breeding programs for patellar luxation, meaning the Chihuahua and the Bichon Frise. This is because these two breeds have official breeding programs for PL, and so their statistics should contain the least amount of bias. One example of this can be seen in the column displaying the p-values for Birth year in Table 2, where p-values are low for the Bichon frise and Chihuahua (0.0097-0.1342), but fairly high on an all breed level (0.3169-0.4202). This is most likely due to the results of the breeds without official breeding programs decreasing the confidence of the data. The heritabilities estimated in this report show high levels of heritability for patellar luxation, which is a categorical trait, in the Chihuahua and the Bichon frise (0.18-0.25). This coincides well with the findings of Lavrijsen et al. (2013), who estimated a heritability of 0.14-0.20 for a Dutch population of Flat-Coated Retrievers. There are therefore good possibilities to lower the occurrence of the condition by selective breeding. Prediction of breeding values could be of great help in this endeavor. However, environmental factors still play a big role in whether or not the condition manifests in the dog.

Estimating the heritability for a certain trait can be very useful, especially for developing effective breeding programs to make some of these traits more or less common within a population. The heritability, h^2, will tell us how much of the variation within a trait can be explained by the genetic composition of the animals. Furthermore, the calculation will correct for how much of the variation can be explained by the various identified environmental factors, such as the sex of the dog or when it is born. Finally, the residual of the model, will let us know how much variation of the trait is still unexplained, meaning there are still environmental factors to be identified that influences the trait.

Since there was little difference seen between heritability estimates for different trait definitions and between the groups where patellar luxation was graded in three classes and when only graded as 0 (unaffected) and 1 (affected), there may be only a small difference in the genetics of dogs with different grading of patellar luxation. In fact, when looking at grading of patellar luxation beyond affected and unaffected, the difference in grading may only be due to the number of and severity of other hind limb deformities, in association with environmental factors such as age, feeding, exercise and examining veterinarians. In other words, all dogs with patellar luxation, regardless of grading, may not be genetically different.

In some of the breeds studied, the Pomeranian and the French bulldog, a lower heritability than expected was found, when comparing to the previous study and also to the other two breeds in this study. This can be due to many reasons. The main factor influencing these results is that, in contrast to the other two breeds, it is not required of the Swedish breeders of Pomeranians and French bulldogs to examine their breeding animals for patellar luxation. It is voluntary and hence, up to each breeder which animals are examined and included in the statistics. The heritability estimate for Pomeranians were 8-12 %, lower than expected compared to the other two breeds and the value achieved for the Flat-coated retriever, but much higher compared to that of the French bulldog, being at 2-3 %. One reason for this could be that there would often be the same breeders within a breed that checks their dogs for patellar luxation. This will make some lines well investigated, and others completely unknown in regards to the prevalence of patellar luxation, decreasing genetic variation. Both of these estimates would likely be higher if these two breeds underwent official breeding programs for patellar luxation, such as the Chihuahua and the Bichon frise.

The residual was fairly high in the statistical calculations of our model, ranging from about 0.13 to 0.30. This tells us that there are still important environmental factor(s) to be identified to further help breeders reduce the incidence of patellar luxation

Future studies

The heritabilities and models used to estimate heritabilities for each breed, can be used to estimate breeding values for each animal within a population. The effectiveness of estimating breeding values to be used in breeding programs will depend on availability and quality of data. For many breeds, more observations are needed before reliable breeding values can be estimated. Since previous studies show that patellar luxation is usually not a inherited deformity in the knee itself, but rather a result of the misalignment caused by deformities in the other structures of the hind limb, it would most likely be very beneficial to future research into the genetic predisposition of the disease, to include measurement results of the other structures of the limb, such as coxa vara, coxa valga, the depth and shape of the knee cap etc. These factors are more objectively measured and hence, not dependent on the subjective diagnosis of any one veterinarian, so they should be more reliable factors to base a breeding program on to increase the effectiveness of this tool. However, factors such as cost must be considered, and today's examination method is a cheap one. With more dogs examined for patellar luxation, variations between veterinarians can be corrected for when estimating breeding values, and could then in part sort out the problem of subjectiveness in the evaluation.

The present analyses did not consider any difference between dogs that have unilateral patellar luxation and bilateral patellar luxation. The data of this study only included the score for the most severely affected limb. Hence, a dog that has one unaffected limb and one affected limb, received the same score as a dog with two affected limbs with the same grading. Since the genetic composition of an animal should affect both sides of the body equally, the difference between the hind legs may be environmental. A dog that has unilateral patellar luxation may in fact have been favoring one leg during development for one reason or another, and so the wear on that leg was larger and hence showing the predisposing PL. The opposite could also be true, and the dog could in fact genetically have healthy knees, but the grading of 1 in one knee could be due to an injury. Further studies into this is motivated. The Swedish Kennel Club are now registering results from both knees of the dogs since about 6 months back (Sofia Malm, 2014-09-30), and so in the future, when more dogs have been examined, it should be possible to include this effect in a study.

There are studies that suggest a difference in incidence of patellar luxation between neutered and intact dogs (Vidoni, 2005). It would be interesting in the future to compare PL prevalence in intact and neutered females, as well as females who had puppies during their lifetime with and females who did not. A previous study also suggest that there is a difference in female/male ratio in regards to patellar luxation between large and small breed dogs, with affected males being more common in large breed dogs rather than females (Gibbons et al., 2006). This should also be further investigated.

In addition to today's screening method of palpation and grading of the patella, new methods of measuring the different parts of the hind limb should be evaluated. This is to further deepen the knowledge of which deformities of the hind limb cause the luxation of the patella in a dog, and in doing so, more accurate measures could be obtained to be used for further genetic studies. Consideration needs to be taken both towards the severity of the abnormality, but also the age and size of the dog, because patellar luxation would most likely get more severe with age. Since Bound et al (2009) showed a connection between coxa vara and PL, it should be examined if the measurement of the AOI (Angle of Inclination) could be a useful measurement when breeding for reduced risk of PL. Making sure the radiographic images are read and interpreted by one or a few veterinarians rather than many, as is done today with hip dysplasia scans, could further speed up the progress. It could potentially be of greater benefit to breeding progress to instead only use measurable data of the different parts of the limb when calculating breeding values for patellar luxation.

Efforts should be made to include more information in the data in the future, such as if the dog is neutered or not, to find more environmental factors that are affecting PL. In this study we found significant effects of breed, sex, age, birth month, birth year and examining veterinarian. When looking at a similar developmental orthopedic disorder in dogs, hip dysplasia, many studies have been performed to investigate these other factors influencing the etiology of hip dysplasia. Scientists found that factors such as feeding and exercise at a young age had a significant impact on whether or not a specific dog would develop the disorder (Frise & Remedios, 1995; Krontveit et al., 2012). This considered in combination with its genetic influence of course. This author would suggest similar studies to be made also for Patellar Luxation.

Conclusions

- Patellar luxation has a clear genetic predisposition, and is also influenced by environmental factors. A few of these have been identified in this study, more should be explored.

- Patellar luxation seems to be inherited in a polygenetic, possibly sex influenced, manner.

- The heritability for the trait patellar luxation was 0.24-0.25 in Chihuahuas.

- The heritability for the trait patellar luxation was about 0.18-0.20 in Bichon frise.

- Heritability estimate for the Pomeranian and the French bulldog were lower than expected, at 0.08-0.12 and 0.02-0.03 respectively. New estimates should be calculated when a higher number of observations within the breeds are available. Most accurate results would be obtained if these breeds also became subject to official screening programs for patellar luxation, such as the Chihuahua and the Bichon Frise, as it would generate more data.

- The effect of breed was highly significant, meaning that there was a clear difference in patellar luxation incidence between the breeds.

- The effect of sex of the dog was highly significant, suggesting there is in fact a difference in incidence (and perhaps also severity) of patellar luxation between males and females, where females appear to have a higher risk of developing patellar luxation.

- The effect of age of the dog at the time of examination was highly significant, suggesting that there is a difference in patellar luxation incidence between the different age groups. A higher age implicated a larger risk of being diagnosed with patellar luxation

- The effect of examining veterinarian was highly significant, suggesting there is a need for higher uniformity when it comes to grading of patellar luxation.

- There was an indication that the birth month of the dog could be influencing the incidence of patellar luxation, hence environmental factors associated with seasonal differences should be further explored.

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