Prevalence of genetic disorders in dog breeds: a literature review

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Contents

Summary

Genetic disorders are common in dogs and in the media it is reported that genetic disorders are more frequent in pedigree dogs than in look-a-likes or in mixed-breed dogs. Here, we consider pedigree dogs as purebred dogs (i.e. matching a breed-specific morphology) with a registered and certified pedigree, whereas look-a-likes dogs are dogs without a certification. Thus, look-a-likes may be non-pure bred or purebred but lacking the supporting evidence. Dutch experts have indicated that more than 40 percent of purebred dogs in the Netherlands suffer from genetic disorders. Uncertainty about the validity of such indications, and if pedigree dogs are at increased risk of genetic disorders, together with societal concerns about the well-being of (pedigree) dogs, incited a Wageningen UR Science Shop project commissioned by the Dutch animal protection foundation Dier&Recht. Genetic disorders are heterogeneous in aetiology and manifestations across dog breeds, which complicates studying them. One feasible approach is to study specific disorders in pre-selected breeds only, as a model for the complex reality.

This report, as part of this project's products, provides a scientific literature overview on prevalence data for two genetic disorders (hip dysplasia and elbow dysplasia) in the German Shepherd and the Rottweiler in various countries including the Netherlands. The prevalence data assembled and compared in this study are based on results of screening programs published from national and international Kennel Clubs and Veterinarian Associations.

In both breeds, the disease prevalence for hip dysplasia (HD), ranging from 10-46% in European and non -European countries, was remarkably variable, with a substantial proportion of the population at risk in, for example, Finland (33-46%). In the Netherlands, the prevalence for HD reported for both breeds (10-18%) was intermediate compared to that in other European countries (8-46%). Different methodology and scoring systems for HD are used in screening programs, whereas interpretations of radiographs to determine the HD grade, and the quality of databases, are critical factors. Methodological differences between studies make a valid comparison between studies difficult. The results for elbow dysplasia (ED) are similar regarding the high variation in prevalence among different countries (7-65%). However, the ED condition is estimated to be at least twice as prevalent in Rottweilers (40-60%) than in German Shepherds (20%). Yet, in the Netherlands, the estimated ED prevalence in both breeds is low (7-14%).

This literature search found no data that allowed to test if the subcategory of look-a-likes are less affected by the specific genetic disorders HD and ED than pedigree dogs. Earlier studies have indicated that purebred dogs are more at risk of genetic disorders than mixed breed dogs, but this need not be the case for every disorder-dog breed combination. The detection of subtle differences in the prevalence of genetic disorders, for example between pedigree dogs and look-a-likes, require data that are presently unavailable as look-a-likes and mixed breeds are not nationally monitored for ED and HD.

Introduction

Pedigree dogs are known to be at risk of a range of genetic disorders and a common assumption is that mixed breed dogs are healthier (Asher *et al.* 2009). Information about the prevalence of genetic disorders in such different dog populations may aid the development of preventive strategies. The prevalence of genetic disorders in dog breed populations is discussed extensively by the Dutch media [1, 2, 3, 4], and based on analyses and statements of genetic experts [4, 6] it is suggested (e.g. Ed Gubbels, gencouns) that more than 40 percent of purebred dogs in the Netherlands suffer from genetic disorders. These statements have remained controversial, but interesting for scientific and societal reasons. The question if hereditary disorders are more prevalent in pedigree dogs than look-a-likes triggered the present project of the Wageningen UR Science Shop [7] in collaboration with the Dutch association Dier&Recht [5]. In the following we consider pedigree dogs as purebred dogs (i.e. matching a breed-specific morphology) with a registered and certified pedigree, whereas look-a-likes dogs are dogs without a certification. Thus, look-a-likes may be non-pure bred or purebred but lacking the supporting evidence.

This literature review addresses the prevalence of genetic disorders in populations of pedigree dogs, look-a-likes and mixed breeds. The international canine organisation, the Federation Cynologique International (FCI) [8], contains the largest registry of dog breeds and recognizes 343 breeds of dogs. In addition, there are a total of 635 genetic disorders/ traits found in dogs[9] and more than 350 genetic disorders have been described in different dog breeds (Sargan *et al*. 2004). Instead of studying many dog breeds and genetic disorders, the present project team [5, 7, 10, 11, 12] decided to take a model approach and focus on two popular dog breeds and two common disorders. In this report, scientific literature data were analysed on differences in prevalence of two common disorders (hip dysplasia and elbow disease) in two popular dog breeds, the German Shepherd and the Rottweiler. Hip and elbow dysplasia are both locomotory diseases, which can cause lifelong disability. For both disorders a polygenic mode of inheritance is considered with multiple genes being involved. Environmental factors like feeding and adequate exercise are also recognized as factors influencing susceptibility to these disorders.
The aim of this report was to summarize literature that compares prevalence of genetic disorders between pedigree dogs, look-a-likes and mixed breeds, focussing on information that may help to assess the situation in the Netherlands. Selection strategies based mainly on phenotypic features, ignoring health and performance, have increased inbreeding and the risk of hereditary disorders in modern dog breeds. To counteract this, dog kennel clubs adopt health surveillance programmes and breeding strategies to combat genetic disorders. The outcomes of these processes should be evident in genetic disorder prevalence studies, and may help deciding how to breed dogs in the future.

Part 1: Hip dysplasia in two dog breeds

1. 1. Prevalence of hip dysplasia (HD) in German Shepherds

The literature search revealed only one study that presented prevalence data for hip dysplasia (HD) in pedigree dogs, including German Shepherds living in the Netherlands (Lavrijsen *et al.* 2014). Confirmation of the pedigree files of the dogs was provided by the Dutch Kennel Club [12]. A prevalence of 18.2% for HD was found in the pedigree German Shepherd dog population (Table 1), as based on the standard Fédération Cynologique International (FCI)-scoring system (FCI, 2010)[8] , see Table 2. The FCI-scoring system is based on radiographic evaluation of the hip (osteoarthritis, congruity, shape and laxity) and there are five different scores, ranging from A to E. Grades A and B are considered nondysplastic hips, whereas grades C to E are considered dysplastic hips. Final scoring is based on the worst of the two hip joints. The minimum age for screening is one year for most breeds but it is 18 months for large and giant breeds. In accordance with the FCI scoring system the study of Lavrijsen *et al. (*2014) recognized a score result of C to E (i.e. not when A or B) as a dysplastic hip, independent of whether or not a dog will develop symptoms of HD later in life. The researchers investigated certified purebred (pedigree) dogs, but not mixed breed dogs. A quite similar result was published by Coopman *et al*. (2008), who showed that the German Shepherd purebred dogs in Belgium showed a prevalence of 23% for HD. Yet, this similarity in breed-specific prevalence rates for HD in the Netherlands (18.2%), and in Belgium (23%) are not matching with breed specific published HD-prevalence data for purebred (i.e. pedigree and look-a-likes) German Shepherd populations in other European countries. For instance, in Finland where the FCI-scoring procedure was used also, a higher prevalence of 33-46% (Leppänen and Saloniemi 1999) and of 39% (Mäki *et al.* 2001) for HD were found in the German Shepherd purebred populations. Researchers examined the population structure and inbreeding trends as one of the causes that could explain the high prevalence. They observed an increase of inbreeding for German Shepard purebred population from the late 1960s onwards and a decrease of inbreeding for the Rottweiler purebred dog populations from the early 1980s onwards and concluded that incomplete pedigree data for individual dogs complicated their examinations and made a comparison of inbreed levels for hip and elbow dysplasia between dog breeds biased and difficult. Additionally, two other important factors were discussed by the researchers that might have contributed to the results. The fact that dogs had been graded according to three different variants of FCI-Systems (two older FCI systems, present FCI System) and screening for HD allowed also older dogs (≥ 24 month) makes it difficult to recognize one leading cause (Mäki *et al*. 2000, Mäki *et al*. 2001). The findings in Belgium and the Netherlands, however, contrast with reports from Germany, that indicate a much lower HD-prevalence of 12.6% (Hamann *et al.* 2003) and 8.5% (Stock *et al.* 2011) for German Shepherd purebred populations.
For non-European German shepherd populations, the present literature search identified three studies from the US focussing on HD rates in German Shepherd populations. Diagnostic methods used in the US such as the evaluation system of the Orthopedic Foundation for Animals (OFA)[13] differ from those used in Europe. The OFA grading system applies radiographic criteria that focus on the hip joint conformations incongruence and degenerative joint disease and hip laxity. In dogs of 2 years or older, a descriptive scoring method is used with hips graded in 7 categories: excellent, good, fair, borderline, mild, moderate and severe hip dysplasia (Verhoeven *et al* 2012). Comparison of different screening systems like the one of the FCI, which is applied in most of the European countries (including Russia) South America South Africa and Asia, and the OFA is difficult. Differences of radiographic phenotypic criteria, differences in timing (i.e. age of the dog) of hip joint screening, and many other factors affect the diagnostic outcome (Table 2). Typically used in the US, the Penn HIP screening method is managed by the University of Pennsylvania and involves radiographic assessment that mainly focuses on passive hip joint laxity. The differences of the main screening methods that are used worldwide are summarized in Table 2 as described by Verhoeven *et al* 2012.

A prevalence of 19% for HD-affected German shepherds registered from 1974 to 2005 was reported by the Orthopedic Foundation for Animals (OFA)[13]. In this US study, the OFA-evaluation system was applied, which is used both in the United States and Canada.
More recent OFA-statistic records from the US showed a similar HD prevalence of 17.8% for the German Shepherds population with dogs registered from 2006-2010. A higher prevalence, namely 25%, was found by the Pennsylvania Hip Improvement Program (PennHIP)[14], where the PennHIP method was used for evaluating German Shepherd hip status (Smith 2005). The third US-study (Rettenmaier *et al*. 2002) where the OFA-method was applied, is the only study in which HD was measured separately in purebred and in mixed bred dogs. The records were collected by the University of Missouri, Columbia, from 1991 to 1995 and were derived from a veterinary clinic database, meaning the results deal with a specific subpopulation of unhealthy dogs and the absolute prevalence found may not be representative for the larger population. The comparison between purebreds and mixed breeds is likely to be sound though. The study did not differentiate purebred dogs with a registered pedigree and known ancestors from look-a-likes. The researchers reported a high HD-prevalence of 33% for the German Shepherds breed (49 HD cases of 149 cases). For registered mixed breed dogs (a total of 649 dogs) the researchers reported an overall prevalence of about half that in purebreds, i.e. 17.7 % (115 HD-cases out of 649 mixed bred

dogs). For all registered purebred dogs a HD-prevalence of 19.7% was found (441 HD-cases of 2236 cases, Rettenmaier *et al.* 2002), meaning that German Shepherds are more prone to HD than individuals of an average other breed.

Taken together, the prevalence of HD in Germans Shepherd dogs seems about 20% in the Netherlands and Belgium, as based on the FCI diagnostic system, which compares with results from the US as based on the OFA method (estimated prevalence of 19%) and PennHIP method (25%). Deviating results, which cannot be attributed solely to the used diagnostic methodology, are reported for Finland (33 to 46%) and Germany (9 to 13%). This means that the prevalence of HD in Dutch (pedigree) Germans Shepherd dogs is about twice or half that of other (purebred) Germans Shepherd populations in Europe and it is intriguing what causes these differences. Differences in genetic background of the populations, including inbreeding status, may be an explanation (Hou *et al.* 2013). Methodological factors that likely play a role include the sensitivity of the screening methods, time period of the screening program, or the screening age of the dog (Paster *et al*. 2005). It would be encouraging if rules that exclude dysplastic dogs from the breeding population contributes to the found variation (Leppänen and Saloniemi, 1999). A within study comparison of purebred Germans Shepherd dogs and mixed breeds, meaning major methodological biases were excluded, detected a near double risk of HD for purebreds as compared to mixed breeds. The purebred category included look-a-likes and the specific situation for the latter cannot be discerned.

1.2. Prevalence of Hip dysplasia (HD) in Rottweilers

For HD in Dutch pedigree Rottweilers Lavrijsen *et al.* (2014) estimated a prevalence of 9.6% (Table 1) which is below the estimated HD prevalence of 15% for all pedigree dog populations in the Netherlands. Similarly, in Belgium a HD prevalence of 10% is reported for the purebred Rottweiler population (Coopman *et al*. 2008). In contrast, the study by Mäki *et al.* (2001) in Finland shows a much higher prevalence of 32% for HD in Rottweilers. In Sweden, two independent studies on Rottweilers reported a HD prevalence of 29-31% (Swenson *et al.* 1997a, b) and 18.8% (Malm *et al.* 2008). Swenson *et al.* (1997a) investigated hip dysplasia of purebred dogs born between 1976 and 1986 and registered by the Swedish Kennel Club. The grading system that was used for the HD-records in Sweden until 1999 and applied in this study is described as a modification of that originally suggested by Schnelle in 1954 and has a 4-point classification system (Normal, grade I, with slightly dysplastic, Grade II moderate, Grade III severe, Grade IV, very severe). Because the 4 point grading system is different from the 5 point FCI-classification system and might bring forward different meanings it is difficult to compare.

Malm *et al.* (2008) investigated hip dysplasia of purebred dogs registered in the Swedish Kennel Club born between 1974 and 2001. Because in this study records from two different scoring systems, the 4 point classification system (until 1999) and the official 5 point FCI-system scoring (from 2000 onwards) were present, the researchers performed a transformation of the HD-grades to a common scale prior to the statistical analyses. Differences in the grading systems and usage of records of different time periods might have contributed to the different prevalence distributions. Similarly as found for Germans Shepherd dogs, in Rottweilers the prevalence of HD is higher in Finland, and seemingly other Scandinavian countries, than in the Netherlands and Belgium.

Outside of Europe, we found three studies on HD in Rottweilers based on data from the US. A prevalence of 33% for HD- affected Rottweiler registered from 1974 to 2005 was reported by the Orthopedic Foundation for Animals (OFA)[13]. This means the OFA-evaluation system was used, which is different from the European standard FCI screening system. More recent OFA statistical records showed a prevalence of 20% of HD-affected Rottweiler's, with dogs registered from 2006-2010[13]. This remarkable decrease with a third stresses the importance of the period of time for screening HD, and it suggests that HD prevalence decreased over the recent years. Possibly, this reflects the success of a screening program within a breed.
A second US study used Rottweiler records from the Pennsylvania Hip Improvement Program (PennHIP)[14], i.e. the PennHIP method for evaluation of hip status, and found a HD-prevalence of 25%. In the third US-study, Rettenmaier *et al.* (2002) where the OFA-scoring method was applied and data set of a veterinary hospital population during a five year period of 1991-1995 were investigated, reported a relatively high HD- prevalence of 35.4% for the purebred Rottweiler population.

The prevalence of HD in Dutch and Belgium Rottweilers is estimated at about 10%, meaning about half of that in German Shepherd dogs. Estimates are up to three-fold higher for Scandinavian Rottweiler populations (estimates of 19 to 32%) as well as for US populations (20 to 35%). Differences in diagnostic methods used across studies are unlikely to explain these discrepancies, but the time of record sampling may be of major importance with more recent data sets revealing lower prevalences.

Table 1: HD in German Shepherd and Rottweiler

Country	HD German Shepherd	HD Rottweiler	Purebred dogs All	Mixed bred dogs All	Time Screening	Method	Author Name
The Netherlands	18.2% N= 2041	9.6% N= 646	15% N= 34 620 (214 breeds)	Not defined	2002-2010	Pedigreed (FCI,2010)	Lavrijsen *et al*. 2014
Belgium	23% N=1245	10% N: 346	20% N: 5883 (40 breeds)	Not defined	2002-2006	HD: FCI, as described by Bass 1993.	Coopman *et al.* 2008
Germany	12.6% N= Total: 21371	Not defined	Not defined	Not defined	1998-2000	Pedigreed Registered by German Shepherd Dog Breeding Organization (SV) Augsburg	Hamann *et a*l. 2003
Germany	8.5% N=48367	Not defined	Not defined	Not defined	2001-2007	FCI Pedigree	Stock *et al*. 2011
Finland	33-46% N: 23 385	38-45% N= 6672	Not defined N: 69349 (22 breeds)	Not defined	1988-1995	95% pedigreed dogs Finish Kennel Club	Leppänen and Saloniemi 1999
Finland	39% N: 12302	32% N: 3985	N: 289569 (6 breeds) Not defined	Not defined	1987-1996	FCI, before 50% of dogs older FCI system (1994)	*Mäki et al*. 2001. Mäki *et al*. 2000
Sweden	22-37% N: 31951	29-31% N: 3197	Not defined N: 83 229 (7 breeds)	Not defined	1976-1988	Modified Grading system originally suggested by Schnelle 1954.	Swenson *et al*. 1997a
Sweden	Not defined	18.8% N: 14693	Not defined	Not defined	1974-2001	Until 1999 Swedish grading acc. Schnelle (1954) Since 2000, FCI, Grading	Malm *et al.* 2008

Switzerland	21-31% N: 933	13-21% N: 250	42% HD N: 3700 (30 breeds)	Not defined	1971-1994	According to Flückinger *et al* 1993	Flückinger *et al.* 1995
Croatia	Not defined	11.2% N=455	18.75% N=5381 (2 breeds)	Not defined	2001-2009	FCI	Stanin *et al*. 2011
Poland	7-12% N: 757	10-19% N: 369	Not defined N: 2113 (16 breeds)			FCI	Aleksiewicz *et al.* 2008
USA	19% N: 107698	20.2% N: 94253	Not defined	Not defined	1974-2005	OFA	OFA-Hip statistics [13]
USA	17.8% N: 9936	15,0% N: 4562	Not defined	Not defined	2006-2010	OFA	OFA-Hip statistics [13]
USA	13% Not defined	25% Not defined	Not defined	Not defined	PennHIP 2005	PennHIP	Smith 2005
USA	32.9% N: 149	35.4% N: 99	19.7% N: 2236 (19 breeds)	17.7 N: 649	1991-1995	OFA	Rettenmeier *et al*. 2002

Table 2: Different screening systems used for canine hip dysplasia demonstrating their impact on screening results for HD prevalence.

Screening system	The Orthopedic Foundation for Animals (OFA)	Federation Cynologique Internationale (FCI)	FCI-Variant	Pennsylvania Hip Improvement Program (PennHIP)
Country	United States, Canada	Europe (84 national members), Russia, South America, South Africa, Asia.	Germany	Unites States, University of Pennsylvania
Age of dogs	≥ 24 months	1 year, 18 months for large breeds	1 year	6 months
Scoring system	7-point scoring method: 1: excellent, 2: good, 3: fair 4: borderline 5: mild, 6: moderate 7: severe _____ 1-3= nondysplastic status 4-7= dysplastic status	5 different scores A: normal B: near normal C: mild hip dysplasia D: moderate E: severe _____ A-B: normal C-E: affected Final scoring is based on the worst of the 2 hip joints. Variations on the FCI System are applied in several European Countries (Verhoeven et al 2012)	10 criteria A1/A2 normal B1/B2 almost normal C1/C2 still acceptable D1/D2 moderate E1/E2 severe _____ Individual breeding organizations decide whether dogs with HD are recommended for breeding.	PennHIP distraction index measurement (DI). _____ DI ranges from 0 to1 or higher, range 0: representing full congruency of the hip joint and range ≥1 : complete luxation and has been correlated with the risk of developing hip joint osteoarthritis.
Radiographic criteria	Hip joint conformation Signs of incongruence and degenerative joint disease and hip joint laxity)	Standard radiographic evaluation with the NA measurement The scoring system combines the subjective standard hip-extended	Standard radiographic evaluation with the NA measurement The scoring system combines the subjective standard hip-extended	Measure of passive hip joint laxity, three separate radiographs: the distraction view, the compression view and the hip-extended view.
Norberg angle (NA) measurement	No	Yes	Yes	No
Evaluation of Radiographs	Consensus of three independent board-certified radiologists	Certified veterinarian, training is not mandatory.	Specialist radiologists or surgeons	PennHIP-certified veterinarians
Database Registration	Voluntary submission of films for evaluation and entry in to the database. Offspring from affected dogs can receive a pedigree.	Voluntary submission of films for evaluation and entry in to the database. In some countries and some breeds, offspring from affected parents do not receive a FCI pedigree.	Voluntary submission, dysplastic dogs can still be used voluntarily for breeding	Mandatory submission

Part 2: Elbow dysplasia in two dog breeds

2.1 Prevalence of Elbow dysplasia (ED) in German Shepherds

The prevalence of Elbow dysplasia (ED) was recently described for the pedigree German Shepherd population in the Netherlands by Lavrijsen *et al.* (2014). The pedigree files of the dogs from 2002 to 2010 were provided by the Dutch Kennel Club[12]. The scoring system that was applied was according to the international Elbow Working Group (IEWG)[15] and is based on the degree of arthrosis present and divided into four categories from Grad 0 (normal), Grad I (mild arthrosis), Grade II (moderate arthrosis) to Grad III (severe arthrosis), depending on the size of osteophytes present in the joint. The minimum age for official ED screening is 12 months.
Interestingly, a relatively low prevalence rate of 6.9% for ED was reported for the pedigree German Shepherd dog population in the Netherlands (Table 3). In the same study the overall prevalence ratio for ED, calculated for all affected pedigree dogs was similar low; 8.9%.The authors pointed out that four radiographic views were applied for scoring of ED. The official ED screening as regulated by the International Elbow Working Group (IEWG) requires at least two, but preferable four radiographic views of each elbow. Because IEWG standard screening methods used by others are not always described in detail, it is difficult to discuss about to which extend this factors could have influenced the evaluation and prevalence data.
In parallel, a percentage of 12% was reported by Coopman *et al. (*2008) in purebred German Shepherds in Belgium. A substantial higher percentage of 19% was reported for the purebred German Shepherd population in Finland (Mäki *et al.* 2001) and in France (Remy *et al.* 2004). For non-European countries, reports of the US statistics for ED showed a similar percentage of 19% for ED in German Shepherd populations (OFA-Elbow statistics)[13].

2.2 Prevalence of Elbow dysplasia (ED) in Rottweilers

ED prevalence for the Dutch pedigree Rottweiler population was recently described by Lavrijsen *et al.* (2014) with a prevalence of 14%. This is a one and a half higher prevalence compared to the overall ED-prevalence of 8.9% calculated across pedigree dogs in the Netherlands, presented in the same study. In other European countries higher prevalences are reported for Rottweilers and possible differences in screening protocols even if they are uniformly based on the IEWG standards and the period of sample collection might have contribute to the different distributions. Prevalences of ED in Rottweilers are estimated to be 33% in Belgium (Coopman *et al.* 2008), 38.7% in Sweden (Malm *et al.* 2008), 47% in Finland (Mäki *et al.* 2001) and 44-65% in Germany (Beuing *et al.* 2000). A similar high prevalence of 39% is estimated for the US Rottweiler population, as reported by the Orthopedic Foundation for Animals[13].

2.3 Summary of results for ED

The prevalence of ED is estimated at 7% and 14 % for Dutch pedigree German Shepherd dogs and Rottweilers, respectively. These estimates are substantially lower than those reported for other European countries or the US, being 19% and 33 to 65% for the respective purbred breeds. The exception is the ~12% prevalence of ED in German Shepherd dogs in Belgium (Coopman *et al.* 2008). What specific features of Lavrijsen's study (2014) could explain the relatively low prevalences is unsure and details on diagnostic methods and the period of sample collection and number of animals considered should be discussed when comparing the prevalence with that in other countries. Like for HD, the recent time of sampling may have played a role, which would suggest that high ED prevalences of about 20% in German Shepherd dogs and double that in Rottweilers, as found across countries, are decreasing as surfaced in the recent Dutch study. Results demonstrate how Rottweilers are more at risk of ED than German Shepherd dogs, but based on the data used in these studies it is not yet possible to assess the specific risk of look-a-likes as compared to purebreds.

Table 3: Breed specific ED in German Shepherd and Rottweiler
ED grading is according to IEWG standards (ED-score >=1) or as described.

Country	ED German Shepherd	ED Rottweiler	Purebred dogs All	Mixed bred dogs All	Time Screening	Method	Author Name
The Netherlands	6.9% N= 480	14% N= 314	8.9% N= 9788 (34 breeds)	Not defined	2002-2010	Predigreed dogs (IEWG standards)	Lavrijsen *et al*. 2014
Belgium	12% N=130	33% N: 135	19% N: 1356 (11 breeds)	Not defined	2002-2006	ED=IEWG standards) Accoring to Flückinger *et al.* 2000 FCI, Predigreed dogs	Coopman *et a*l. 2008
Germany	16.1% N=28011	Not defined	Not defined	Not defined	2001-2007	FCI Pedigree, according to IEWG	Stock *et al.* 2011
Germany Lit print		44-65% N:2114			1996-1999	With pedigree according to IEWG	Beuing *et al.* 2000
Finland	19% N=2566	47% N: 2972	Not defined	Not defined	1987-1996	according to IEWG	Mäki *et al.* 2001 Mäki *et al.* 2000
Sweden	Not defined	38.7% N: 11981	Not defined	Not defined	1974-2001	according to IEWG	Malm *et al.* 2008
France	Not defined	19.4% N: 520				Accoring to Remy *et al* 2004 Defined in the methods	Remy *et al*. 2004
USA	19% N: 36523	39% N: 36523				1974-2006 OFA-three specific etiologie, FCP,OCD ,UAP	OFA-Elbow statistics [13]

Part 3: Discussion and conclusions

3.1 Discussion

The estimated prevalences for hip dysplasia (HD) and elbow dysplasia (ED) in Dutch German Shepherd dogs are, respectively, roughly 20% and 10%, whereas for Rottweilers these are about 10 and 15%. Estimates for dog populations in Belgium tend to be similar, where data are available, and in Germany this is true for ED in German Shepherd dogs, though the estimated risk of HD in German dogs is about half of that in Dutch German Shepherd dogs and twice of that in Rottweilers. Typically, prevalences of HD and ED in other European countries, especially Scandinavian, and the US are two-fold to three-fold higher than those reported for the Netherlands. The use of different diagnostic principles are unlikely to explain the large differences in prevalences reported across studies, though in more detail the use of different thresholds for identifying positive cases has the potential to cause such major differences across studies. Related to this, it should be noted that prevalence estimates summarized are in part based on subclinical cases, meaning dogs without detectable manifestations of the disorder that are however at increased risk of developing these. Debate about the absolute level of prevalence for a given disorder has little influence on answering the question if pedigree dogs are at increased risk of HD or ED, as here the relative outcomes compared to those on look-a-likes or mixed breeds matter. In one study on HD in German Shepherd dogs, purebreds had a near double health risk compared to mixed breeds. The comparison between pedigree dogs and look-a-likes cannot been made as studies typically do not indicate if purebred dogs have pedigree certificates. A Dutch study with purebred dogs with a pedigree certificate reported low disorder prevalences, but did not make the comparison with other subpopulations.
Different aspects have been discussed critically by researchers regarding the comparison of prevalences of genetic disorders (Wahl *et al.* 2008). For instance, the different scoring systems that are used to evaluate the quality of the hips influence the prevalences (Table 2). In Finland, for example, all the radiographs of dogs that are screened are officially recorded and receive an official evaluation, which is not the case in Belgium (Coopman *et al.* 2008) where in most instances a single observer of the breed club is responsible for screening radiographs. Because the individual breed club selects the observer and a qualification is not mandatory, a possibly more subjective classification of radiographic findings is performed (Verhoeven *et al.* 2012). It should also be mentioned that the different countries started the official screening program for HD and ED at different time periods. For example in France the first elbow dysplasia screening programme was established in 1997 in German Shepherds and the researchers stated that the screening was still not mandatory and only well-motivated owners or breeders submitted radiographs (Remy *et al*. 2004). Also in Finland, Rottweilers were included in the official HD screening program in 1994 (Leppänen and Saloniemi 1999). Therefore, fewer publications of prevalence data were found for the Rottweiler breed because official HD screening programs started later from 1994 onwards.

Assuming that at least partly the pronounced variation in estimated prevalences, for a specific genetic disorder within the same breed, are based on true biological differences among populations, this may reflect inbreeding status (Hou *et al.* 2013).

Regardless of the different factors that might have contributed to the reported variation of prevalences seen in different countries, our literature study showed that the two conditions, hip dysplasia and elbow dysplasia, are present in all purebred German Shepherd populations and in Rottweiler purebred populations and is also found in mixed breed dog populations. Therefore, this condition remains a concern in the Netherlands, and in other European and non- European countries. More stringent standardizations and detailed definitions will be needed to compare purebred populations and other categories of look-a-likes and mixed breed dog populations. Differences in quality of databases and many other factors described previously might have contributed to the screening results of prevalence. Whether the prevalence percentage in other populations, including look-a-likes or mixed breed dog populations, is different, higher, or lower, compared to pedigree dog populations cannot be estimated from the literature screened here. These data are not available because look-a-likes are not nationally registered and are not evaluated with the same method as pedigree dogs are for ED and HD.

3.2 Conclusions

In conclusion, the literature reviewed here provides an overview over prevalence data found for two genetic disorders in two different dog breeds. To this point, this investigation confirms that these two conditions, hip dysplasia and elbow disease are worldwide present in the German Shepherds and in the Rottweiler. The study revealed that screening results for prevalence of one or both genetic disorders can vary strongly between population studies. Whether the wide variations of prevalence for a genetic disorders between population of the same breed is representing a true prevalence difference or is the result of various factors that have biased the data collection is not clear. The study demonstrates that various factors including different screening systems and quality of databases are important and critical factors that make a comparison of prevalence results across countries difficult.
Databases that were used typically included purebred dogs with and without a pedigree certificate and a distinction between purebred pedigree dogs and look-a-likes could not be made.
Up to date, the prevalence for HD and ED in the pedigree German Shepherds and in the pedigree Rottweiler populations living in the Netherlands are monitored. For look-a-likes and mixed breed dogs such monitoring programmes do not exist in the Netherlands, making it difficult to assess the difference in prevalence of such genetic disorders among subpopulations. In this scientific literature study, two breeds and two genetic disorders were investigated. Even within this focussed area, reported prevalences in purebred dogs varied from less than 10% to over 60%, and claiming a specific number of purebred dogs being "affected" by genetic disorders seems unfounded. If worldwide, a considerable proportion, e.g. somewhere between 10 and 60%, of German Shepherds and Rottweilers is at increased risk of developing clinical HD or ED, summation of these figures for multiple disorders seemingly produce extreme risks of developing any genetic disorder. Obviously not all dogs identified as a case actually develop clinical symptoms and as such the prevalence numbers are subjective, strongly reflecting diagnostic criteria decisions. The monitoring of prevalence of genetic disorders, even if there is debate about the "real" absolute levels, remains useful as it allows to follow trends over time and to assess the effects of preventive strategies. Because the available databases of kennel clubs did not provide clear information to distinguish between look-a-like dogs and mixed breed dogs, screening results should be added to the databases. This could help to get a clearer picture on whether specific dog subpopulations are especially at risk of genetic disorders, and how this changes in time.

Part 4: Literature:

4.1 Scientific literature

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10: German Shepherd Association, in the person of Anja Boonemmer (Representative of the Dutch German Shepard Club)

11: Rottweiler Association, in the person of Andrea Lapere (Representative of the Dutch Rottweiler Club

12: The Dutch Kennel Club, Raad van Beheer. URL: www.radvanbeheer.nl

13: Orthopedic Foundation for Animals (OFA) URL: http://www.offa.org/

14: Pennsylvania Hip Improvement Program (PennHIP) URL: http://info.antechimagingservices.com/pennhip/

15: The International Elbow Working Group (IEWG). URL: www.vet-iewg.org

Part 5: Definitions in this report:

Pedigree dogs
Pedigree dogs are dogs having an officially registered family tree (pedigree) with acknowledged paternity. In most cases the pedigree is recorded and verified by the authorized association of breeders or others, for example, by the Fédération Cynologique International (FCI)[8]. The pedigree dog is registered as a purebred dog and therefore officially qualified and certified as descent from a purebred dog having a clearly defined set of characteristics and meet their breed's standards(i.e. matching a breed-specific morphology).

Look-a-like dogs
Dogs that do not have a registered and certified pedigree (family tree) and are without acknowledged paternity Thus, look-a-like dogs are without an official certification as a pedigree dog and may be non-pure bred or purebred but lacking the supporting evidence..

Mixed breed dogs
Mixed breed dogs are used for dogs that do not belonging to a recognized breed and that have a mixed breed background, and share many traits. Mixed breed dogs include such dogs that are recognized as crossbreed dogs and that are of uncertain ancestry or arise from two different breeds, not just from dogs with uncertain ancestry. Mixed breed dogs have not a clearly defined set of characteristics.

Prevalence
Proportion of all individuals affected by the disorders including new affected individual at a particular time in a population.
Prevalence is a term used for a population found to have a condition, typically a disease or a risk factor. Prevalence describes a proportion, typically expressed as a percentage and is a measurement of all individual affected by the disorder at a particular time. Prevalence is a measurement that is distinct from incidence. Incidence is a measurement of the number of new individuals who contract a disease during a particular period of time

Hip dysplasia (HD) and different scoring system for HD diagnoses
Hip dysplasia is a common hereditary skeletal disorder in dogs. This orthopedic condition causes instability and subluxation of the hip with secondary signs of osteoarthritis and clinical signs of lameness. It is known that it is a quantitatively inherited trait (Leppänen and Saloniemi 1999), with estimates of its inheritability ranging from 0, 17 to 0, 6. Dysplastic dogs have a higher risk of producing affected offspring (Swenson *et al*. 1997a). Numerous methods are used to screen dogs for the condition. The Pennsylvania's Hip Improvement Program (PennHIP) system tests the hip capsule for passive laxity (PennHIP 2007)[14]. The methods of the Fédération Cynologique International (FCI)[8,] the Orthopedic Foundation for Animals (OFA)[13] and the British Veterinary Associating/Kennel Club (BVA/KC) evaluate osseous conformation and evidence of osteoarthritis, but also signs of subluxation (Coopman *et al.* 2008).

Elbow dysplasia (ED) and different diagnoses for ED
ED is a combination of four different disorders, which, according to the International Elbow Working Group (IEWG)[15] are primary defects. Osteoarthritis

and osteophytes are describes as secondary lesion. The disease is known to be partly inherited in many dog breeds (Beuing *et al.* 2000). Elbow joint classification according to the IEWG are used in most studies. However, when comparing ED across studies, it must be taken into account that ED classification may differ between countries even if it is uniformly based on the IEWG standard. In the Scandinavian countries and in the USA, dogs are diagnosed with the disease if they are positive for the secondary lesions, whereas in Germany, the Netherlands, Switzerland, Belgium and France, dogs with only a primary defect may also be diagnosed with the disease.